

# Research Involving Adults With Impaired Decision-Making Capacity

Scott Kim, MD, PhD

Department of Bioethics  
Clinical Center  
NIH

# Disclaimer

The views expressed in this talk are my own.  
They do not represent the position or policy of  
the NIH, DHHS, or US government.

# Outline

- What is the problem?
- What is decision-making capacity (DMC)?
- What is the current policy situation?
- How do data inform policy? Selected topics.

# The Problem

---

## Consider the following scenario....

Researchers want to begin testing a treatment for Alzheimer's disease where doctors insert genetic material (DNA) into the brains of Alzheimer's patients using brain surgery.

This is to be the first study of this kind involving humans and the main purpose is to test its safety in just a few people, before moving on to larger studies.

One risk of brain surgery is a 1-4% chance of bleeding into the brain. This is usually minor, but rarely it can cause serious harm. It is possible that gene transfer could make Alzheimer's symptoms worse, cause brain tumors or cause brain inflammation. No one knows how likely these risks are.

# Questions:

Suppose Mr. S has AD but is too impaired to give his own consent.

- Is it ethical to enroll a decisionally incompetent person in such research?
- If it is, under what conditions should we allow it?

# Relevant to one of the biggest public health issues of our time...

- Research involving adults lacking decision-making capacity → most commonly in Alzheimer's disease research.
  - Highly vulnerable subjects
    - Usually unable to provide informed consent
    - Unable to take care of own welfare during study
  - Yet, need for research is great
    - Devastating and costly disease
    - 80million with AD by 2040 worldwide (Ferri 2005)
    - Without research no progress likely.

# Other areas of research are also affected

- Applies to other types of research as well
  - Some types of ICU research
  - Some research on psychiatric disorders
- Today, we are not talking about:
  - Pediatric research
  - Emergency research without consent



**What is decision making capacity?**

---

# Decision-Making Capacity (DMC)

- Part of the informed consent doctrine
  - Decision-Making Competence/Capacity
  - Adequate disclosure
  - Voluntary decision

# DMC is function based

- Actual abilities relevant to the decision
- Task specific
- NOT diagnosis (“senile”) or label based (“unsound mind”).

# Definitions: Three Levels

- *Adjudicated capacity/competence*—what a judge determines in a court of law (probate in MI)
- *Capacity/Competence*—a clinician's approximation of what the courts might say; usually this carries the day.
- *Abilities* relevant to capacity (e.g., Grisso and Appelbaum 1988):
  - Understanding
  - Appreciating
  - Reasoning
  - Communicating a stable choice

# Decisional Capacity Abilities

(4 abilities model of Grisso and Appelbaum 1988):

- Understanding—factual understanding and comprehension; in this sense, it is a technical use of the term and narrower than ordinary language.
- Appreciation—applying the facts to oneself and one's own situation; implies a certain level of rational belief (e.g., believes key points laid out by doctor)

# 4 abilities/standards

- Reasoning—formal aspects of manipulating information to arrive at a choice; least defined legally.
- Evidencing a choice—at least stable enough for the choice to be implemented

