The Mother test for trialists

Would you enroll your Mother in that trial? How often have you been asked that question as a designer or conductor of trials?

Mothers are special. Sure, Fathers are great, but Mothers are special.

How many times have you seen 300 pound tackles mouth "Hi Dad" in front of TV camera? It is away "Mom". How many residents of nursing home do you hear calling out for their Dads? They call for their mothers.

Who do you call when you need a shoulder to cry on? Who do you call when you just want to talk? Mom of course!

Because Mothers are our most prized possession, in trials, they serve as an operational measure of the appropriateness and adequacy of the trials we plan and conduct. Technically, the Mother test comes down to a single question: *Would you enroll your Mother in the trial*? If your answer is *no* you need to work to change the design and conduct procedures so you can answer *yes*. Or you need to walk away from the trial.

The expectation is, when you have finished designing a trial and have established operating procedures for its conduct, that it will be possible to answer all questions in the test *yes*. Questions answered *no* serve to identify areas in need of change or "fixing".

It may be useful to have investigators take the test prior to starting a trial. Investigators should be polled for *no* answers and should be asked to give their reasons.

The test may also have utility when deciding whether to respond to an RFA or RFP for a trial. If you are not able to answer questions because the information provided in the RFA or RFP is sketchy, maybe you should not respond.

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The essence of the Mother test is contained in question 40 below: *Assuming your Mother is eligible and willing to be enrolled into the trial, would you be willing to randomize her to treatment and to have her treated and followed as proposed?* If, as a designer or conductor of that trial, the answer is *no*, you need to indicate your reasons for the *no* and work to change the design and conduct procedures so as to be able to answer *yes* to the question. The goal should be to produce a trial where it is possible to answer all questions preceding question 40 in the affirmative.

Your name . . . . . _____

Name of trial being evaluated? _____

Date (day, Mon, year) . . . . . __ __/__ __ __/__ __

Position in trial (check one)
- ( ) Center director
- ( ) Deputy director
- ( ) Coordinator
- ( ) Other (specify) _____

Discipline/training (check one)
- ( ) Physician
- ( ) Statistician/epidemiologist
- ( ) Other (specify) _____

1. Is the trial necessary?
   . . . . . (y) (n)
   Answer *no* if the trial is a demonstration trial or if you believe the answer to the question being addressed in the trial is known.

2. Is the trial large enough and the period of treatment and followup of sufficient length to make it likely that the trial will yield fruitful results?
   . . . . . (y) (n)

3. Does the trial address a medically relevant question?
   . . . . . (y) (n)

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4. Is the primary outcome measure a relevant measure of treatment effect?
. . . . . (y) (n)

5. Is there good reason to believe that the test treatment(s) is (are) safe?
. . . . . (y) (n)
Lean toward *no* in the absence of data bearing on safety, especially if the treatments carry risk, eg, as is likely to be the case with most invasive forms of treatment involving surgery and implanted devices and with most forms of treatment involving drugs or biologics.

6. Is there reason to believe that the test treatments will be effective in treating or preventing the condition targeted in this trial?
. . . . . (y) (n)
Lean in favor of *no* if the only basis for the belief is theoretical, not buttressed by other trials or observational studies.

7. Is there likely to be a favorable benefit-risk ratio for persons in the trial?
. . . . . (y) (n)

8. Is the risk of harm to persons from the trial minimized?
. . . . . (y) (n)

9. Does your Mother stand to benefit from participation?
. . . . . (y) (n)

10. Is there a state of clinical equipoise underlying the treatments being tested?
. . . . . (y) (n)
In answering, remember that clinical equipoise in this context, is a collective state of legitimate doubt as to choice or proper course of treatment due to absence of agreement among medical experts. The state is considered to exist even if individual persons are certain as to choice or course so long, as together, they are more or less equally divided. States of doubt are legitimate only if informed, ie, based on careful study and review of existing information bearing on choice or course.

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11. Are the study treatments (test and control treatments) compatible with prevailing norms and standards for care and treatment?
. . . . . (y) (n)
Answer *no* if persons enrolled into the trial are denied access to accepted forms of treatment, are likely to receive substandard care, or if the control treatment is considered to be substandard. Note that in answering, you must decide whether the "prevailing norms and standards for care" are judged on a regional or on a global basis.

12. If the control treatment involves use of a placebo or a nil or null form of treatment, is that treatment consistent with prevailing norms and standards for care and treatment?
. . . . . (y) (n)
Answer *no* if there is a proven accepted mode of treatment. In answering, you must determine your basis for assessing norms and standards. If you believe that norms and standards for care and treatment are global then the locale of the trial is irrelevant. If your believe that they are regional then the country or locale of the trial is relevant.

13. If treatments are administered in double-masked fashion, can they be safely administered in that way?
. . . . . (y) (n)
Answer *no* if you believe that the masking increases the risk of harm to your Mother, if the protocol fails to allow for physician judgment in regard to whether to continue treatment, or if the protocol places higher value on the importance of adherence to treatment than on patient safety.

