

LETTER

An unattractive hypothesis – RCTs' descent to non-science

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To the Editor

Eyal Shahar's essay review [1] of James Penston's remarkable book [2] seems more inspired playful academic provocation than review or essay, expressing dramatic views of impossible validity. The account given of modern biostatistical causation reveals the slide from science into the intellectual confusion and non-science RCTs have created:

".... the purpose of medical research is to estimate the magnitude of the effect of a causal contrast, for example the probability ratio of a binary outcome ..."

But Shahar's world is simultaneously not probabilistic, but of absolute uncertainty: *"We should have no confidence in any type of evidence We should have no confidence at all"*. Shahar's "Causal contrast" is attractive. It seems to make sense, but bypasses in two words the means of establishing causation by the scientific method. This phrase assumes a numeric statistically significant "contrast" is causal rather than a potential correlation requiring further investigation.

The concept of "causal contrast" is a slippery slope from sense into biostatistical non-science. This can be illustrated with an hypothetical RCT where 100% of interventions exhibit a posited treatment effect and 0% of placebo controls. Internal validity is seemingly quite reasonably assumed satisfied (common-sense dictating the likelihood of an awesome magnificent fraud, bias or plain error of the magnitude required is infinitesimal). Scientific method appears satisfied. The RCT demonstrates: (1) strict regularity of outcome in the presence of posited cause; (2) the absence of outcome in its absence and (3) an intervention (experiment) showing the direction of causation is from posited cause to posited effect.

Now travel further down the slope from science. Assume 50% of interventions and 0% of controls are positive. We compromise scientific method, but justify this by assuming a large subgroup which we say surely

must on these figures be exhibiting the posited treatment effect. But what of 10% of interventions and 9% of placebo controls exhibiting the posited treatment effect? Our biostatistician says the 1% "causal contrast" is statistically significant. But we have: (1) minimal evidence of regularity; (2) the posited outcome irrespective of presence of posited cause and (3) our intervention is at the highest equivocal in demonstrating any form of causation. This is not science. It is, however, where biostatistics has unthinkingly taken us, as Penston has shown comprehensively [2].

We, the audience of published medical research, are now for the 10% / 9% example well down the slope from science.

An unattractive hypothesis results requiring numerous assumptions similar to these:-

"There is a 'contrast' which is 'causal', albeit the method employed is not scientific. An effect of the intervention has been observed in a very small subgroup. This subgroup is susceptible to treatment. The similar number of placebo controls exhibiting the outcome sought is irrelevant, because the 1% difference between intervention and controls is statistically significant. The statistical analysis is valid and reliable. The RCT's internal validity is sufficiently satisfied. No funding or bias or fraud has affected the results or their analysis."

As Penston notes:

"Confirming and refuting the results of research is crucial to science But ... there's no way of testing the results of any particular large-scale RCT or epidemiological study. Each study ... is left hanging in the air, unsupported."

It gets worse. To identify a rare serious adverse reaction of a frequency of 1:10,000 can require a trial of 200,000 or larger split between controls and interventions. This is not done. But for every 100 who prospectively

benefit from the intervention, 9,900 also receive it. And for every 100 benefiting one person (who likely gains no benefit) will suffer a serious unidentified adverse reaction. This is also without taking account of more common adverse reactions whether serious or otherwise.

References

- [1] Shahar, E. (2011) Research and medicine: human conjectures at every turn. *International Journal of Person Centered Medicine* 1 (2), 250-253.
- [2] Penston, J. (2010). stats.con: How we've been fooled by statistics-based research in medicine. London: The London Press, UK.