# Assessing DMC: Two-Step Model

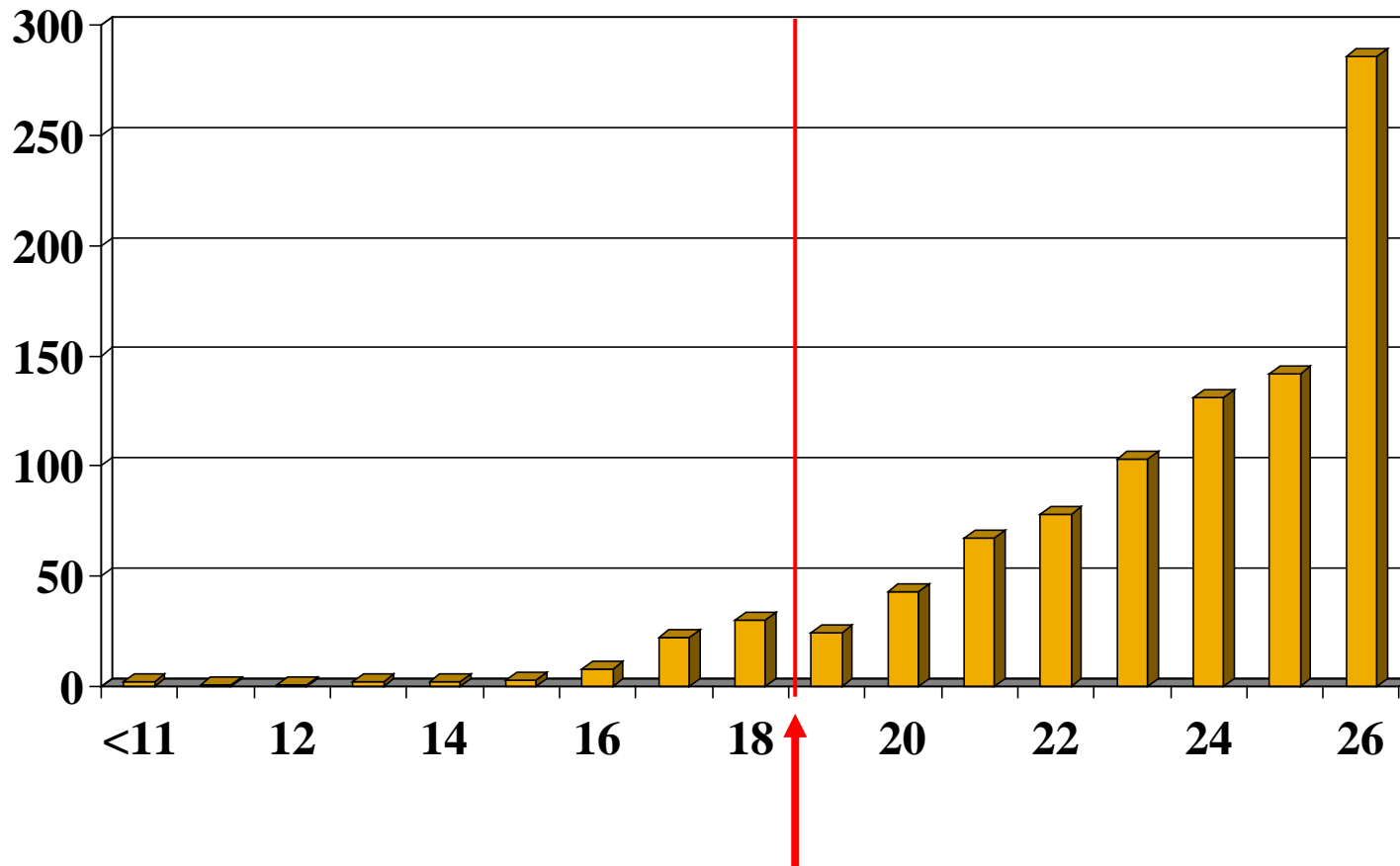
1. Assess the elements:
  - A. Decision-making abilities
    - Individual abilities can be reliably and validly measured
    - But they are only a part of the picture
  - B. Contextual factors
    - Most important are the likely risks and benefits resulting from decision at issue
2. Using A and B, determine decision-making authority
  - Virtually no specific legal or ethical guidance
  - Matter of judgment