14. If the trial is double-masked, do clinic personnel have the means to unmask treatment in the case of medical emergencies?
. . . . . (y) (n)

15. If your Mother is masked to treatment, will she be informed of treatment assignment when she leaves the trial or when the trial is finished?
. . . . . (y) (n)

16. Will your Mother be told the results of the trial when it is finished?
. . . . . (y) (n)

17. Is it likely that your Mother will be treated with respect by clinic personnel?
. . . . . (y) (n)

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18. Will she be treated as an autonomous person?
. . . . . (y) (n)

19. Is subject selection equitable in the trial?
. . . . . (y) (n)
Answer *no* if the trial is designed to exclude a gender group, persons of a particular race or ethnic origin, or persons of a specified age if the condition being treated in the trial effects both gender groups, is no respecter of race or ethnic origin, or is present in other age groups. Answer *no* also if the trial is designed to concentrate on vulnerable or disadvantaged persons for no apparent reason.

20. Will the information your Mother provides and will the data collected on her be kept confidential?
. . . . . (y) (n)

21. Will study personnel respect and protect her privacy?
. . . . . (y) (n)

22. Will your Mother be provided with the information necessary for her to make an informed judgment regarding participation?
. . . . . (y) (n)
Answer *no* if you consider information provided in consent form(s) to be inadequate, incomplete, or misleading or if the reading level is too high.

23. Is the consent process adequate?
. . . . . (y) (n)
Consider answering *no* if consent is not solicited in a quiet private setting, if you think she will feel pressured to make a decision on the spot, if staff do not have the time or patience to answer her questions concerning the trial, or if she does not have time to discuss the pros and cons of enrolling with family members prior to deciding.

24. If she agrees to enroll, will she be free to terminate her participation at any time without prejudice?
. . . . . (y) (n)

25. Are investigators in charge of the trial and its conduct?
. . . . . (y) (n)
Answer *no* if investigators cannot modify the protocol without sponsor approval or if a treatment group or the trial cannot be stopped without sponsor approval.

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26. Is the study protocol written in such a way that makes it clear that investigators are obliged to depart from it if doing so is considered to be in the best interest of persons enrolled?
. . . . . (y) (n)

27. Are investigators competent?
. . . . . (y) (n)
Answer *no* if you believe they lack the knowledge, skill, training, or experience necessary for the proper and safe conduct of the trial.

28. Are the investigators trustworthy?
. . . . . (y) (n)

29. Is the data collection schedule reasonable and practical?
. . . . . (y) (n)

30. Are the procedures to which your Mother will be exposed necessary and safe?
. . . . . (y) (n)

31. Is the primary analysis to be by intention to treat?
. . . . . (y) (n)
Answer *no* in the absence of statements in the protocol indicating that the primary analysis will be by intention to treat.

32. Are the results of the trial being monitored by a body constituted for that purpose (typically referred to as a data and safety monitoring committee or by other names such as treatment effects monitoring committee or data monitoring committee)?
. . . . . (y) (n)

33. Is that monitoring body charged with responsibility for recommending whether the trial should be stopped or altered based on interim looks at study data?
. . . . . (y) (n)

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34. Are the analyses presented to that body based on a timely flow of data from collection to analyses and performed by a competent data coordinating center?
. . . . . (y) (n)
Lean toward answering *no* if flow is not designed to be continuous, if the case report form of data flow is employed (ie, where forms for a person are submitted for processing as a package at the end of treatment and followup for that person), if data entry and processing is not continuous, or if data analyses are not done by personnel trained for data analyses.

35. Is the monitoring body free of constraint in regard to what it may look at or in how it may look?
. . . . . (y) (n)
Lean toward answering *no* if the body is masked, if is required to operate under externally imposed stopping rules, or if it is empowered to address only issues of safety.

36. Is there an inalienable link of the monitoring body to study investigators?
. . . . . (y) (n)
Answer *no* if the monitoring body is charged to report to the sponsor and the sponsor has not provided written assurance to investigators that any recommendation for change, regardless of whether supported or opposed by the sponsor, will pass to study investigators in a timely fashion. Answer *yes* if the body reports directly to study leaders or simultaneously to investigators and sponsor.

37. Are investigators free of financial, operational, and philosophical conflicts of interests in regard to the trial?
. . . . . (y) (n)
Answer *no* in the absence of a system, within the trial, for disclosure of conflicts, for reviewing disclosures, and for, when indicated, insulating the trial from persons considered to have conflicts serving to disqualify them from participation or serving to place limits on participation.

38. Are investigators free to publish results from the trial as they deem reasonable and necessary without fear or prospect of interdiction by sponsors?
. . . . . (y) (n)
Answer *no* if the funding agreement with the sponsor places restrictions or limitations on publication or if the sponsor has right of approval of what or when something is published.

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39. Are investigators committed to publishing results of the trial regardless of the nature or direction of the results?

. . . . . (y) (n)

Lean toward answering *no* in the absence of study policy indicating such intent.

40. The Mother test: *Assuming your Mother is eligible and willing to be enrolled into the trial, would you be willing to randomize her to treatment and to have her treated and followed as proposed?*

. . . . . (y) (n)

If you answer *yes* and you answered *no* to one or more of the questions above either you are not as devoted to your Mother as you think or you do not believe that issues addressed in questions you answered *no* are important in applying the Mother test. Please explain.

If you answered *no* even though you answered *yes* to questions 1 through 39, either you do not believe in randomized trials (if so, you should find some other profession) or the list of questions does not cover issues central to your value system. Please explain.

If you answered *no* because you answered *no* to one or more of questions 1 through 39, detail the changes or conditions that would have to be satisfied in order for you to allow your Mother to enroll into the trial. Please explain.

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