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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: On how to succeed in trials without really trying

I wrote, a few weeks back (9 May), about my record as a trialist. It is a modest record. A lifetime to do just twelve trials. Not great. For the 60 years I have been doing trials, that is 5 years per trial on average, to say nothing about time spent to get them funded. It makes me wonder if I have earned my keep.

Below are suggestions for ways to make trials easier and faster. This essay was stimulated by a spread in the Wall Street Journal, 29 May 2018, entitled *Are Big Clinical Trials Relevant* by Lucette Lagnado.

1 Pick a condition common to males and females

This will make recruiting easier and having a condition common to both gender groups will save you the aggravation of having to explain to your IRB why you are enrolling only one gender group, especially if limited to males.

2 Gravitate toward conditions that have been in the popular press

This will make recruitment easier and put you in good stead in your community by doing worthwhile research, instead of squandering money on esoteric conditions.

3 Avoid rare conditions requiring multiple clinics to achieve enrollment goals

Leave those for others to do. Multicenter trials are PITA. They are much harder to fund and take much longer to fund than the usual single-center trial, and if you do manage to get one funded there is a good chance you will have sold part of your soul to the funding agency.

4 Opt in favor of short-term treatment and followup, a few weeks or so.

It is much easier to show change short-term than it is to sustain change over long periods of time. Short-term treatment and followup avoids the problems common to long-term trials, like noncompliance, dropouts, and censoring due to death, or serious illness making continuation in the trial impossible.

5 Choose change as the measure of interest

It is easier to effect change for some designated measure than waiting to see if there are changes in the rate of clinical events over extended periods of time and treatment.

6 Avoid choosing hard outcomes such as death or low occurring clinical events as the outcome of interest

The choice will commit you to having long-term treatment, followup, and probably a multicenter trial to achieve enrollment goals.

7 If you are inclined to focus on a clinical event as the outcome, choose a surrogate for the outcome

We know from Dem Bones (spiritual by James Weldon Johnson; 1871–1938) that

Your toe bone connected to your foot bone,
Your foot bone connected to your ankle bone,
Your ankle bone connected to your leg bone,
Your leg bone connected to your knee bone,
Your knee bone connected to your thigh bone,
Your thigh bone connected to your hip bone,
Your hip bone connected to your back bone,
Your back bone connected to your shoulder bone,
Your shoulder bone connected to your neck bone,
Your neck bone connected to your head bone,
I hear the word of the Lord.

So if, in your trial, you are interested in the head bone it is sufficient to study the toe bone because it is connected to the head bone. It is easier and faster to study the toe bone than the head bone and if the assumption of connectivity is correct then the toe bone is a suitable surrogate for the head bone. (We could have saved a lot of time doing the UGDP if we had used blood glucose control as a surrogate for clinical events because everybody knows that blood glucose control translates into benefits in reducing the late complications of diabetes – except for one small problem -- the assumption is false. Oh well. Sometimes the toe bone is not connected to the head bone.)

8 Steer clear of phase 4 trials

To be useful they will have to be large, likely multicenter, and long-term. Besides they may well produce results the world does not want to hear.

9 Muster arguments to convince your IRB and sponsor that an independent data and safety monitoring board (DSMB) is not necessary

Staffing and creating a monitoring board is an administrative burden, best avoided if possible. It should not be needed if the trial is short-term and the treatments are low risk.

10 Be modest on power requirements in sample size calculations

Remember, the higher the power specified for a calculation, the bigger the sample size requirement

11 Have some fancy esoteric twist in your design; the more esoteric the better

The twist will draw attention to the trials, perhaps causing some to label it as innovative and ground breaking. The fewer who understand the twist the better causing people to believe it is clever beyond their comprehension

12 If possible choose so your trial will produce results the world wants to hear

It is better to receive accolades for your work than brick baths. If you produce results the world does not want to hear, chances are you will be assumed to have done something wrong because the world is never wrong.

13 If results are nil data dredge to find something significant and report as a surprising result

Remember: The world loves statistical significance

14 Publish. Use a headline style for titling and do not spare on self laudatory terms like unique, novel, and innovative

15 Mine big data files and avoid trials completely