Competing Commitments in Clinical Trials

Charles W. Lidz

Paul Appelbaum

Steven Joffe

Karen Albert

Jill Rosenbaum

Lorna Simon

Why a Clinical Trial

- Effort to determine causation
- Does one treatment work better than another
- Control many variables
  - Expectations
  - Clinician biases
  - Clinical features of the subjects
  - Effects of other medications
  - Etc.

Typical Structure of Trials

- Randomization of patients
- Tight control of who is eligible
- Blinding of subjects and providers
- Comparison intervention that is the best available treatment
- Limitations on dosages
- Limitations on other medications

These features are essential

- Differences in effect between two treatments are often minimal
- The idea is to definitively determine causation and all other determinates must be controlled or eliminated.

The Problem

- Most staff in clinical trials have clinical training
- They have a deep-seated commitment to their "patients" as most clinicians do.
- They generally, and mistakenly, think that the experimental intervention is likely to be much better for their subjects.

The Question

- How do clinical trial staff manage their competing commitments to research standards and clinical commitments?

Why does this matter?

- Clinical trials are the means by which we determine whether treatments are used
- Pharmaceutical companies, and universities, have enormous stakes in their outcomes
- You and I have an enormous stake in their outcomes

Methods 1

- Use semi-structured interviews at UMass and Harvard to learn how clinical trial staff think and talk about these issues.
- Use data to develop a survey that can ask touchy questions and still leave subjects willing to answer

Methods 2: Sample

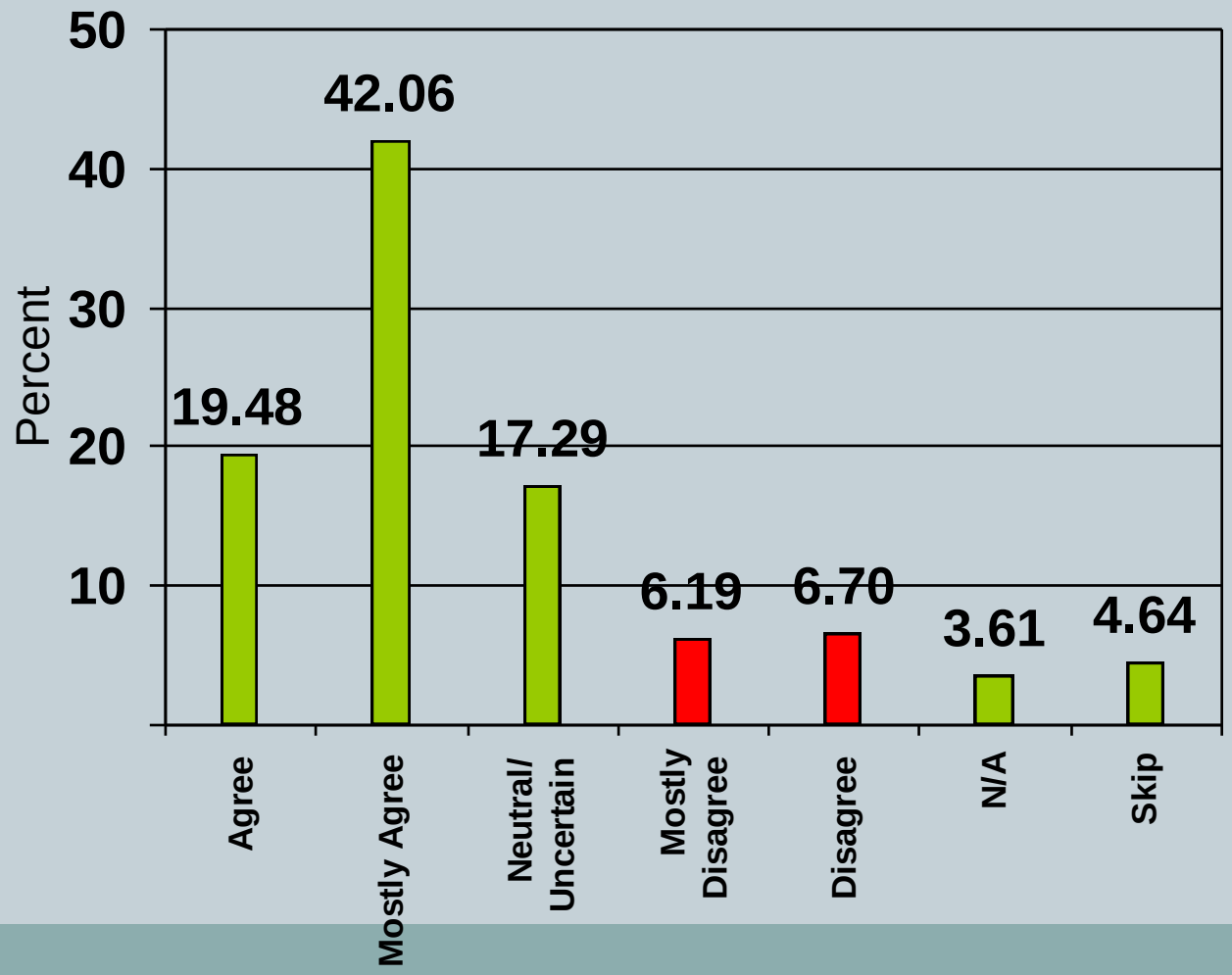
- Drawn from contacts on patient oriented website - Centerwatch.com

Methods 3: Surveymonkey and Dilman Method

- Jill and Sue created a poster
- 6 rounds of different types of contacts
- Make the contacts as personal as possible
  - Real signed letters
  - Personal notes written on letters
  - Jill's interpersonal charm on the phone
- Response rate >75%

Attitudes about Clinical Trials

Research centers should choose which trials to participate in based on how much the trials contribute to science.



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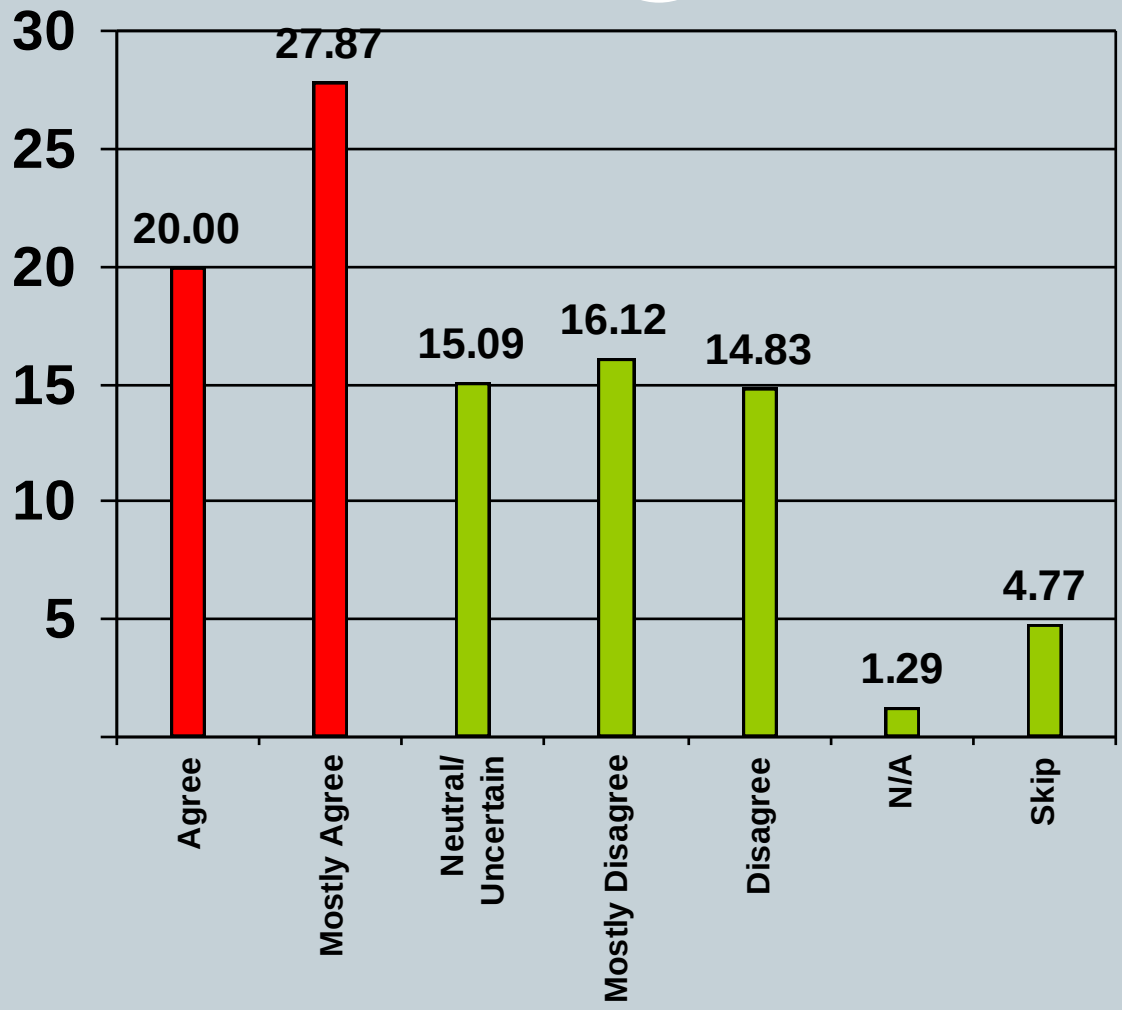
Researchers should only participate in trials that are likely to help the subjects that take part.



