



A new type of bias in research: The research ethical committees' bias

Many types of bias which alter the results of research have been described and investigated, but to my knowledge nobody has yet described the research ethical committees' (RECs) bias. Bias is something that induces a distortion of research results from the reality.

The main role of RECs in human research is to ensure the ethical standards and scientific merit of research involving human subjects. RECs have to protect research participants by ensuring that they receive sufficiently clear and correct information, which can be easily understood, and that are protected from potential adverse consequences of the research. RECs, on the other hand, also have some obligations to the researchers by treating research proposals with due respect, consideration and understanding. RECs should ensure that research meets the high ethical and scientific standards required. This is the theory – but what about reality?

I will briefly describe my personal failures with RECs. I have experienced many RECs in many different countries, usually with a great deal of success, though often they take (in my opinion) too much time in their decisional process, further slowing down the already naturally slow pace of clinical research. In fact, in few instances when the ethical approval finally arrived, years after the original proposal, most of the investigators had lost interest in the proposed research or had become involved in other more rewarding projects.

My first failure was due to inexperience. I worked for more than 20 years in Sweden, Norway and UK. When I started to plan my first clinical trial in Italy, my proposal was not even taken into consideration because the clinicians involved were private dentists rather than academicians or hospital doctors. In Italy, only academics and hospital doctors are allowed to conduct clinical research, which is quite paradoxical

since more than 90% of clinical research in dentistry is conducted by self-employed professionals, and by some academics in their own private clinics. To be correct on paper, Italian private dentists can acquire a special accreditation licence to run clinical research by following some regional rules, which in most of the regions were never made. As a result, the number of accredited private dentists in Italy is less than the fingers on one hand. I personally see this as an unjust discrimination and I do not see any ethics in it.

I recently had a second failure in Australia for a multicentre trial, in which, against my advice, different countries were involved. The research question was simple, if not banal: on the market, there is a chlorhexidine-based mouthwash with an added decolourant agent to eliminate or limit the known and unpleasant side effect of teeth staining. Some trials evaluated this mouthwash, which all reported efficacy in reducing staining, but 50% of them reported no statistically significant difference and even trends in the antiplaque capacity versus the placebo. It was decided the matter should be clarified, but the Australian REC of the University of Sydney did not allow the study on the grounds that no placebo can be used in patients when some effective treatment is already known about. This clinical question was generated by reviewing the published literature on the matter that suggested contradictory results on the effectiveness of the mouthwash under investigation; therefore, it is not clear whether this treatment is effective or not. Can anybody explain to me or the REC what are the potential health issues of using a placebo mouthwash after periodontal/oral surgery for 2 weeks that patients have to be protected from? I myself would have absolutely no problem to volunteer as a patient to this study, despite being considered unethical in Australia.



My third failure is even more emblematic. We presented to the REC of Bologna University (considered the oldest university in the world) a protocol of a particularly well-designed multifactorial randomised controlled trial with an ad hoc sample size calculation, strictly conducted according to the international standards for this specific type of trial and reported in full detail. The protocol was discussed for more than 1 year, until it was rejected because of the sample size calculation. In addition, they requested and obtained 4500 Euros before evaluating the application.

I feel the RECs in some situations abuse their dominating authority, making clinical research such a difficult challenge that puts off even the most diligent and enthusiast researcher. However, the task of RECs should not be that of frustrating the lives of researchers; on the contrary, they should be helping researchers improve their protocols, if needed. To obtain REC approval, research is biased towards what is believed more likely to obtain an ethical approval and not towards what researchers believe is of actual interest. In my experience, and if you allow me to generalise (I am not being evidence-based now!), there are strong cultural differences which play an important role. The Germanics and Scandinavians are very pragmatic, mixing the right balance of ethical needs to protect patient with the right degree of flexibility to test new products and interventions. The Anglo-Saxons are dominated by unbreakable rules, leaving almost no space for flexibility and innovation. The Latin RECs, with the exception of the French ones that apparently have a high degree of affinity with the Anglo-Saxon ones, are heterogeneous, extrovert and rather unpredictable, ranging from exceptionally high degrees of flexibility to senseless stubbornness. This attitude is likely to influence the decision of which country to

run the clinical research, especially for large trials, and some countries might be self-penalised a little too much. In addition, in some countries, you need to present your request locally – and in the case of multicentre trials, each centre must apply individually, with the not-unusual consequence that the same research protocol approved in one town or hospital is not approved, or is approved in a rather different form in the neighbouring hospital or town. If your protocol is rejected in your town, you are not allowed to present it in another town.

To conclude, the ideal REC should be:

- Ethical – it should focus on patient rights protection, ensuring an acceptable standard of research.
- Competent – it should be able to really understand the research question using a right degree of flexibility, since not all treatments pose the same level of risk for the patients.
- Supportive – it should help improve research protocol with competent and constructive suggestions.
- Accessible – anybody that has the required titles and the competence to run research should be able to apply without being discriminated against, as which happens in some places against private practitioners.
- Universal – it is not acceptable that the same protocol is ethical in one place and unethical in another.
- Free of charge – to ask for money to give authorisation to run or not a certain research is not ethical and leads to corruption.

Please take the time to think about these issues, since they are biasing research.

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