




# BMJ Open Public reporting of clinical trial findings as an ethical responsibility to participants: a qualitative study

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## ABSTRACT

**Objective** To understand how the experiences and views of trial participants, trial investigators and others connected to clinical trial research relate to whether researchers have a duty to participants to publicly report research findings.

**Design** Qualitative interview study.

**Setting** Semistructured interviews held in person or by telephone between March 2019 and April 2021 with participants in the Canadian provinces of Alberta, British Columbia and Ontario.

**Participants** 34 participants, including 10 clinical trial participants, 17 clinical trial investigators, 1 clinical research coordinator, 3 research administrators and 3 research ethics board members.

**Analysis** We conducted a thematic analysis, including qualitative coding of interview transcripts and identification of key themes.

**Main outcome measures** Key themes identified through qualitative coding of interview data.

**Results** Most clinical trial participants felt that reporting clinical trial results is important. Accounts of trial participants suggest their contributions are part of a reciprocal relationship involving the expectation that research will advance medical knowledge. Similarly, comments from trial investigators suggest that reporting trial results is part of reciprocity with trial participants and is a necessary part of honouring informed consent. Accounts of trial investigators suggest that when drug trials are not reported, this may undermine informed consent in subsequent trials by withholding information on harms or efficacy relevant to informed decisions on whether to conduct or enroll in future trials of similar drugs.

**Conclusion** The views of trial participants, trial investigators and others connected to clinical trial research in Canada suggest that researchers have an obligation to participants to publicly report clinical trial results and that reporting results is necessary for honouring informed consent.

## INTRODUCTION

A systematic review indicated approximately 4 in every 10 randomised controlled trials included in trial registries were not reported in journal articles after a period of 2 or more years from study completion.<sup>1</sup> Clinical studies

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The use of qualitative interviews allowed for an in-depth exploration of experiences and views relating to clinical trial reporting as an ethical responsibility towards trial participants.
- ⇒ The study was strengthened by the inclusion of a range of participants, including past trial participants, trial investigators, research administrators and research ethics board members.
- ⇒ As the sample of past trial participants interviewed for this study was small, caution is warranted in generalising from these interviews.
- ⇒ The study focused on clinical trials in Canada, so it is not clear to what extent our findings apply to clinical trials in other countries.
- ⇒ It is possible that attitudes towards clinical trial reporting differed in those who participated compared with those who did not take part in the study.

with results favourable for the experimental treatment are more likely to be published, leading to bias in the medical literature.<sup>2</sup> Studies have also found low compliance with regulatory requirements for timely reporting of clinical trial results within ClinicalTrials.gov and the EU Clinical Trials Register.<sup>3 4</sup> A study of clinical trials conducted in Canada, including trials registered in ClinicalTrials.gov and completed between 2009 and 2019, found that only 39% of trials had reported results in the registry by early October 2021.<sup>5</sup> Moreover, the problem of non-publication of clinical trials has been documented across many areas of medicine<sup>6–10</sup> and, although more frequent in earlier phase trials, for all phases of clinical trials.<sup>2</sup> Selective reporting of trials has led to less informed patient care, unnecessary harm to patients and a waste of research resources.<sup>11–13</sup>

Advocates of full reporting of clinical trials have argued non-publication betrays trial participants and violates an implicit contract between participants and researchers.<sup>14–18</sup> They reason that when individuals agree

to participate in trials, they expect their participation will contribute to medical knowledge and help future patients. When trial findings are not reported, this expectation is not fulfilled. More fundamentally, as individuals may reasonably expect trials to contribute to knowledge when deciding to participate in a trial, non-reporting of clinical trials may undermine informed consent.<sup>17 18</sup>

Arguments that clinical trial investigators have a duty to trial participants requiring them to report findings are strengthened by previous research suggesting that motivations for participation in trials include altruism.<sup>19–22</sup> In addition, a survey of non-critically ill patients in an emergency department setting found that most felt it was important to make clinical trial results publicly available.<sup>23</sup> However, trial participant views on the importance of reporting research findings and trial investigator views on the responsibility to report findings are unclear.

We conducted a qualitative study of clinical trial reporting in Canada. Our broader study aimed to investigate factors contributing to non-publication and publication bias in clinical trials and related ethical issues.<sup>24 25</sup> The analysis reported in this paper aimed to understand how the experiences and views of trial participants, trial investigators and others relate to whether researchers have a duty to trial participants to publicly report research findings in journals or trial registries.

## METHODS

### Study design

We conducted a qualitative study involving semistructured interviews and thematic analysis of interview data to investigate experiences and views related to clinical trial reporting.<sup>26</sup> This study used a qualitative approach because this provided the flexibility to investigate emergent themes and to collect rich data regarding views and experiences relating to reporting of clinical trials—for example, through prompting interviewees to elaborate on unanticipated or important points raised in their responses.<sup>27 28</sup> The research team for this project included a clinical trial investigator (SG), an expert in qualitative methods (GG), a health research analyst (RLM) and researchers in epidemiology and health policy (BM, MRL and CRD). The researchers had no prior relationship with those interviewed for the study.

### Sampling

We sought to interview clinical trial participants, clinical trial investigators, clinical research coordinators, research administrators and research ethics board (REB) members (inclusion criteria are listed in [table 1](#)). We used a purposive sampling strategy to involve trial participants who had participated in trials for a range of treatments, trial investigators in diverse medical fields and others connected to clinical trial research to provide additional perspectives. Snowball sampling was used to as a complementary strategy to gain referrals to additional trial investigators and REB members. We chose to include

**Table 1** Types of interviewees and inclusion criteria

Interviewee type	Inclusion criteria	Rationale
Past trial participant	Participated in ≥1 clinical drug trial while at least 18 years of age; participation in the 5 years prior to interview, but has now ended	Will have experience related to trial participation and trial reporting
Clinical trial investigator	Conducted ≥1 clinical drug trial	Will have experience relevant to trial reporting
Clinical research coordinator	Coordinated ≥1 clinical drug trial	May have experience relevant to clinical trial reporting
Research administrator	Knowledge of policy and practice related to dissemination of clinical trial findings and/or relations with trial sponsors	Contribute experience, knowledge and views from policy or administrative perspective
Clinical REB member	≥1 year of experience as clinical REB member	Experience in ethical review and familiarity with practice and policy relating to clinical trial reporting