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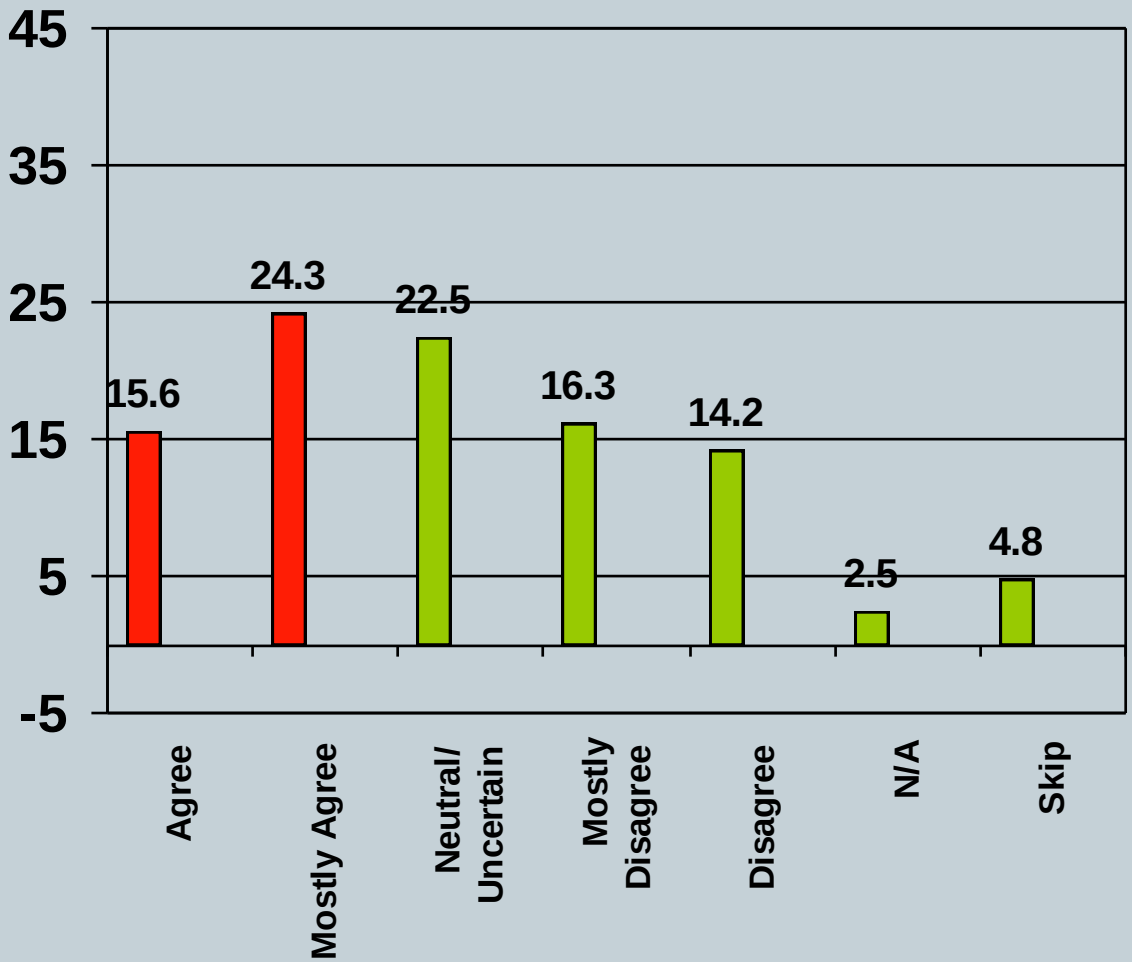
When several subjects at a site do considerably worse than would be expected in ordinary care, that site should stop recruiting for that study.



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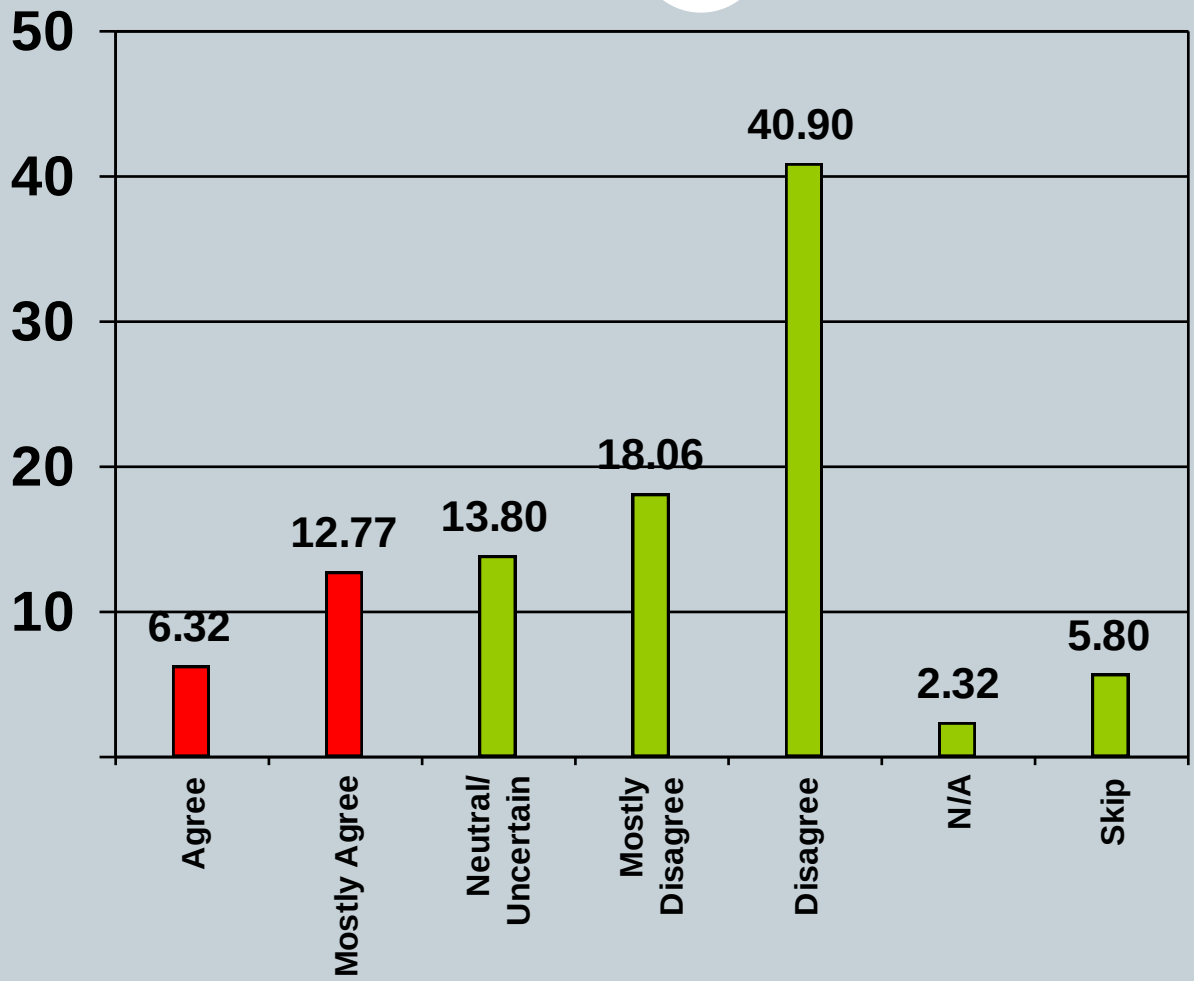
Researchers should deviate from the protocol if doing so would improve the subject's medical care.



