Challenges stemming from NIH's extended registration and reporting requirements

To the Editor — The new National Institutes of Health (NIH) policy requires that investigators register NIH-funded clinical trials and report their results on ClinicalTrials.gov; investigators also have to submit full protocols when they submit results on ClinicalTrials.gov[1]. Although the definition of 'clinical trial' has not changed since 2014[1,2], the new policy extends existing registration and reporting requirements beyond hypothesis-testing trials to include all clinical trials (for example, Phase 1 or exploratory, non-drug or non-device). The policy presents challenges for behavioural investigators and others who do not consider their work 'clinical'.

As it is ethically and scientifically imperative to share the results of research involving human participants, we support the new NIH registration and reporting policy[3,4]. Nonetheless, because the ClinicalTrials.gov and protocol structures were designed for Food and Drug Administration-related trials[5], we believe modifications of existing systems are needed, and we give three examples.

Registration and reporting requirements should be aligned with the purposes or goals of clinical trials. At present, investigators conducting 'exploratory' trials have to adhere to registration and reporting requirements more applicable to hypothesis-testing trials. For example, an exploratory trial of a behavioural intervention might comprise a single intervention group and examine the feasibility of one component of a planned complex intervention; nevertheless, a trial must be described using the standard ClinicalTrials.gov format, which assumes certain components that may be more relevant to hypothesis-testing than exploratory goals. Different data items might be appropriate for exploratory trials.

Appropriate registration and reporting options for complex designs are needed. Investigators find ClinicalTrials.gov data entry forms are difficult to complete for designs other than parallel trials. We looked at the entry for the SMART Weight Loss Management Trial (NCT02997943), a two-stage trial in which participants were assigned randomly to one of two behavioural interventions in stage 1 (A versus B), and participants who did not lose weight were assigned randomly to one of two additional interventions in stage 2 (C versus D). Given ClinicalTrials.gov requirements and the trial's complex design, it appeared that information about the trial could not be entered in a manner consistent with all trials in the registry. Inconsistent and unclear records reduce the utility of ClinicalTrials.gov for meta-research, and they create challenges for compliance monitoring.

The new NIH policy could also contribute to inconsistencies across multiple reports of the same clinical trial (for example, grant proposal, registration on ClinicalTrials.gov, protocol)[6]. This is particularly likely when the NIH requires different information, or information appearing to be different, across reports. For example, ClinicalTrials.gov requires that investigators define 'outcomes' using five elements (that is, domain, measure, metric, method of aggregation and time point). In contrast, the NIH protocol template refers to 'endpoints' (instead of 'outcomes') and does not ask investigators to define the five elements[7–9]. The NIH could create a linked system to reduce burden on investigators and to improve consistency across reports of individual trials. For example, information provided for the NIH protocol could be used to register trials automatically on ClinicalTrials.gov. ❐

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Competing interests

Up to 2008, K.D. served as an unpaid expert witness for the plaintiffs' lawyers (Greene LLP) in litigation against Pfizer related to reporting of gabapentin trials. Thomas Greene has donated funding to Johns Hopkins University for scholarship related to reporting clinical trials. E.M.-W. and K.D. conduct research about reporting clinical trials, and they have received funding for their research from multiple funders including the National Institutes of Health and the US Food and Drug Administration.