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in our study sample both those who had participated in trials and those involved in the conduct, administration or ethical review of trials for two reasons: first, each type of interviewee might provide insights from a different perspective, and second, this would allow for triangulation of findings.<sup>27</sup>

### Recruitment

Strategies to recruit past trial participants included advertising in a free newspaper and requesting assistance from clinical research coordinators and managers, who sought consent from past trial participants for us to contact them about our study. We emailed or telephoned 11 individuals who expressed interest following the advertisement or consented to be contacted (10 participated and 1 did not respond). We identified other types of interviewees through online sources (ClinicalTrials.gov, Canadian Clinical Trials Asset Map database and websites of research institutions and REBs) and referrals. We invited participation from 61 trial investigators by email (17 investigators participated, 2 responded but were unavailable for an interview during the study, 36 did not respond and 6 declined). Investigators who declined stated they were too busy (n=1), not interested (n=1) or lacked relevant experience (n=4). A clinical research coordinator

who worked with a participating trial investigator also volunteered to take part in an interview. In addition, we emailed 12 research administrators (3 participated and 9 did not respond) and 15 REB members (3 participated and 12 did not respond). Trial participants and trial investigators were eligible to receive a US\$50 honorarium for participation.

### Data collection

We conducted semistructured interviews from March 2019 to April 2021. Interview guides for each type of interviewee were used (online supplemental appendix). Interviews were primarily based on open-ended questions and allowed for exploration of unanticipated issues. Data collection included initial interviews in person or by telephone with 34 individuals and follow-up telephone interviews with 4 individuals to collect additional information. The duration of interviews was approximately 45–60 min for initial interviews and 20 min for follow-up interviews. In-person interviews were held in a public library meeting room or at the interviewee's workplace. RLM conducted the research interviews and coded the interview data. Data collection continued until the data allowed for a detailed analysis addressing the study's research questions.

### Data analysis

Interviews were audiorecorded and transcripts were analysed using ATLAS.ti (V.8), including coding and deriving themes from the data. Analysis included initial coding with an open-ended approach, followed by additional analysis to retain and develop key themes for analysis.<sup>26</sup> Collection of data from different types of interviewees allowed for triangulation of data during analysis.<sup>27</sup> The Consolidated Criteria for Reporting Qualitative Studies checklist was used to guide reporting of findings.

### Patient and public involvement

A patient advocate was consulted during the planning of this study regarding the importance of pursuing this research and strategies for recruiting past trial participants for interviews. All participants in this study who are interested will receive a summary of the study results, including past trial participants who took part in a research interview.

## RESULTS

Overall, 34 individuals took part in the study, including 10 clinical trial participants, 17 clinical trial investigators, 1 clinical research coordinator, 3 research administrators and 3 REB members. (See table 2 for interviewee characteristics). The study included individuals from the Canadian provinces of Alberta, British Columbia and Ontario. Past trial participants varied by sex (three male; seven female), age (38–77 years at the time of their initial interview) and highest level of education completed (from elementary to university). They had taken part in trials of 6 months to 5 years in duration, testing treatments

**Table 2** Interviewee characteristics

Characteristic	Past trial participants (n=10)		
<b>(A) Past trial participants</b>			
Sex			
Female			7
Male			3
Age			
≤65 years			5
>65 years			5
Education, highest level completed			
Elementary			1
Secondary			3
Community college			1
University			5
Province			
Alberta			3
British Columbia			7
<b>(B) Trial investigators</b>			
Characteristic*	Trial investigators (n=17)		
Primary appointment			
University or academic teaching hospital			10
Other (eg, private practice, cancer centre)			7
Experience in role			
≤5 years			0
>5 years			17
Province			
Alberta			0
British Columbia			9
Ontario			8
Types of funding			
Non-industry only			0
Industry only			0
Both industry and non-industry			17
Most senior role			
Principal investigator for site			3
Principal investigator for trial			14
Trial type			
Single site only			0
Multiple site only			1
Both single and multiple site			16
<b>(C) Clinical research coordinators, research administrators and research ethics board (REB) members</b>			
Characteristic	Research coordinator (n=1)	Research administrators (n=3)	REB members (n=3)
Primary appointment			
University or academic teaching hospital	0	3	1
Other (eg, private practice, cancer centre)	1	0	2

Continued

**Table 2** Continued

(C) Clinical research coordinators, research administrators and research ethics board (REB) members			
Characteristic	Research coordinator (n=1)	Research administrators (n=3)	REB members (n=3)
Experience in role			
≤5 years	0	0	1
>5 years	1	3	2
Province			
Alberta	0	1	1
British Columbia	1	0	2
Ontario	0	2	0

Table 2 was created by the authors. A version of table 2 has previously been published, and it is reprinted in a modified form with permission.<sup>24</sup>  
 \*Classifications were based on those used for an investigator survey by Rochon *et al.*<sup>39</sup>  
 REB, research ethics board.

for cardiovascular disease, *Clostridioides difficile* infections, chronic pain, diabetes, eye disorders and multiple sclerosis. Among interviewees who were involved in the conduct, administration or ethical review of trials, some spoke about both conducting trials and playing a role in research administration or reviewing ethics applications. Trial investigators who took part in the study had conducted trials in cardiovascular medicine, endocrinology, hepatology, infectious diseases, oncology, psychiatry and rheumatology.

Our study results are presented below by theme. This includes themes relating to trial participant experiences and views (motivations for participating in a trial and trial participant views on reporting research findings), accompanied by quotations from trial participants (P1–P10). The findings below also include themes related to accounts from those involved in the conduct, administration or ethical review of trials (views on clinical trial reporting as a responsibility to research participants and linking clinical trial reporting to informed consent), presented with quotations from trial investigators (T1–T17).