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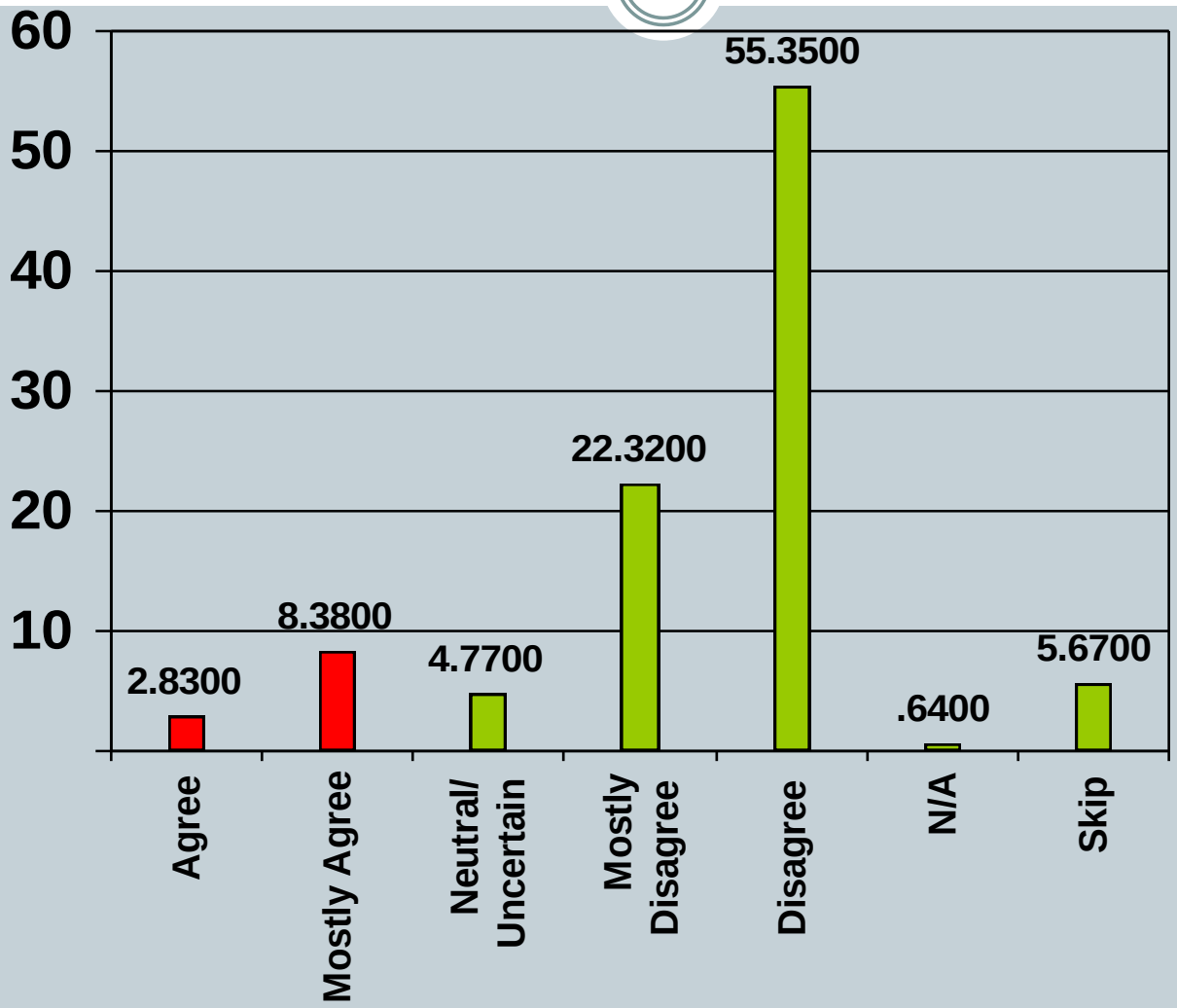
The protocol should be used as a guideline rather than something to be strictly followed under all circumstances.



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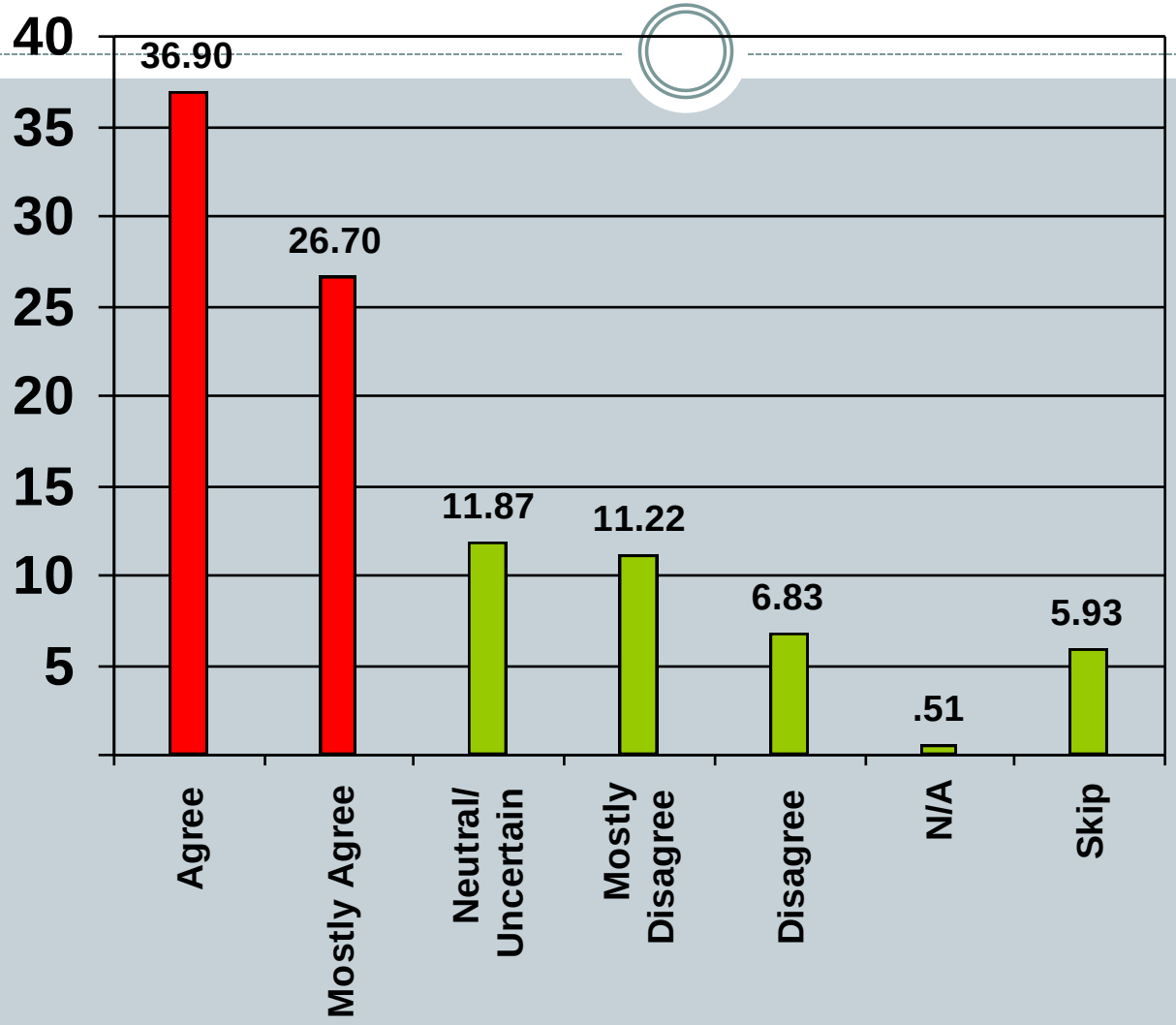
Even if patients are technically eligible for a trial, they should only be recruited if being in the trial will be in their best medical interests.