# Impaired decisional capacity is common in Alzheimer's disease research

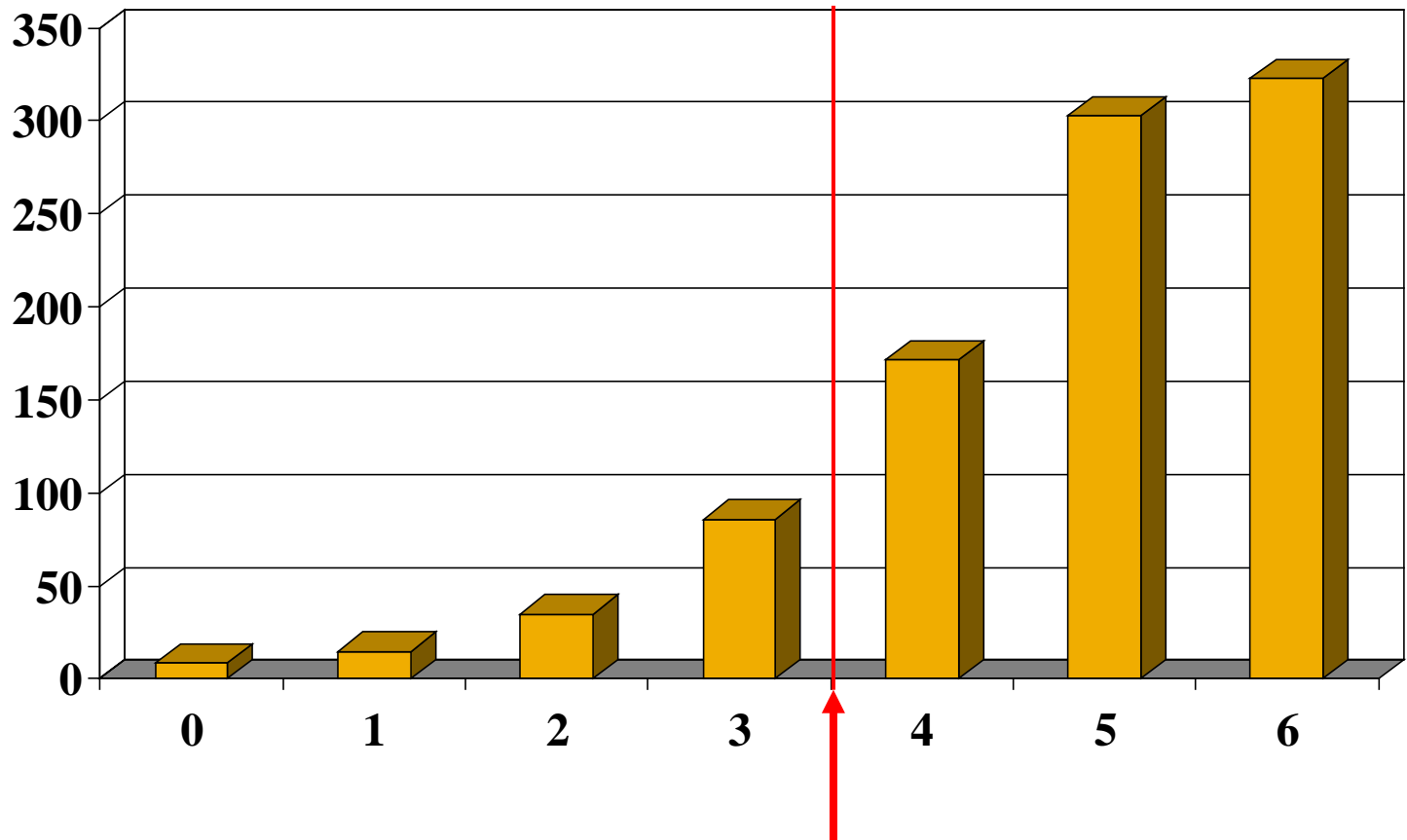
- 40% of pts with even Mild Cognitive Impairment (MMSE  $27.8 \pm 1.8$ ) lack capacity to consent to RCT (Jefferson, JAGS 2008)
- 62-76% of AD patients (MMSE 22-23) in a typical RCT probably lack capacity (Kim, *AJP* 2001; Warner, *JME* 2008)



# CATIE Schizophrenia Study: Understanding Score Distribution at N=900 (S Stroup)



# Appreciation Score Distribution



# Prevalence of decisional incapacity: Very rough estimates (Kim, 2010)

- General hospital inpatients: 30-40%
- Nursing homes: 44-69%
- Psychiatric hospital/units: 30-86%
- Chronic psychoses: ~25-50%
- Mild-moderate depression: Relatively little impact
- Depression, inpatients: 5-24%
- Severely depressed  
(inc. those with psychosis and  
cognitive impairment): prob >25%

# Current policy situation

---

# Regulatory guidance unclear

- Federal regulations speak to two issues:
  - Legally authorized representatives (46.102c)
    - But defers to local and state laws to define LAR
    - Therefore, OHRP guidance turns on state and local laws
  - Additional safeguards provision for “mentally disabled” (46.111b)
    - But seems to specifically addressed to issue of coercion and undue influence, not capacity

# Current Situation

- U.S.
  - Only few states (CA, NJ, VA) have 'modern' laws explicitly addressing this issue
- Elsewhere...
  - UK: three different guidelines (depends on location and type of research)
  - Canada: varying laws in provinces

# Brief History of (Failed) Attempts at Policy Consensus in US

- The only report by the National Commission that did not become part of federal regulations (*Research involving those institutionalized as mentally infirm*)
- President's Commission in early 1980's.
- National Bioethics Advisory Commission 1998
- Maryland and New York state efforts in 1998-9.
- Other federal advisory groups since then, including two DHHS secretary's advisory groups