### Views of clinical trial participants

#### Motivations for participating in a clinical trial

Most trial participants stated they were motivated to take part in the clinical trial in part to help future patients. Patients with a less urgent need to improve their health condition were more likely to identify helping future patients as their primary reason for joining a trial. For example, a patient with type 1 diabetes recalled that she had joined multiple clinical trials over time because she ‘figured if there isn’t research being done to help people, then nothing is ever going to improve.’ (P7) Patients who were in more urgent need to improve their health condition were more likely to identify access to treatment as their primary reason for participating in a trial. However, they also often wanted to help future patients and conceived of their participation as an act of solidarity with others like them. A patient who had experienced a

recurring *C. difficile* infection recalled that at the time of joining a clinical trial she had told family members: ‘Nobody should have to suffer this way, and if there’s anything that I can do to help medical science move forward so that other people don’t have to suffer like this in the future, I’m all for it.’ (P6) Although most participants were motivated to join a trial in part to help others, this was not always the case. One trial participant, who joined a trial to access treatment after suffering from a sudden deterioration of her vision due to an eye disorder, recalled that her initial motivation was solely to address her own health needs. Trial participants typically had multiple reasons for participating in a trial. Motivations varied among participants but included access to free medication or medical supplies, access to better care and helping one’s health provider or researchers.

#### Trial participant views on reporting research findings

Most past trial participants felt it was important for the results of clinical trials to be published. Trial participants stated various reasons they felt publishing research findings was important. Some suggested if results were not published, this would represent a waste of time or resources. A patient who had participated in a trial to test a treatment for *C. difficile* felt it was important to avoid wasting the effort and resources invested in a trial: ‘If we’re doing the work, spending the dollars and not using that information to further medical science, then what was the point of doing all that work in the first place?’ (P6) Another patient, who had taken part in a trial to test a treatment for relapsing-remitting multiple sclerosis, emphasised the importance of reporting results to help future patients: ‘If you don’t publish... then how is it to be paid forward to help other people?’ (P5) Some trial participants stated it was important to publish trials to learn from negative or incomplete trials, inform the medical community, demonstrate transparency and improve future research. However, not all patients stated that publishing trial results was important. One patient felt it was hard for her to judge whether it was important to publish results from a trial suggesting a treatment did not work. Another patient spoke about how he would feel about publication of results of the trial he participated in, rather than about the importance of reporting in general, saying: ‘I would feel a little better knowing that my participation helped in something.’ (P9)

When some participants described the value of clinical trial reporting, they highlighted the contribution of trial participants to research. A patient with type 1 diabetes felt it was important to publish trial results, ‘because of a lot of effort that a lot of people put into it—not just the researchers, but the people that were participating in the trial.’ (P7) Similarly, another trial participant said she felt it was important to publish trial results in part because ‘people were gracious enough to be part of it.’ (P2) One trial participant reflected that she was quite willing to be a ‘guinea pig’, but she would feel ‘cheated’ if the trial she had participated in were not published, because she



had participated ‘not just for me.’ (P5) Taken together with statements from a larger number of trial participants that they had participated in part to help other patients, these comments suggest reporting the results of trials is important as a form of reciprocity between researchers and trial participants. However, none of the trial participants was aware of whether the results of the trial they had participated in had been published, although in some cases the trials they had taken part in were either ongoing or so recent that it would be reasonable that results might not have been published at the time of their interview. In effect, reciprocity between trial participants and researchers may require reporting of trial results, but trial participants may often not be able to observe whether this is fulfilled.

### Views of those involved in the conduct, administration or ethical review of trials

#### Clinical trial reporting as a responsibility to research participants

Among investigators, administrators and REB members interviewed for this study, many felt researchers have an obligation to trial participants to report the results of clinical trials. Comments highlighted that trial participants contribute their time and expose themselves to risk, yet may not directly benefit through their participation. Several comments suggested reporting results is necessary as a kind of reciprocity, or to fulfil an implicit agreement, between trial participants and researchers. A trial investigator who studied treatments for infectious diseases felt publishing was important as a responsibility to trial participants: ‘Well, they’ve spent their time ... There’s a potential risk of entering a clinical trial, so I think as researchers we have a responsibility to hold true to their commitment and altruism to enter into a clinical trial.’ (T16) An endocrinologist who conducted clinical trials said: ‘I think most people understand that this may or may not benefit them, but hopefully this will benefit society... If it’s not even published, then we’re not fulfilling our side of the bargain.’ (T14) Similarly, a couple of investigators suggested that a ‘contract’ between participants and researchers obligated researchers to report results. Notably, the chronology of this reciprocity or ‘bargain’ involves the trial participants contributing their time and exposing themselves to risk without knowing whether researchers will fulfil their implicit obligation to report the research findings. This was reflected in the comment of one trial investigator, who noted: ‘People have volunteered, given their time, given their samples *in good faith* that some science is going to come out of it.’ (T7, emphasis added)

Some trial investigators felt a responsibility to trial participants to publicly report trials results existed but it could be difficult or less important to publish in certain circumstances. A cardiovascular investigator, who spoke about the difficulty of publishing incomplete trials, stated: ‘To me, not publishing is unethical, but I can see some situations where it’s just not possible.’ (T10) He also suggested trials stopped early following a decision by

an industry sponsor to halt development of a drug could be less important to publish due to a lack of statistical power and lack of relevance. Similarly, some interviewees mentioned that trials which are unable to recruit many patients may not be published and that it can be difficult to make inferences from or publish an incomplete trial. In addition, some investigators highlighted that a lack of time or resources may be a factor contributing to non-reporting or delays in reporting. While trial results could be reported in trial registries such as ClinicalTrials.gov, which could be particularly helpful if results were difficult to publish in a journal, not all trial investigators were aware of the possibility of reporting results in registries.