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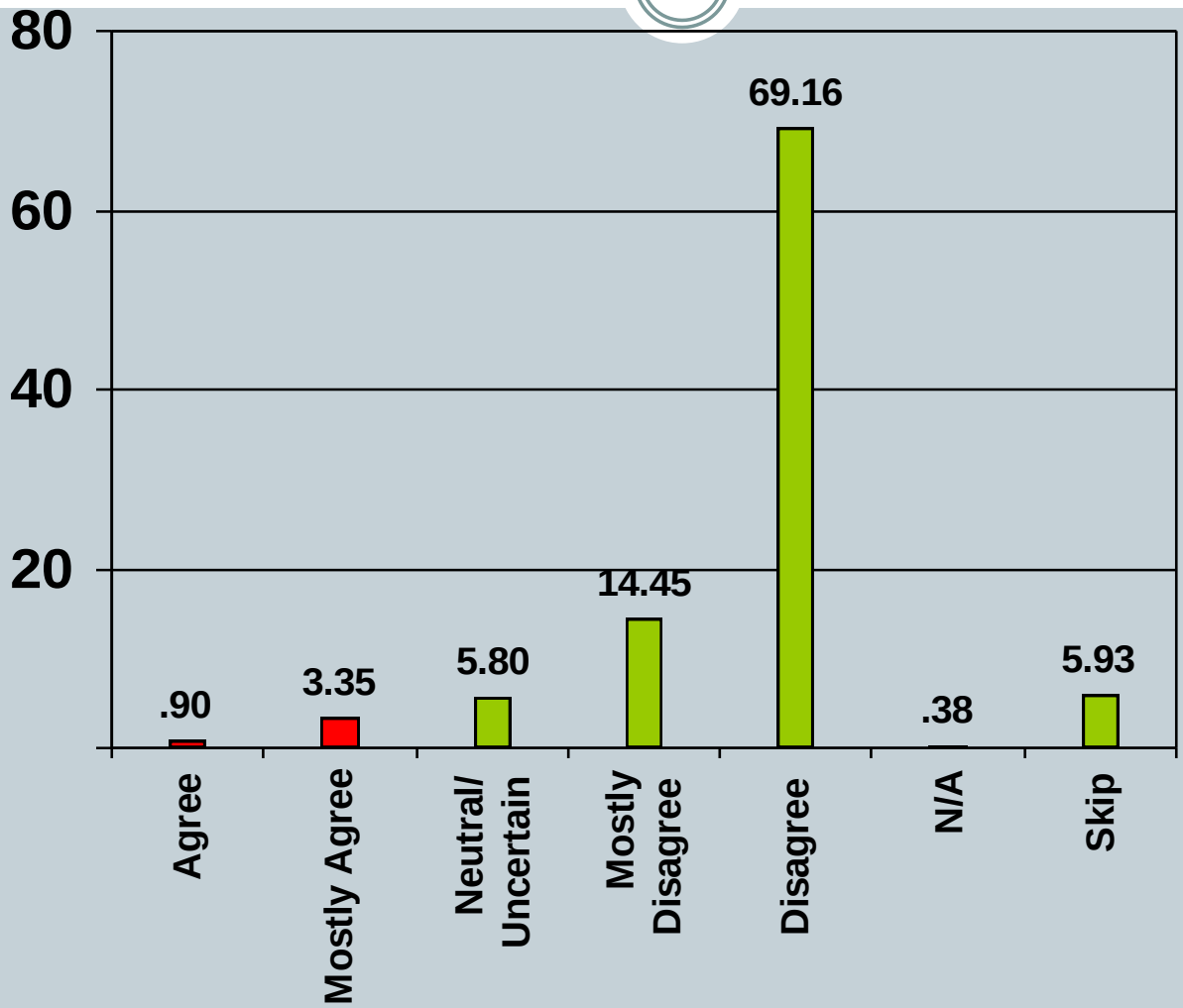
It is acceptable to disregard minor entry criteria if a patient will benefit from being in a trial.



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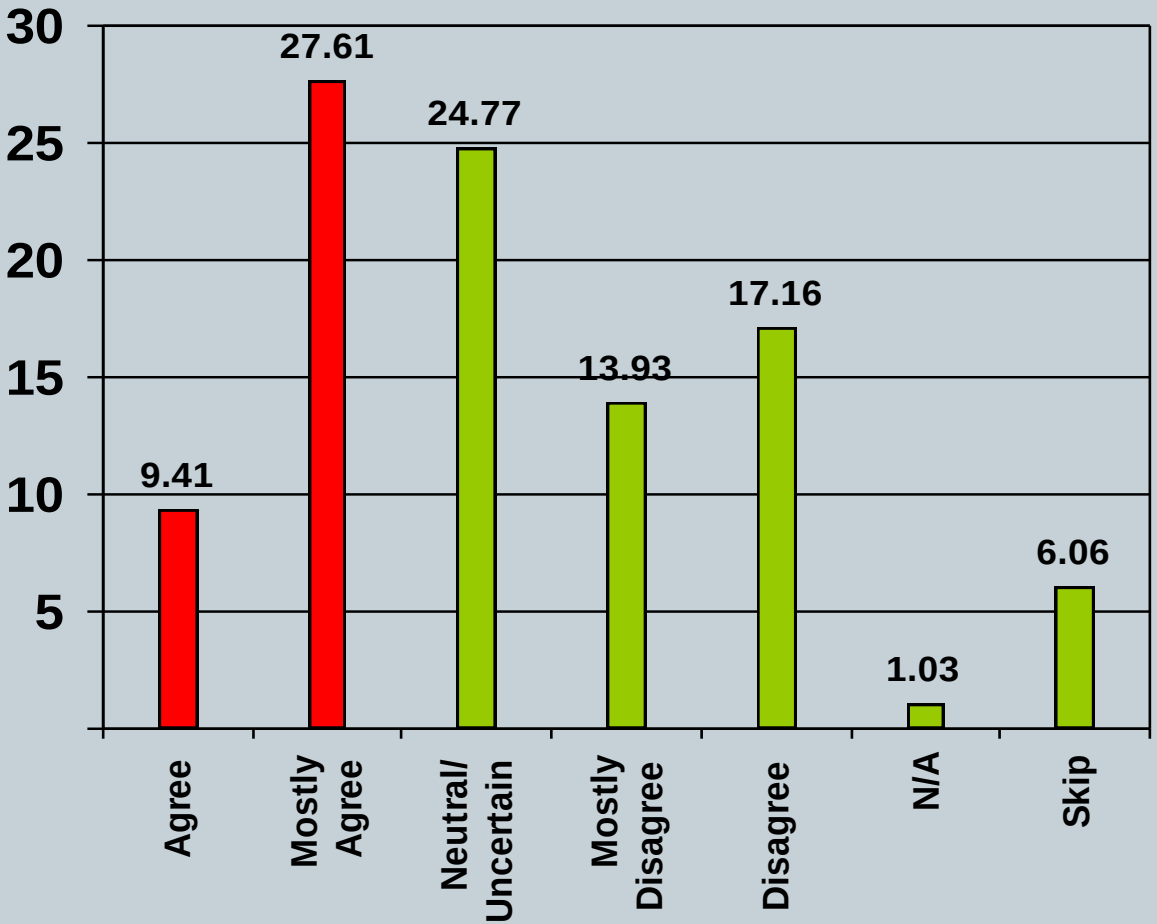
Patients who are not doing well with standard care should be recruited most actively so that being in the trial can help them.