# Effects of lack of clear policy

- Lawsuits in NY, California (schizophrenia research)
- Temporary, voluntary suspension of research at UCLA
- Mandated suspension of research at Vanderbilt and all Tennessee institutions, until special state regulations enacted
- Series of OHRP compliance letters to various institutions regarding some dementia RCTs as well as ICU studies of ventilator settings
- Continued uncertainty, and danger of overreaction with dramatic events.
- **Leaves both institutions and research subjects vulnerable?**



# Necessary Elements of Policy for Involving Decisionally Impaired Adults in Research

- Involve incapable subjects only when their condition or situation is being studied (w/ some exceptions)
- Risk-benefit analysis :
  - Potential benefit versus none
  - Risk/burden
    - Minimal?
    - Minor increase over minimal?
    - Greater than minor increase?
  - Most controversial when:
    - No potential for benefit, greater than minor increase over minimal risk.

# Elements of policy, cont'd

- Who should be allowed to give permission in subject's place?
  - Family? Legal guardian? Health care proxies? Research proxies?
  - OHRP will seek
    - Specific state law, regulation or interpretation (See OHRP determination letters & FAQ response)
- Assessment of capacity: by whom, how, when?
- Role of assent, dissent?
- Other protections? E.g., monitors, advocates, etc.

# Summary of some policy relevant data

1. What does the public think about surrogate consent for dementia research?
2. How reliable is assessment of decision-making capacity?
3. What is the ethical importance of “preserved” abilities in persons with dementia?

# U.S. public attitudes about family surrogate consent for dementia research.

**Table 2** Proportion\* of respondents providing positive responses for each of the four surrogate-based research scenarios for the three main survey questions

Questions	Lumbar puncture	Drug RCT	Vaccine	Gene transfer	p Value
Societal perspective: If patients cannot make their own decisions about being in studies like this one, should our society allow their families to make the decision in their place? (n = 1,463)					
[allow, not allow]	72.0	82.5	70.5	67.5	<0.001
Self perspective: Suppose you wanted to give a close family member instructions for the future, in case you ever became unable to make decisions for yourself. Would you say you would want to participate in the study? (n = 1,444)					
[yes, no]	70.8	79.7	57.4	68.7	<0.001
Leeway question: How much freedom or leeway would you give the close family member to go against your preference and instead [opposite of answer to 2: enroll/not enroll] you in the study? (n = 1,456)					
[In descending order in the column: no leeway, some leeway, complete leeway] <sup>†</sup>	41.4	33.2	45.2	39.6	
	39.3	40.6	37.9	39.2	0.09
	19.3	26.2	16.9	21.1	

# Public attitudes toward family surrogate consent for dementia research: after one day deliberation exercise (n=173)

	LP	Drug RCT	Vaccine RCT	Gene transfer
<b>Societal perspective</b>  % definitely or probably allow family consent	95%	97%	79%	68%
<b>Self perspective</b>  % definitely or probably want to participate	93%	97%	70%	54%

# How clear is the line between capacity and incapacity?

- When the person is impaired yet still conversant and cooperative (as in mild to moderate stage of dementias), often not clear.
- Although we can reliably measure each ability relevant to capacity (i.e., understanding, appreciation, reasoning), translating that into a categorical judgment is less reliable.

# Do experienced capacity evaluators agree? (Kim et al, 2006)

Results of capacity determination, using a video portraying a man with AD being interviewed for capacity to consent to a drug RCT study. N=52 psychiatrists.

Judgments of Capacity Evaluators (Psychiatrists)	N(%)
Definitely not capable	5 (9.6)
Probably not capable	16 (30.8)
Probably capable	22 (42.3)
Definitely capable	9 (17.3)

1. **40% saw subject as incapable vs 60% said capable**
2. This case was chosen to represent a 'gray area' example, but not uncommon type of case.

# Variability of capacity judgments

(Kim et al, 2011)

	Capacity to Consent to Drug RCT ( <i>n</i> = 181)
	N (%)
<b>Capacity</b>	<b>75 (41.4)</b>
3 judges agree	20 (11.0)
4 judges agree	30 (16.6)
5 judges agree	25 (13.8)
<b>No capacity</b>	<b>106 (58.6)</b>
3 judges agree	21 (11.6)
4 judges agree	29 (16.0)
5 judges agree	56 (30.9)

MMSE score<sup>a</sup>

Mean (SD)	20.8 (5.0)
<12, No. (%)	12 (6.4)
12-17, No. (%)	27 (14.4)
18-23, No. (%)	87 (46.3)
≥24, No. (%)	61 (32.4)

3 agree in 23% of cases  
 4 agree in 33% of cases  
 5 agree in 45% of cases

Pairwise kappa statistic range: 0.17 (slight agreement) to 0.64 (substantial agreement)



# In practice, perhaps even greater variability

...(Karlawish et al. 2002)

- In a survey of 30 AD research centers, asked what proportion of research subjects in their studies were capable.
- Range 0-100% of AD research subjects were seen capable, depending on the site!