#### Linking clinical trial reporting to informed consent

Several investigators linked an obligation to report trial results in a journal or trial registry to informed consent. In some cases, consent forms signed by trial participants actually indicate research findings will be published. More generally, trial participants may reasonably expect or be told a trial will contribute to medical knowledge. An investigator in hepatology trials suggested this requires researchers to report their findings: ‘We specifically say the benefit will be greater knowledge to the scientific and medical community, which will hopefully benefit other people in the future. So if we’re not sharing the results of the study, then that’s not true... We are not honouring that consent.’ (T15)

When trials showing drug harms or a lack of efficacy, including early phase trials, are not reported, this may also undermine informed consent in future trials. An investigator noted that trials identifying safety concerns may provide information relevant to future trials of similar drugs. Although another investigator was less concerned about this issue because drugs in the same class would not necessarily be associated with the same adverse effect, in some cases information about harms of one drug in a class is deemed important enough to add to consent forms used in trials of drugs in the same class. Similarly, a trial investigator and an REB member involved in conducting trials each highlighted that publishing trials showing harms may inform other trialists that trials of the same or similar drugs would expose patients to excessive risk. In addition, the REB member commented that non-publication of negative trials may lead to redundant research which unknowingly involves patients in trials of drugs lacking efficacy.

### DISCUSSION

The accounts of trial participants, trial investigators and others connected to clinical trial research suggest that when researchers enrol patients in clinical trials there is often an implicit understanding among researchers and trial participants involving an obligation to publicly report research results. Most trial participants were motivated to enter clinical trials in part to advance science, and most felt that reporting the results of clinical trials is



important. Trial participant accounts suggest their contributions are part of a reciprocal relationship involving the expectation that research will advance medical knowledge. Similarly, comments from trial investigators suggest that reporting trial results is part of reciprocity with trial participants and is a necessary part of honouring informed consent. In addition, when trials are not reported, this may undermine informed consent in subsequent trials by withholding information on harms or efficacy relevant to informed decisions on whether to conduct or enrol in future trials of similar drugs.

### Comparison with existing literature

Our finding that many trial participants were motivated to join trials in part to help future patients is consistent with previous studies on reasons for participation in trial research.<sup>19–22</sup> Our study adds that even patients who are strongly motivated to participate by the opportunity to access treatment may feel it is important to help future patients out of a sense of solidarity with others like them.

A survey of non-critically ill patients in an academic emergency department in the northeastern USA found that most felt it was important to report trials results.<sup>23</sup> Our study indicated most individuals who had recently taken part in a clinical trial felt it was important to report trial results, while highlighting trial participants may view their own contributions as part of a reciprocal relationship involving the expectation that trials will contribute to medical knowledge. However, this reciprocity which involves a responsibility for researchers to report trial results may be weakened for various reasons. First, trial participants may often not find out whether trial results are published by the researchers, which might diminish a researcher's sense of the obligation to publish as a responsibility to the trial participants. Second, trial participants might be unlikely to question whether results have been reported, due to losing contact with researchers who are not their regular health providers, respect for the authority and expertise of the researchers, or gratitude for other benefits received in the trial (such as access to treatment or greater medical attention).

Importantly, our study strengthens empirical support for arguments that when trial results are not reported, this violates an implicit agreement or contract between researchers and participants and undermines informed consent.<sup>15–18</sup> Trial participants may consent to enter a trial with the understanding that research will benefit future patients. However, this consent is not respected when trial results are not reported and this potential benefit is not fulfilled. In effect, the core ethical principle of respect for persons is undermined, as informing trial participants of the risks and benefits of research is part of respecting their autonomy as research participants.<sup>29 30</sup>

Notwithstanding the responsibility to publicly report trial findings, some investigators noted it may be difficult to complete a trial due to low recruitment or other reasons, and it may be difficult to publish certain findings such as those from an incomplete trial. Estimates of the

rate of discontinuation of clinical trials vary, but discontinued trials are less likely to be published.<sup>31–33</sup> A focus group study of biomedical researchers found that many felt it was difficult to publish negative or 'no difference' results.<sup>34</sup> It may even appear questionable to report a trial that encountered problems such as difficulty in recruitment or high drop-out rates. However, trial registries provide an avenue to report trials that might be difficult to publish in a journal, and may, like ClinicalTrials.gov, allow authors to provide reasons for early termination of a trial and to describe limitations or caveats regarding a trial's results.<sup>35</sup>

### Policy implications

While the analysis reported in this paper highlights an ethical responsibility to report research results, this responsibility does not lie with trial investigators alone. Previously reported findings from our broader study of clinical trial reporting, based on the same interviews analysed for this paper, indicated that industry sponsors of clinical trials may exert influence on whether results are reported and that clinical trial reporting practices are shaped by incentives within the research system favouring publication of positive or negative trials, such as funding opportunities and academic promotion, bonuses and recognition.<sup>24 25</sup> Similarly, a survey study found researchers were 'aware of being the main culprits of non-publishing or selective publishing of results from clinical trials' but felt that 'blame rested not solely with them but with the system that encourages and supports practices that lead to publication bias—from funders and research institutions to journals and trial registries.'<sup>36</sup> The responsibility to ensure trials are publicly reported is shared by trial investigators with other actors in the research system who shape the context in which trial reporting takes place.

Stronger regulatory measures could improve clinical trial reporting policy or practices of research institutions, sponsors and individual investigators. In Canada, it is important to adopt regulatory measures to require reporting of clinical trial results within a recognised trial registry. While phase 1 trials are largely excluded from current regulatory reporting requirements in the USA and European Union,<sup>4 37</sup> our study highlights reporting early phase trials is necessary for fulfilling informed consent. The effectiveness of mandatory reporting requirements depends on both enforcing existing requirements and expanding their scope to cover all clinical trials of drugs and biologics.<sup>3 4 38</sup>

### Strengths and limitations of this study

The use of qualitative interviews allowed for an in-depth exploration of experiences and views relating to clinical trial reporting as an ethical responsibility towards trial participants. A strength of our study was the inclusion of a range of participants, including past trial participants, trial investigators, research administrators and REB members. Our study also had limitations. As the sample of past trial participants interviewed for this study was

small, caution is warranted in generalising from these interviews. However, this limitation was mitigated by triangulation of findings among different types of interviewees regarding reciprocity between researchers and trial participants and the responsibility to report results. More generally, it is not clear to what extent our findings apply to clinical trial settings outside Canada, as experiences and views of clinical trial reporting might vary due to differences in funding, policy or healthcare systems. In addition, it is possible that attitudes towards clinical trial reporting differed in those who participated compared with those who did not take part in the study.