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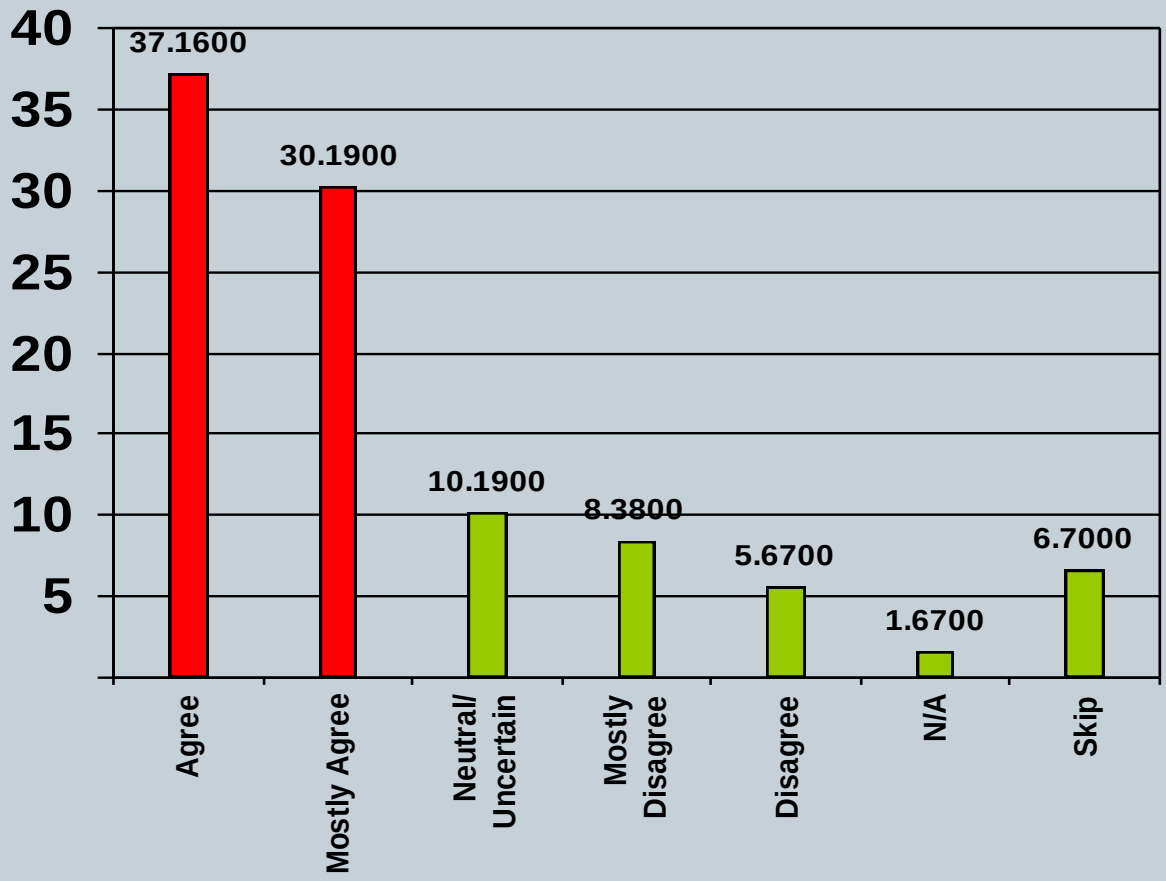
Clinical judgment, rather than strictly following the protocol, should be the basis for deciding to remove subjects who are not doing well.



