The Ethics of N-of-1 Studies
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Problem

N-of-1 studies are randomized controlled trials (RCTs) that involve multiple crossover and blinding in a single individual. Multiple such RCTs of single individuals can be analyzed together. This evolving field of research is described in more detail by Lillie et al. (2011).

In the United States, there is no standard policy about the ethics of N-of-1 studies. AHRQ has published a discussion of the ethics of N-of-1 studies (AHRQ, 2014). There is no consensus about whether N-of-1 trials qualify as research under the federal definition, which would then require IRB review. Some IRBs consider them as research, while others think they are simple case studies.

Purpose

To determine whether AAHRPP accredited IRBs in the United States consider N-of-1 studies to be research. Do they meet the definition of human subject research (45 CFR 46.102) that requires IRB approval or not?

Method

To summarize the opinion among AAHRPP accredited IRBs in the United States about N-of-1 studies, a survey was conducted using SurveyMonkey as a data-collection tool (https://www.surveymonkey.com/). A questionnaire was sent in March 2014 to the 169 IRBs that were accredited by AAHRPP.

Results

According to the policy you have, are N-of-1 studies considered research by the definition of 45CFR46.102(d)?

According to the policy you have, do N-of-1 studies need IRB approval?

Discussion

Although the vast majority (79%) of responding IRBs said they didn’t have a policy about N-of-1 studies, almost half of the responding IRBs thought N-of-1 studies were research and even more (54%) said they need IRB approval. Only 21% of respondents had a policy regarding this issue and they all thought that N-of-1 studies were not research and therefore didn’t need IRB approval. There were 4 non-responding IRBs that had a policy about N-of-1 studies being research on their websites.

Limitations of this study include the response rate of 35% and that the responder for each IRB may be stating what that IRB thinks, or might be stating their personal view. Even with these limitations the survey does provide an interesting insight into the variety of views held by IRBs in the US about N-of-1 studies.

An inquiry was made to OHRP about this issue by one of us (JB) and their e-mail response on 2/6/2014 stated, “The regulations do not define a minimum number of subjects needed to constitute research. The regulations recognize research development as an activity that falls within the definition of research. One can make a distinction between ‘case reports’ which, in the clinical context, typically consist of retrospective descriptions and discussion of one individual’s condition and treatment; and ‘n of 1 case studies’, which generally use qualitative research methods to study an individual or group, and may fit the regulatory definition of research. For example, an ‘n of 1’ might in some cases be sufficient to refute a generally accepted rule.”

Conclusion

The issue of whether N-of-1 studies are research is currently confusing for the IRB community. This is partly explained by newness of the topic and hence many are not familiar with the how n-of-1 studies can be RCTs. This topic deserves wider dissemination in the IRB community.

REFERENCE