## CONCLUSIONS

The views of trial participants, trial investigators and others connected to clinical trial research in Canada suggest that researchers have an obligation to research participants to report clinical trial results and that reporting of results in registries or journals is necessary for honouring informed consent. This highlights the need for Health Canada to adopt regulatory measures to require timely reporting of clinical trial results within a recognised trial registry. Future studies could investigate views on clinical trial reporting in other countries.

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**Patient and public involvement** Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

**Patient consent for publication** Not applicable.

**Ethics approval** The study received ethics approval from the University of British Columbia Behavioural Research Ethics Board (H18-03458) and the University of Alberta Health Research Ethics Board (Pro00096201), and all participants provided informed consent. Participants gave informed consent to participate in the study before taking part.

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**SUPPLEMENTARY APPENDIX**

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## A. Interview guide for clinical trial participants\*

1. Involvement and expectations
  - a. How did you come to be involved in the trial? (e.g., sought trial to participate in, invited by physician, saw advertisement; change in health condition)
  - b. How did you understand the purpose of the trial? (e.g., drug, health condition, research question, outcomes, efficacy, safety and efficacy for regulatory approval, postmarket safety)
  - c. How would you describe what motivated you to enroll in the trial?
    - How important did you feel it was to get access to the treatment?
    - How important did you feel it was that it might help future patients?
    - How important were other factors in your decision to enroll in the trial? (e.g., having your health monitored closely, having a good relationship with your physician)
  - d. Do you recall how you felt about enrolling in the trial? What were your expectations of the trial?
  - e. What did you understand about how the trial was designed? (e.g., controlled or not, placebo or comparison drug, randomization, blinding, duration of treatment, study population) What did you understand to be the potential benefits or risks of participation?
  - f. How was information about the purpose, design and benefits or risks of participation in the trial communicated to you?
2. Activities in the trial
  - a. When did your participation in the trial begin and end?
  - b. What did participating in the trial involve? (e.g., taking medication, clinic visits or medical tests)
  - c. Did you receive the trial medication from your regular physician? Who did you interact with as part of the trial? (e.g., clinical research coordinator, regular physician, other physician or nurses)
  - d. What did participating require of you, in comparison to your prior therapy or routine? (e.g., travel to clinic, investment of time)
3. Experience of trial
  - a. How would you describe the experience of participating in the trial? (e.g., what was it like to participate in the trial, what did you think of the experience at the time, how did it feel to participate in the trial)
  - b. Did you feel you benefited from participating in the trial? In what ways? (e.g., health benefits, satisfaction)
  - c. Did you feel you experienced any adverse effects from the treatment or participation in the trial? How would you describe these effects? (e.g., health effects, stress)
  - d. Did you complete the treatment in the trial? If not, what led to withdrawal from the trial?

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\* The interview guides in this appendix were created by the authors. The interview guides were previously published and have been reprinted with permission.<sup>1</sup>

- e. Are you aware of whether the trial has concluded? Do you know when it was (or was expected to be) concluded?
4. Reporting of trial results
- Clinical trials are important for developing new drugs and providing the best medical care. However, about 4 in every 10 clinical trials are not published or only published after a long delay.<sup>2</sup> When clinical drug trials remain unpublished, they are unavailable to the larger wider scientific community. This makes it harder for researchers, doctors and others to understand which drugs are safe and effective.
- a. If the trial has concluded:
- Were you informed about the results of the trial? If so, how did this occur? How did you feel about being informed about trial findings (or about not being informed)?
  - Are you aware of whether results of the trial have been published?
    - If aware, how did you become aware of this? How do you feel about the fact the results were published / were not published?
    - If not aware, how do you think you would feel if the results of the trial were not published?
- b. If the trial has not concluded:
- How do you think you would feel if the results of the trial were not published?
- c. Importance of reporting and of participants being informed of results:
- Given your experience as a trial participant, how would you describe the importance of whether trial results are published? Could you explain why you think that?
  - How would you describe the importance of trial participants being informed of the results of the trial they participated in? If you feel this to be important, what do you think would be a good way to communicate the findings to participants? (e.g., summary in lay language or information shared by physician)
- d. Additional comments:
- Is there something we have not talked about that you think I should know to understand your experience of the trial?
  - Similarly, is there something we have not discussed that you think I should know to understand your views on the publication of trial results?

#### Short answer questions

5. Could I ask you to tell me your age? (<30 years, 30-39, 40-49, 50-64, >=65)
6. Could I ask you the highest level of education that you have completed? (<= grade 8, high school, community college, university, graduate school)

## B. Interview guide for clinical trial investigators

Clinical trials are important for developing new drugs and providing the best medical care. However, about 4 in every 10 clinical trials are not published or only published after a long delay.<sup>2</sup> In this study, I am interested in trying to better understand this phenomenon, in part by talking to trial investigators about their experiences and views related to trials and trial reporting.