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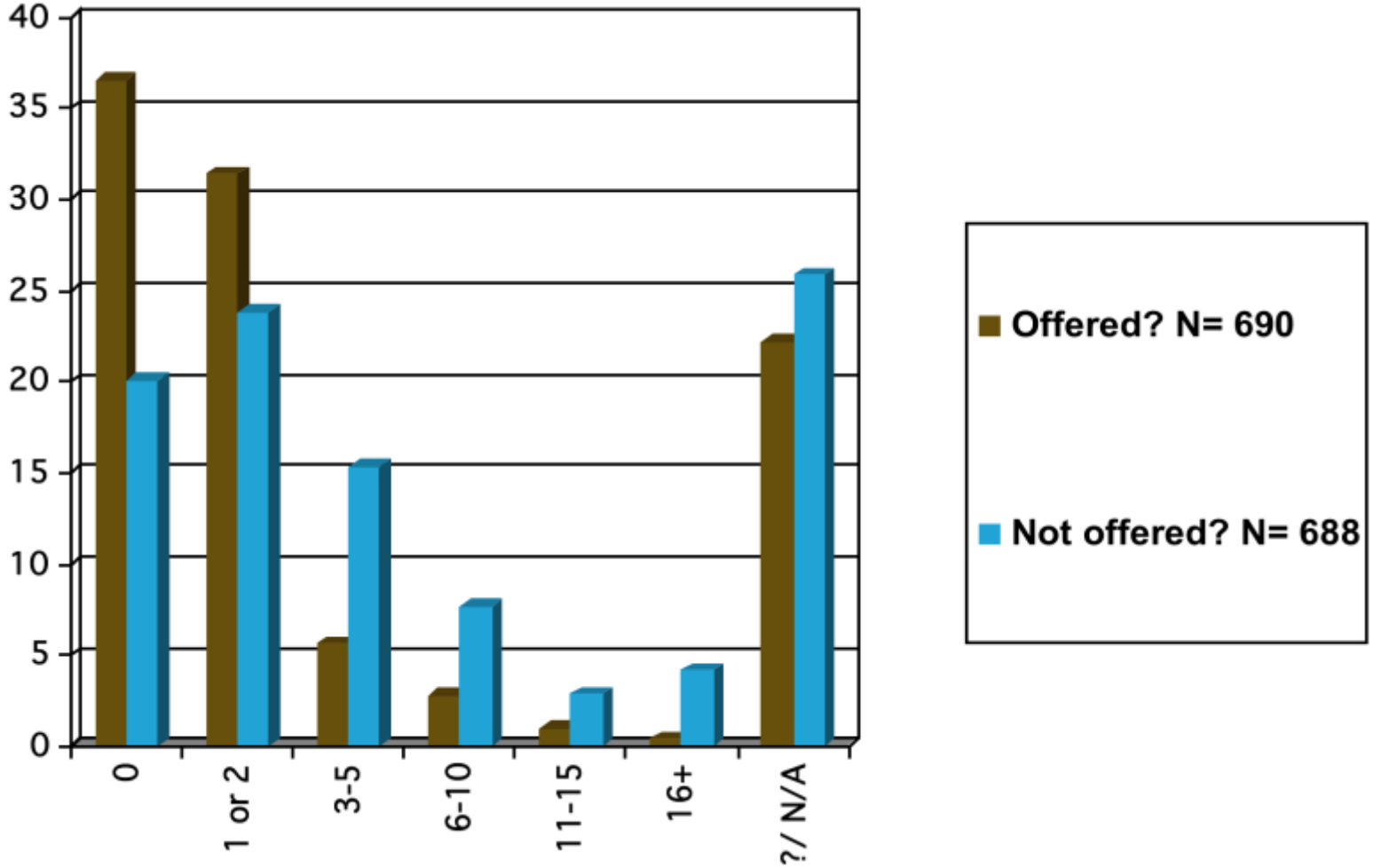
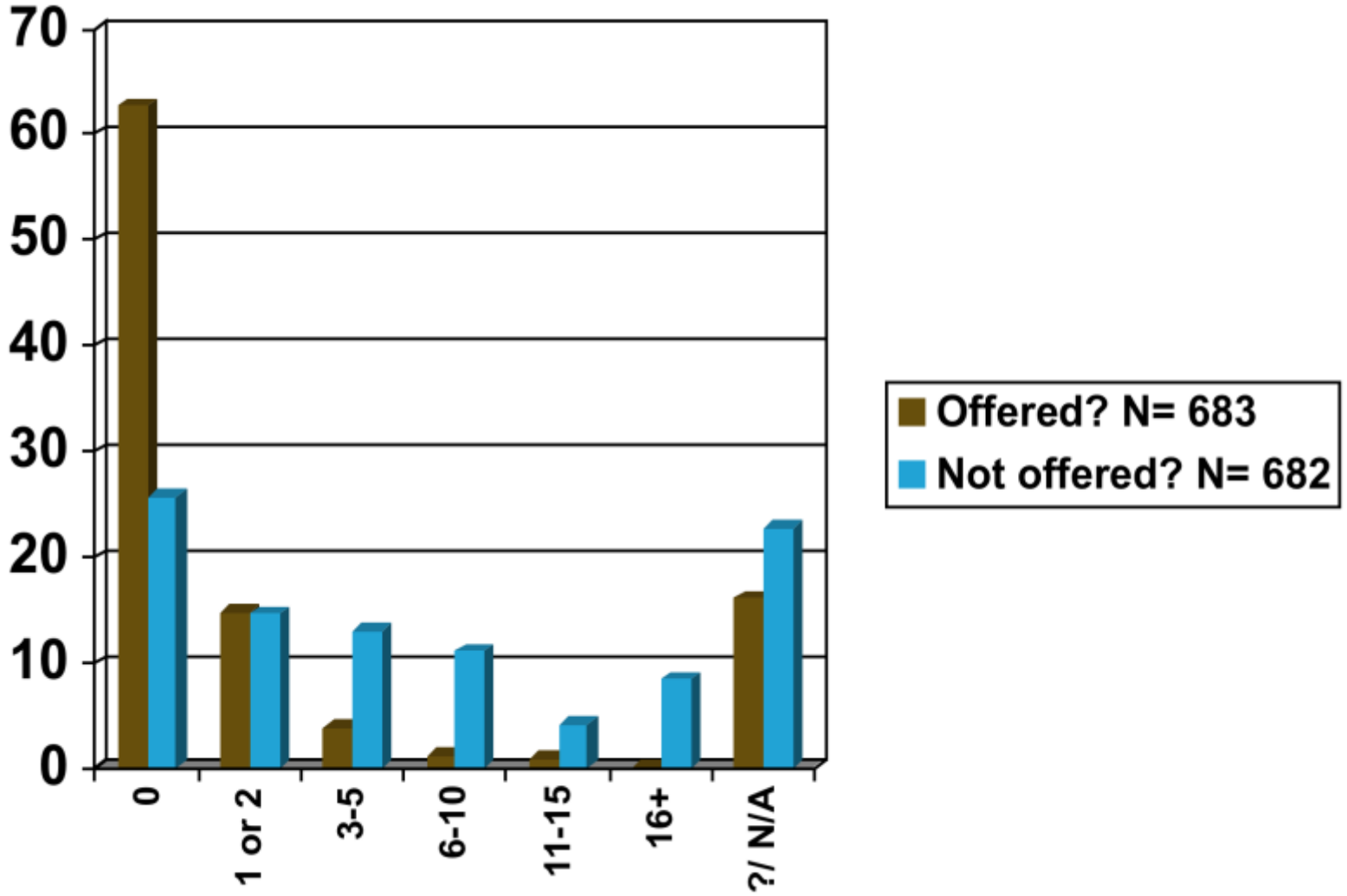
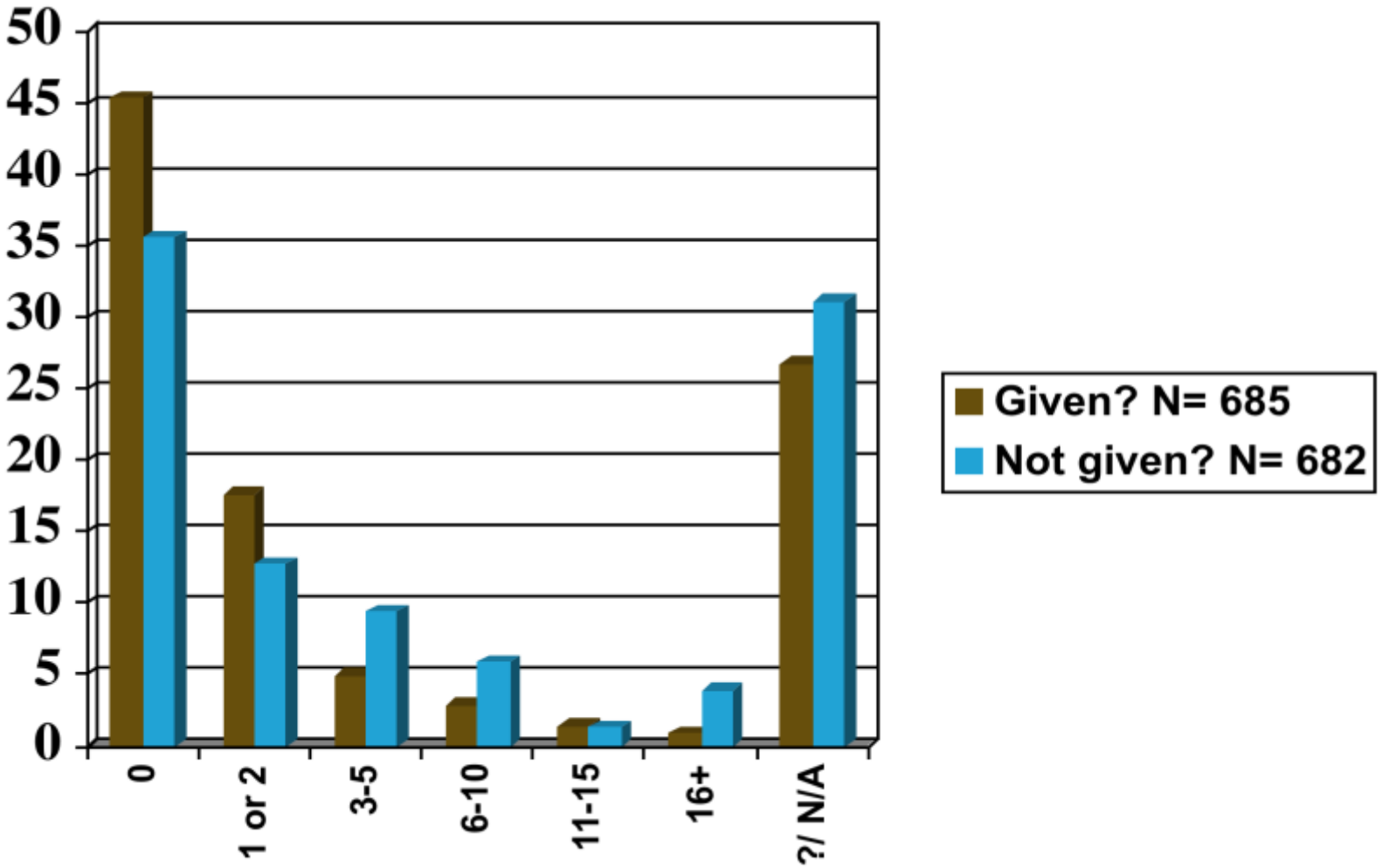
Think of all the times during the past 2 years when you had a patient who was eligible for a clinical trial, but being in the trial seemed *not* to be in the patient's best medical interests.