# Why the variability?

- Conflicts of interest?
- Inherently difficult concept to operationalize?
- Value laden—can vary among evaluators?
- Underdeveloped methods for assessment?
- Different views of what “capable” means?

# Implications for policy?

- If a single evaluator's judgment is not reliable, then ...
  - Shouldn't policy guidelines address this?
  - Are there scenarios (high risk/invasive?) in which multiple evaluations are warranted?
  - How much weight do we want to place on capacity status as lynchpin of policy?
- It seems at minimum, we should not just assume we can validly draw a bright line between capacity and incapacity.

# Preserved abilities: ethical relevance

- What can Mr. S still contribute to the process?  
Or do we bypass him altogether?
- 'Assent' requirement in most guidelines recognizes this aspect to some (minimal) degree.

# Preserved abilities of incapacitated persons with dementias

In theory, a person deemed incompetent to decide X can be competent to decide Y. What is the evidence that ...

- A person who lacks capacity can voice “reasonable” and even “authentic” preference?
- Capacity varies by risk-benefit context?
- A person who is incapable of giving informed consent can still do something else, like appoint a proxy?

# AD patients and controls in general give similar responses regarding willingness to participate in various types of research (Kim et al. 2002)

		AD (N=34)	Normal (N=14)	
	Response	N (%)	N (%)	p
Blood Draw	Willing	29 (85)	14 (100)	.30
Drug Clinical Trial	Willing	22 (65)	14 (100)	.01
PET/Challenge Study	Willing	18 (53)	8 (57)	1.0
Brain Surgery	Willing	7 (21)	3 (21)	1.0

# Capacity to appoint a proxy is preferentially preserved (Kim et al 2011, Arch Gen Psych)

**Table 4. Relationship Between Capacity to Appoint a Research Proxy and Capacity to Consent to the 2 Randomized Clinical Trials (RCT)<sup>a</sup>**

Capacity to Appoint Research Proxy	No. (%)			
	Capacity to Consent to Drug RCT (n=181)		Capacity to Consent to Neurosurgical RCT (n=186)	
	Yes	No	Yes	No
Yes	72 (39.8)	40 (22.1)	29 (15.6)	86 (46.2)
No	3 (1.7)	66 (36.5)	0	71 (38.2)

<sup>a</sup>A total of 188 participants completed the first interview, which included the Capacity to Appoint a Proxy Assessment (CAPA) and either the drug RCT or the neurosurgical RCT MacArthur Competence Assessment Tool–Clinical Research (MacCAT-CR)(decided randomly) as well as the Mini-Mental State Examination (MMSE). One person finished CAPA during the first interview but did not finish MMSE or MacCAT-CR; and this person declined the second interview as well. This person is 1 of 8 who declined the second interview. The remaining 7 of 8 persons who declined the second interview did finish the CAPA, MMSE, and 1 of 2 MacCAT-CRs, but are missing the second MacCAT-CR.

**38% of those deemed incapable of consenting to drug RCT and 55% of those deemed incapable of consenting to neurosurgical RCT are still capable of appointing a proxy.**

# Implications?

- Even after diagnosis of Alzheimer's disease, usually possible to obtain a valid proxy directive.
- As much as possible, involve the patient with dementia in the decision-making process.



# Final Thoughts: Practical Steps

0. Is the involvement of impaired subjects necessary for the scientific aims?
1. What is the risk/benefit analysis?
  - Perhaps the most important question
2. What kind of capacity assessment is appropriate?
  - Tailored to the risks and benefits
  - Formal versus informal
  - Threshold for capacity
  - Who will conduct it? Independent versus researcher team

# Cont'd

3. Caregiver/family role:
  - a. As proxy/surrogate?—
    - i. What is the state's law or regulation re LAR?
    - ii. How does your IRB treat LAR research?
    - iii. Formally appointed versus de facto?
  - b. As informal support?
  - c. As part of risk management?
4. Assent/Dissent issues.
5. Consider asking subjects to appoint someone they trust to help them.