1. Introductory questions
  - a. Could you tell me about the types of trials that you do? (e.g., research areas, phase of trials, single or multi-site trials, funding source)
  - b. How much of your work involves conducting clinical trials? If this is only part of your work, how does it fit into your other work? (e.g., clinical practice, teaching, administration)
  - c. Could you describe your typical role and responsibilities when conducting a clinical drug trial? (e.g., Principal Investigator/ co-investigator, trial design, recruiting patients, administering treatment, collecting data, reporting findings, grant-writing, liaising with sponsor)
  - d. Optional, time-permitting: When you are conducting a trial, who would you typically have occasion to interact with during the course of a trial, from the planning to implementation and reporting? (e.g., co-investigators, clinical research coordinator, clinical research associate or monitor from contract research organization, project manager from contract research organization, patients)
2. Specific clinical drug trial
  - a. Could I ask you to think about an example of a trial you were involved with as an investigator, which concluded prior to the last 12 months?
  - b. Could you describe the trial?
    - Purpose of the trial (e.g., research question, drug, health condition, importance)
    - Generally how was it designed? (e.g., multi-site or single site, phase of trial, study population, intervention and control group, randomization, blinding, duration)
    - How was the trial funded? (e.g., industry, non-industry grant, unfunded)
  - c. Experience of the trial
    - How did this trial come about?
    - Could you talk about your role and responsibilities in this trial?
    - How would you describe the experience of conducting this trial? (design, recruitment, treating patients, collecting data, interactions with others, etc.)
    - What were some things that went well in this trial? What were some challenges in this trial? (e.g., recruitment, treatment, analysis, reporting)
    - Was the trial completed? If so, when did the trial conclude (i.e., year and month)? (Could I ask what the main findings were?) If not, could you describe the factors that led to stopping the trial?
  - d. Have the results of this trial been disseminated to the scientific community? If so, in what ways? (e.g., conference presentations, peer-reviewed publications, trial registry) Was the trial registered in clinicaltrials.gov or another registry?



- If the results have been reported in a registry or peer-reviewed journal: Could you talk about the events leading to the publication of the trial findings? (e.g., steps involved, any barriers or challenges) How long after trial completion were results reported?
  - If the results have not been reported in a registry or peer-reviewed journal (more than 1 year following completion of the trial): It is relatively common that results from a trial are not published. Could you talk about events leading to the trial findings not being reported in this particular case? (For example, in comparison to trials you have been involved with that were published, what differed in this trial?)
3. Experience in other clinical drug trials
- a. If the trial discussed above was not published
    - Was your experience in the trial you just described typical or different from other trials you have been involved with, particularly with respect to delays or challenges in reporting the trial results? Could you provide an example? (purpose, design, role, experience, recruitment, treatment, analysis, results, reporting, interactions with others)
  - b. If the trial discussed above was published
    - Could I ask whether you have participated as an investigator in trials for which the findings were not published in either a registry or peer-reviewed journal (1 or 2 years after trial completion)?
    - It is relatively common that results from a trial are not published. If we consider a trial you participated in that was not published, could you talk about events leading to the trial findings not being reported? (For example, in comparison to the trial you described above, what differed in this trial?)
    - Was your experience in the trial you just described typical or different from other trials you have been involved with, particularly with respect to delays or challenges in reporting the trial results? Could you provide an example?
  - c. In your experience as a trialist, have you encountered (or could you talk more about) barriers to reporting the trial's findings? If so, could you describe those? (e.g., difficulties with co-investigators, constraints in clinical trial agreements or informal influences from a sponsor)
  - d. Optional, time-permitting: Are you aware of instances in which colleagues have conducted trials and the results have not been reported? Could you describe an example? Could you talk about events leading to the results not being published? Are you aware of (or could you talk more about) barriers to reporting trial results that have been experienced by colleagues? (Could you give an example?)

- e. Possible follow-up questions, if applicable:
  - How was the decision made on whether to publish?
  - Was the sponsor able to influence the decision to publish? If so, how did this occur? (clinical trial agreement, control of data, funding dependency)
  - In your experience of multi-site trials, is a given site allowed access to data from other sites? Does this differ between industry and investigator-initiated trials?
  - Could you talk more about an investigator's incentive to publish positive vs. negative findings?
4. Addressing the issue of unpublished trials
  - a. In your view, how important is it to address the issue that many trials are not published, or not published within 1 or 2 years of trial completion?
    - Could you explain why you think that?
    - Do you feel there is a responsibility to the trial participant to ensure that trials are published?
  - b. What do you think would help ensure that trial results are published? (e.g., resources, policies, education)
    - For example, in the unpublished trials that you or your colleagues have participated in, can you think of something that might have helped ensure that a trial was reported?
    - Based on your experience, do you have any advice for clinical investigators for navigating challenges or barriers to reporting trial results?
  - c. Similarly, what role would you envision for others to help ensure that clinical trials are reported:
    - Research ethics boards?
    - Administrators at universities or other research institutions?
    - Health Canada?
  - d. As academic or career incentives may be related to delays in publication or whether results are reported, do you think anything could be done to change incentives?
5. Additional comments
  - a. Is there something we have not talked about that would help me to understand the experience of conducting a clinical trial?
  - b. Similarly, is there something we have not talked about that would contribute to understanding of the phenomenon of unpublished trials?

**Short-answer questions** (Based on background questions from survey by Rochon et al 2011.)<sup>3</sup>

6. Could you describe your primary appointment?
  - a. University or academic teaching hospital
  - b. Non-academic community-based hospital
  - c. Other (e.g., private practice, cancer centre, pharmaceutical)
7. How many years experience do you have in conducting clinical trials?
  - a. ≤5 years
  - b. >5 years
8. What types of funding have the trials you have conducted had?
  - a. Non-industry trials only
  - b. Industry trials only
  - c. Both industry and non-industry trials
9. What is the most senior role you have had in a clinical trial?
  - a. Principal investigator for the entire trial
  - b. Principal investigator for site
  - c. Other
10. Have you conducted the following types of trials?
  - a. Only single site trials
  - b. Only multiple site trials
  - c. Both single and multiple site trials

### C. Interview guide for research administrators

Clinical trials are important for developing new drugs and providing the best medical care. However, about 4 in every 10 clinical trials are not published or only published after a long delay.<sup>2</sup> In this study, I am interested in trying to better understand this phenomenon, in part by talking to trial investigators and research administrators about their experiences and views related to trials and trial reporting.