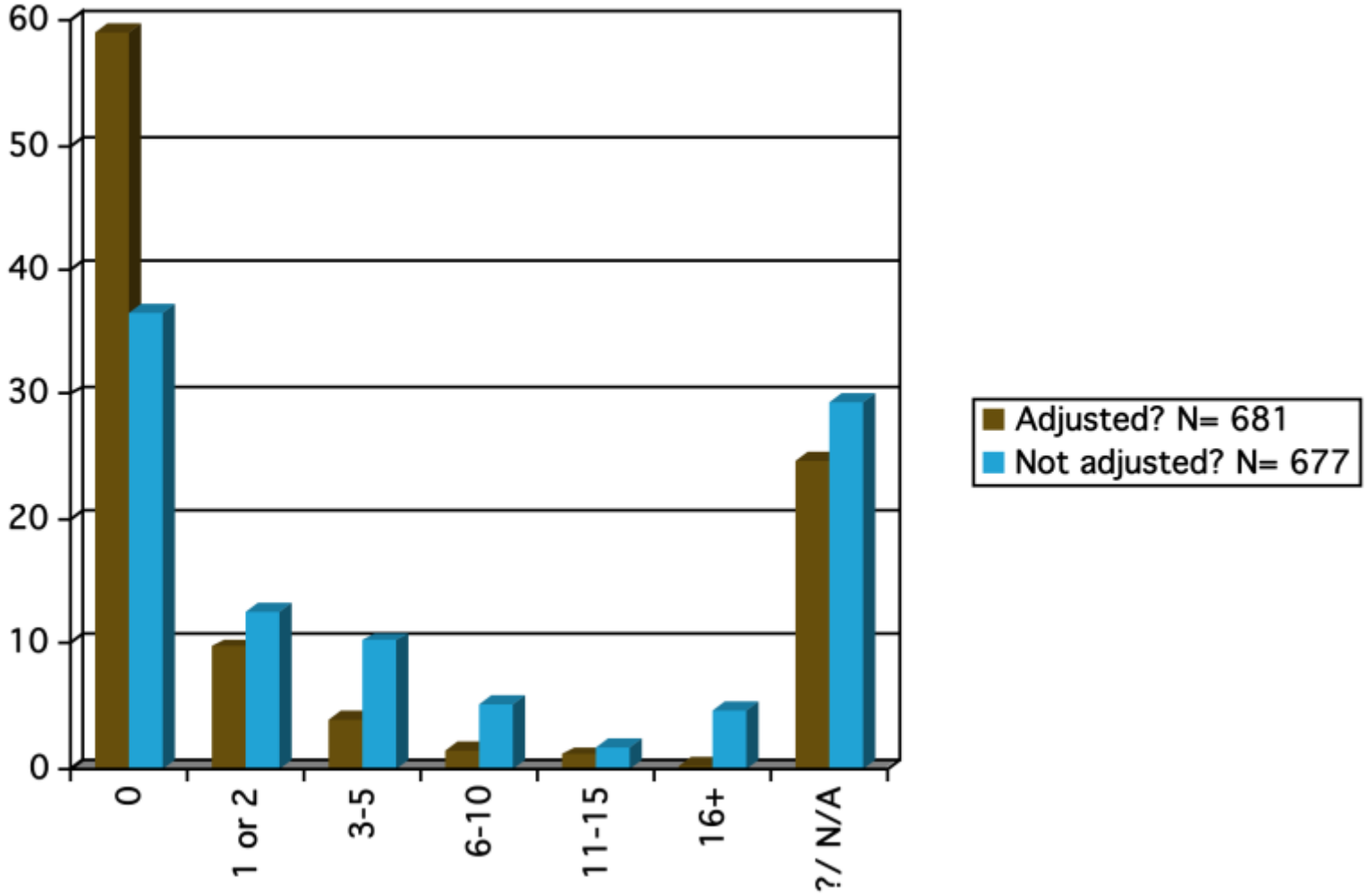
Think of all the times during the past 2 years when you have had a patient who was not technically eligible for a clinical trial, but being in the trial seemed to be in the patient's best medical interests.



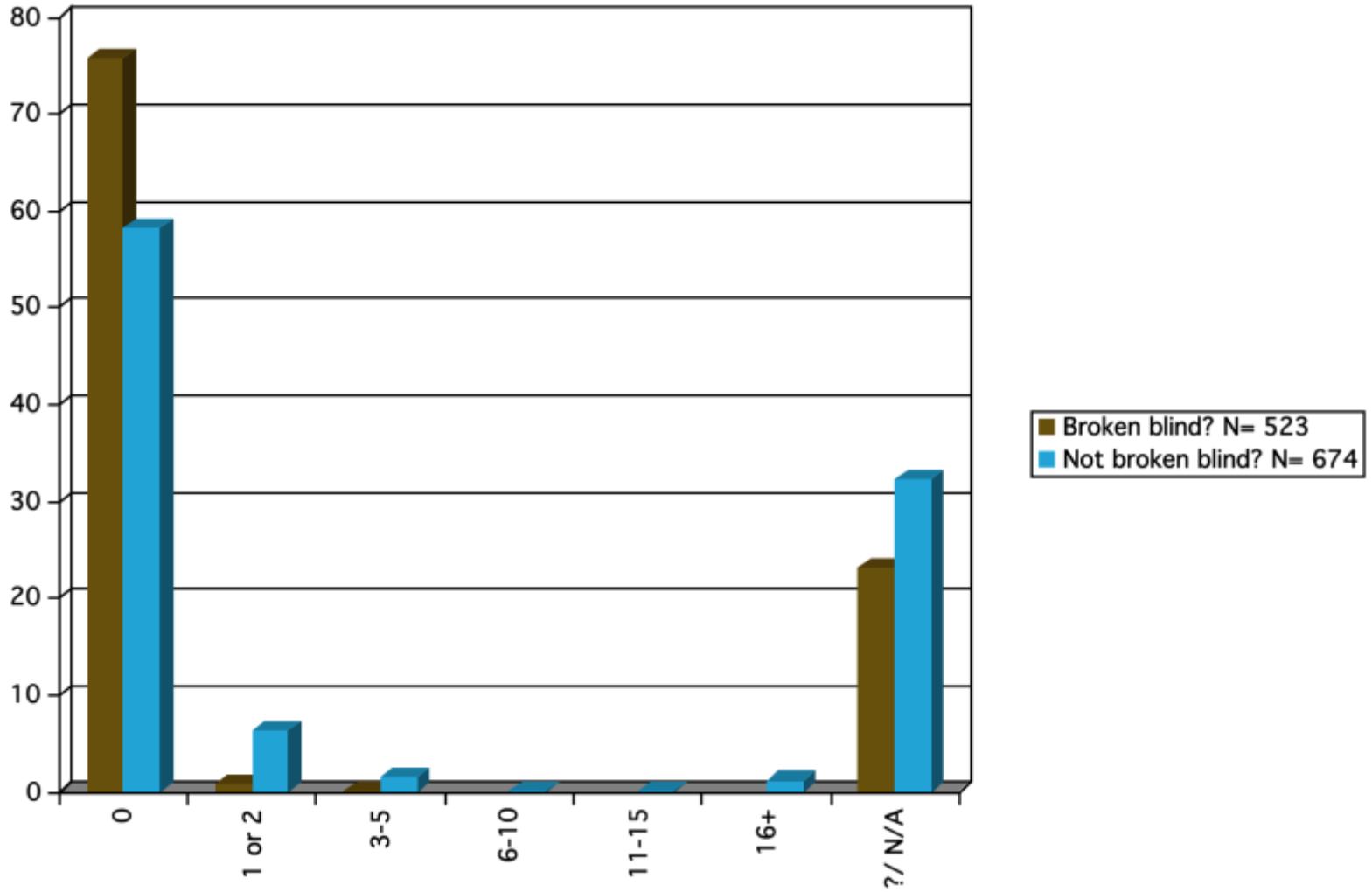
Think of all the times during the past 2 years when a medication was restricted by protocol, but giving the medication seemed to be in the subject's best medical interests.