*What follows include questions for (1) administrators involved in oversight of clinical research, and (2) administrators involved with oversight, review or negotiation of clinical trial agreements or other agreements with industry sponsors. Questions specific primarily to one of these groups are denoted A1 or A2, respectively.*

1. Introductory questions
  - a. Could you describe your experience with
    - A1: Administration of research including clinical trials? (Do you also have experience conducting clinical trials? If so, could you describe your experience conducting clinical trials?)
    - A2: Review, drafting or negotiation of clinical trial agreements with industry funders?
  - b. What is your current role and responsibilities with respect to involvement in
    - A1: Administration of research including clinical trials?
    - A2: Clinical trial agreements (CTAs) with industry funders? What types of clinical trial agreements are you involved with? (e.g., CTAs for industry-sponsored trials, CTAs for investigator-initiated trials with industry funding)
2. Research institution policies on dissemination of trial research (A1)
  - a. In your view, does your research institution have a role in ensuring that the results of trials conducted at your institution or affiliated institutions are published? How do you see your institution's role in that?
  - b. Does your research institution have a policy to require trial registration? Does policy also require reporting of findings in a trial registry or in a peer-reviewed journal? If so, is reporting required to occur within a particular timeframe?
  - c. Does your research institution monitor the proportion of clinical trials conducted at your institution that are published in a timely way or do other monitoring of trial reporting?
  - d. Does your research institution have other types of policies to try to ensure that trials conducted at your institution or affiliated institutions are published?
  - e. Has your research institution considered introducing such policies or additional policies? Could you elaborate on the types of policies considered?
3. Clinical trial agreements (A2)
  - a. Review of agreements
    - Does your research institution require that clinical trial agreements between researchers and funders of clinical trials be reviewed by the institution? Are you aware of whether there are sometimes publication agreements with industry funders separate from clinical trial agreements? If so, would your institution also review the publication agreements?



- For university administrators: If an investigator affiliated with the university is involved in a clinical trial with industry funding, would the CTA typically be reviewed by your office? Are there cases where the CTA would only be reviewed by a hospital affiliated with the university?
- b. For CTAs for clinical trials of pharmaceutical drugs, who would the parties to the agreement typically be? For example, would the industry partner typically be a drug company or a contract research organization? (Are independent academic research organizations sometimes involved?)
- c. Does your research institution allow clauses in clinical trial agreements with industry relating to clinical trials in which:
  - The funder can decide on whether trial results are published? If so, how common would that be in CTAs for industry-sponsored trials (or in investigator-initiated trials that have industry funding?)
  - The funder can delay publication of trials results? If so, what types of delays are permitted in terms of duration and rationale? (e.g., delays of 6 months to seek patent protection for a drug)
- d. Ownership of data and access to data
  - Does your research institution allow clauses in clinical trial agreements with industry in which the funder would have ownership of the data? How common would it be for the industry funder to own the data in industry-sponsored clinical trials? Does this differ in investigator-initiated trials that have industry funding, as compared to industry-sponsored trials?
  - If so, in the context of a multi-site trial, how common would it be for the clinical trial agreement with industry to specify that investigators have access to data collected from all sites of the trial? Again, does this differ in investigator-initiated trials that have industry funding, as compared to industry-sponsored trials? In CTAs for multi-site trials, how is the issue of access to data from all sites by investigators typically addressed, if at all? (e.g., who has access, process for accessing data from all sites)
  - Are you aware of contracts which specify that an academic research organization would be part of the study organization in an industry-sponsored study and must have an identical copy of the study database? (to allow shared data access and validation of analyses conducted by the sponsor)
- e. Protection of the right to publish trial results
  - Do some clinical trial agreements require publication of trial results in a peer-reviewed journal or trial registry? (in investigator-initiated trials with industry funding, in industry-sponsored trials)
  - Does your institution require language to be included in clinical trial agreements with industry that would protect the investigator's right to publish clinical trial results? What type of language is required?
  - If language is required that would protect the investigator's right to publish: In the context of a multi-site trial, would the investigator's right to publish trial results apply only to data from the local site or would it include the right to publish results based on all of the data collected in the trial? Would this apply to industry trials or only investigator-initiated trials with industry funding?

- o Does your institution require language to be included in clinical trial agreements with industry to set out timelines for publication? If so, what would need to be specified?
  - f. Do you feel that clinical trial agreements (or other agreements such as publication agreements) between your research institution and industry provide sufficient protection of the right to publish clinical trial results? Or do you feel this could be strengthened?
  - g. Are you aware of difficulties or challenges in negotiating clinical trial agreements with industry? Could you describe some of the challenges?
  - h. Publication agreements. If publication agreements are reviewed, what issues are typically addressed in the publication agreement and how do these compare with CTAs?
  - i. Some investigators have expressed that industry funders can sometimes influence the decision to publish clinical trial findings. Do you have thoughts on how clinical trial agreements may help create the context for that to occur?
- 4. Experience or examples related to dissemination of research (A1)
  - a. It is relatively common that results from clinical trials are not published. Could I ask if you have become aware of cases of unpublished trials at your research institution during your time as an administrator? If so, could you describe an example?
  - b. In your view, how does the case you have described relate more generally to policies or practices at your research institution with respect to dissemination of trial research? Would you say the case you described reflects a pattern?
  - c. Are you aware of cases where investigators from your research institution have had difficulties with industry funders in relation to publishing of trial findings? Could you describe a case? Again, how would you relate this case to policies or practices at your research institution with respect to dissemination of trial research?
- 5. Academic or career incentives (A1)

Some trial investigators I have spoken to have expressed the view that there is a stronger incentive to publish trials with positive findings as compared to negative trials. For example, positive trials might be more likely to lead to additional grant funding, and there is a perception among some investigators that positive trials are easier to publish in prestigious journals, which could help their careers.

  - a. In your view, is it possible that trial investigators at your research institution have a stronger incentive to publish positive trials as compared to negative trials?
  - b. Do you think that it would be worthwhile to try to change incentives in a way which might encourage full reporting of trials? If so, how might this be done?

6. Addressing the issue of unpublished trials
  - a. A1: In your view, how important is it to address the issue that many trials are not published, or not published within 1 or 2 years of trial completion?
    - Could you explain why you think that?
    - Do you feel there is a responsibility to the trial participant to ensure that trials are published?
  - b. A1/A2: Are there policies or actions your research institution, or other research institutions, could take to better address the need for trial findings to be disseminated? Could you elaborate on those?
  - c. A1/A2: Are there policies or actions that could be taken by others to help ensure that clinical trials are reported, such as:
    - Research ethics boards?
    - Health Canada?
  - d. A1/A2: Are there policies at your research institution that it might be useful for me to review to understand issues relating to trial reporting and/or clinical trial agreements?

7. Additional comments (A1/A2)

Is there something we have not talked about that would contribute to understanding of policy issues regarding trial reporting?

**Short-answer questions (A1/A2)** (Based on background questions from survey by Rochon et al 2011.)<sup>3</sup>

8. Could you describe your primary appointment?
  - a. University or academic teaching hospital
  - b. Non-academic community-based hospital
  - c. Other (e.g., private practice, cancer centre, pharmaceutical)
9. How many years experience do you have either in administration at a research institution that conducts clinical trials?
  - a.  $\leq 5$  years
  - b.  $> 5$  years

#### D. Interview guide for clinical research ethics board members

Clinical trials are important for developing new drugs and providing the best medical care. However, about 4 in every 10 clinical trials are not published or only published after a long delay.<sup>2</sup> In this study, I am interested in trying to better understand this phenomenon, in part by talking to members of research ethics boards about experiences and relevant policies.

1. Introductory questions
  - a. Could I ask you how long you have been involved with ethics review of clinical trials?
  - b. Could you describe your current role in ethics review of clinical trials? Has your role changed over time, since you became involved?
  - c. Do you also have experience conducting clinical trials? If so, could you describe your experience conducting clinical trials?
2. Review of clinical trials and clinical trial reporting
  - a. Could I ask you to describe the typical process for review of a clinical trial, from your point of view as an REB member (for example, in relation to a clinical drug trial that has come before the REB)? (documents, key questions, discussion, time required)
  - b. Does the REB have a policy to require registration of clinical trials prior to enrolment of patients? If so, does the REB require that the trial be registered as a condition of ethics approval?
  - c. Does the REB require that trial results are reported in a trial registry or in a peer-reviewed journal? If so, is reporting required to occur within a particular timeframe?
  - d. Does the REB track whether each trial has been registered and whether results have been reported in a registry or peer-reviewed journal? If so, are you aware of whether the REB monitors the proportion of trials that have been registered and/or have reported results in registries or peer-reviewed journals?
  - e. Are the past practices of investigators in terms of clinical trial registration or reporting considered at the time of ethics review for a clinical trial?
3. Protocols, contracts and other agreements with funders
  - a. Responsibility for review
    - Does the REB review not only protocols but also contracts and other agreements between clinical trial investigators and funders?
    - Or is review of contracts and other agreements delegated to others at your research institution? If so, who has responsibility for reviewing these?
    - If responsibilities are divided, are the agreements reviewed for consistency periodically?
  - b. Does the REB/ your research institution allow clauses in protocols, or clinical trial agreements with industry funders, in which:
    - The funder can decide on whether trial results are published?
    - The funder would have ownership of the data and may not give permission to site investigators to access all of the data collected in the trial?



- The funder can delay publication of trials results? If so, what types of delays are permitted in terms of duration and rationale? (e.g., delays of 6 months to seek patent protection for a drug)
  - c. Protection of the right to publish trial results
    - Does the REB/ your research institution require language to be included in protocols or clinical trial agreements with industry that would protect the investigator's right to publish clinical trial results? What type of language is required?
    - If language is required that would protect the investigator's right to publish: In the context of a multi-site trial, would the investigator's right to publish trial results apply only to data from the local site or would it include the right to publish results based on all of the data collected in the trial? Would this apply to industry trials or only investigator-initiated trials with industry funding?
    - Does the REB/ your research institution require language to be included in protocols or clinical trial agreements with industry to set out timelines for publication? If so, what would need to be specified?
  - d. Do you feel that protocols, or clinical trial agreements between your research institution and industry, provide sufficient protection of the right to publish clinical trial results? Or do you feel this could be strengthened?
4. Experience related to dissemination of research
- a. It is relatively common that results from clinical trials are not published. Could I ask whether, in your experience as an REB member, you have become aware of clinical trials that have not been published? If so, could you describe an example?
  - b. In your view, how does the case you have described relate more generally to policies or practices at the REB/ your research institution with respect to dissemination of trial research? Would you say the case you described reflects a pattern?
  - c. Potential influence of industry funders
    - Are you aware of cases where investigators from your research institution have had difficulties with industry funders in relation to publishing of trial findings? Could you describe a case? Again, how would you relate this case to policies or practices at the REB/ your research institution with respect to dissemination of trial research?
    - In your experience in ethics review, have you seen protocols or clinical trial agreements for industry-funded trials that may constrain full reporting of clinical trial results? If so, could you describe an example? Could this still occur or would current policy or practices likely prevent this?
    - In your experience, have you observed other barriers to publications due to influence of industry funders? If so, could you describe an example? Could this still occur or would current policy or practices likely prevent this?
5. Addressing the issue of unpublished trials
- a. In your view, how important is it to address the issue that many trials are not published, or not published within 1 or 2 years of trial completion?
    - Could you explain why you think that?
    - Do you feel there is a responsibility to the trial participant to ensure that trials are published?

- Do you think this relates to informed consent or other aspects of research ethics?
- b. How do you view the role of REBs, if any, in addressing the issue of unpublished trials? Are there other policies or actions that could be taken on this issue? What barriers to such policies or actions exist, or what could facilitate these?
- c. Are there policies or actions that could be taken by others to help ensure that clinical trials are reported, such as:
  - Others at research institutions?
  - Health Canada?
- d. Is there something we have not talked about that would help contribute to understanding why many trials are not published or the role of the REB in addressing this?

**Short-answer questions**

How many years experience do you have as a member of an REB?

- a. 1 to 2 years
- b. 3 to 5 years
- c. >5 years

## E. References

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3. Rochon PA, Sekeres M, Hoey J, et al. Investigator experiences with financial conflicts of interest in clinical trials. *Trials* 2011;12(1) doi: 10.1186/1745-6215-12-9