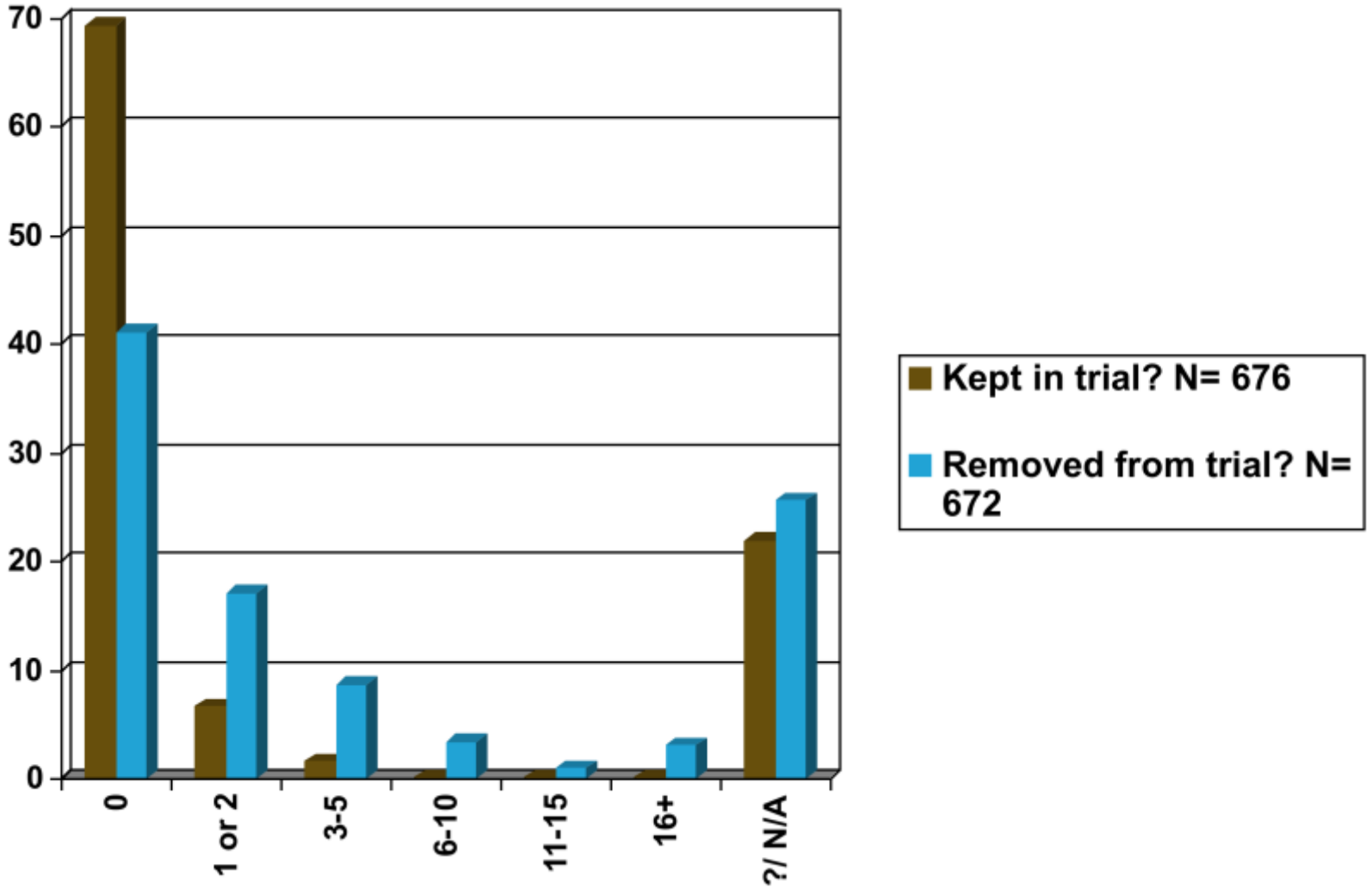
Think of all the times during the past 2 years when adjusting the dose of a study medication seemed to be in the subject's best medical interests, but making the adjustment was not permitted by the protocol.



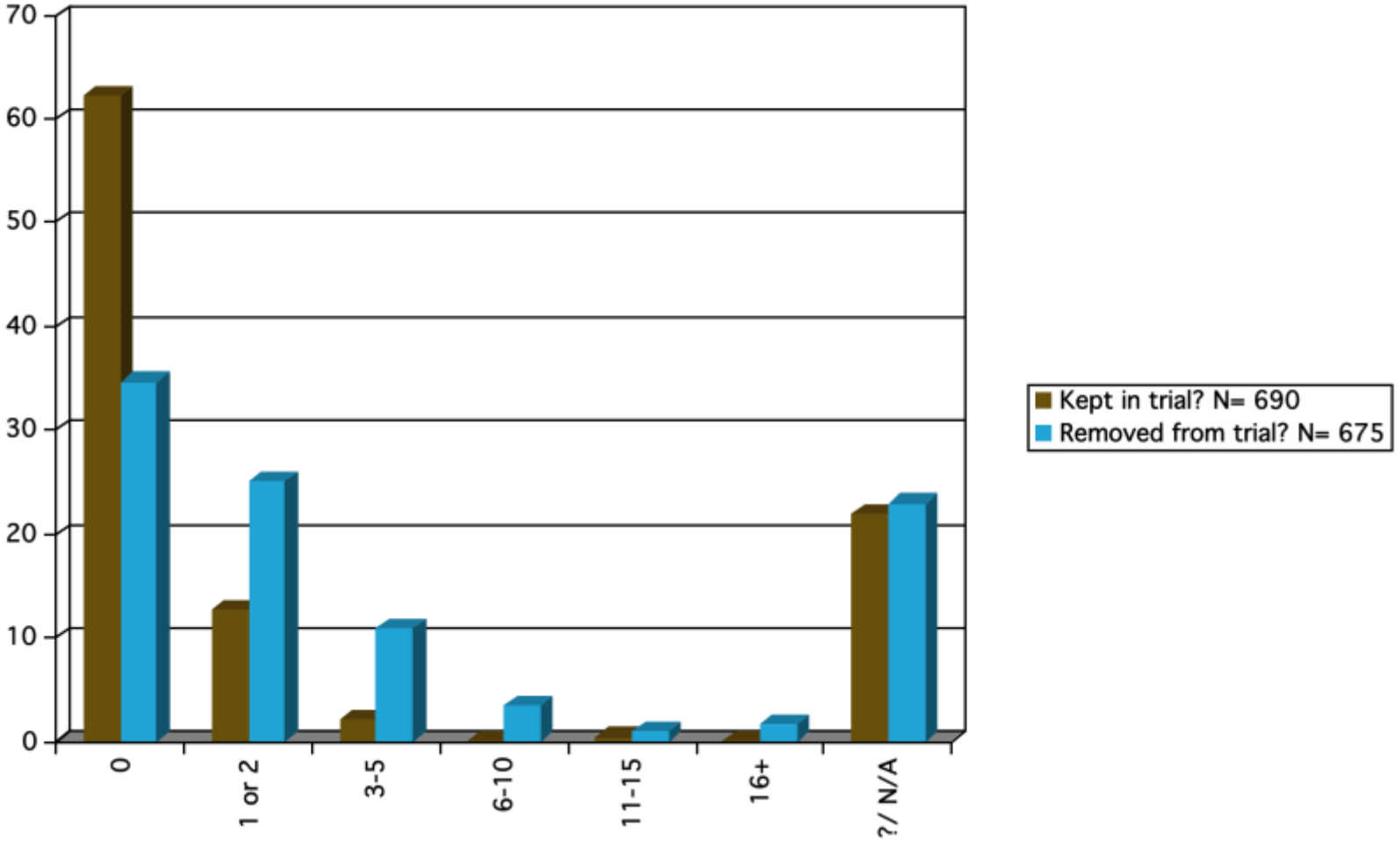
Think of the times during the past 2 years when breaking a blind without reporting it seemed to be in the subject's best medical interests.



Think of all the times during the past 2 years when you had a subject who met termination criteria, but remaining in the trial seemed to be in the subject's best medical interests.



Think of all the times during the past 2 years when you had a subject who did *not* meet termination criteria, but remaining in the trial seemed to be contrary to the subject's best medical interests.



What do we make of his?

- Most clinical researchers follow the rules
- Most researchers try to provide good care to patients within that context.
- A significant number of clinical researchers sometimes violate the protocol in the interests of good clinical care
- There is good reason to worry about biased samples
- Because, in many cases, statistical significance depends on only a few cases, these are important problems.