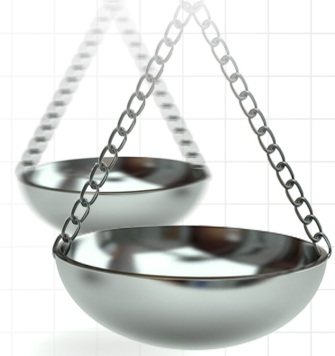
Research Article



Journal of Comparative Effectiveness Research

Physicians' perspectives regarding pragmatic clinical trials

Aim: Practicing physicians inevitably become involved in pragmatic clinical trials (PCTs), including comparative effectiveness research. We sought to identify physicians' perspectives related to PCTs. **Methods:** In-depth semistructured interviews with 20 physicians in the USA. **Results:** Although physicians are generally willing to participate in PCTs, their support is predicated on several factors including expected benefits, minimization of time and workflow burdens and physician engagement. Physicians communicated a desire to respect patients' rights and interests while maintaining a high level of care. **Conclusion:** Future work is needed to systematically assess the impact of PCTs on clinicians in meeting their ethical obligations to patients and the burdens clinicians are willing to accept in exchange for potential benefits.

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Considerable efforts are now being directed at conducting pragmatic clinical trials (PCTs), including comparative effectiveness research (CER), to inform medical practice [1,2]. In contrast to conventional research, these trials are typically "designed for the primary purpose of informing decision makers regarding the comparative balance of benefits, burdens and risks of a biomedical or behavioral health intervention at the individual or population level" [3]. In addition to CER, which typically compares two or more treatment options, PCTs can be used to evaluate interventions intended to improve clinicians' practice behaviors as well as medical center operations.

Much pragmatic research involves physicians either as direct subjects or as facilitators. In a physician education/support study, physicians may be the direct subjects of the research (e.g., a study in which individual physicians are randomly assigned to learn new techniques either online or in person) [4]. Medical center operations studies (e.g., the use of different electronic ordering procedures) might impact physicians' workflow or influence their decision making [5,6]. Alternatively, in a PCT comparing commonly prescribed interventions, patients may be the direct subjects [7].

While there is a growing body of literature regarding the ethical and regulatory challenges associated with fielding PCTs in the USA [3] and some empirical work examining patients' perspectives on pragmatic research conducted in usual care settings in the USA [8–10], comparatively little attention has focused on physicians' attitudes toward such research. A 2009 study found that while more than half of the physicians surveyed believed CER would improve clinical care, 65% thought it would restrict physicians' practices [11]. A later study reported that nearly half of primary care physicians surveyed were unfamiliar with CER, with 22% being moderately or very familiar. In that study, while over 70% of physicians agreed that CER could improve the quality of patient care, 36% believed that CER

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would restrict physicians' freedom to make treatment choices [12]. A more recent survey had similar findings: half of primary care physicians surveyed were not at all familiar with CER, although after they were given a definition of CER, 71% believed CER could improve the quality of patient care. However, 21% of respondents believed CER would restrict their freedom to choose treatment options [13]. Although these data suggest the need for broader dissemination of information about PCTs, there is also a need to more deeply understand what physicians believe (and why) about their involvement in PCTs, particularly in regard to their practices and ethical obligations to their patients.

Accordingly, the objective of this study was to conduct a qualitative exploration of physicians' views toward pragmatic clinical research. To do so, we conducted in-depth interviews with practicing general internists in inpatient and outpatient settings.

Methods

The Johns Hopkins Medicine and Duke University Health System Institutional Review Boards (IRBs) approved this study.

Interview guide design

A semi-structured interview guide was developed by the study team based on existing literature and the team's experience working on large-scale efforts being directed at PCTs, including the NIH Health Care Systems Research Collaboratory and PCORnet [1,2]. Nine pilot interviews were conducted between June and November 2014, after which the team met to discuss initial findings and revise the interview guide (Supplementary Materials).

The guide included hypothetical study scenarios representing three types of pragmatic research: CER, medical center operations and physician support interventions. The hypothetical studies, described in Table 1, consisted of an individually randomized drug comparison study, a cluster randomized study comparing sanitizing hand gels, and an individually randomized comparison of pop-up alerts to prevent adverse drug interactions. The scenarios were tailored to be relevant to general internists in two distinct practice settings: outpatient practices and hospitalists. To minimize respondent burden, each respondent discussed two of the three types of studies. The two scenarios and the order in which they were presented were systematically alternated across interviewees. In total, 14 physicians discussed the CER scenarios; 13 discussed the medical center operations (hand gel); and 13 discussed the physician support (pop-up alert) study (Table 1).

For each scenario, participants were asked a series of questions to ascertain their familiarity with the type of PCT depicted and their opinions about its implementation. Interviewees were asked about their perceptions of the hypothetical study's risks, burdens and benefits in comparison to clinical care and conventional clinical trials (e.g., a Phase III drug study); whether patient and/or physician notification or consent were believed to be ethical obligations or regulatory requirements; and their preferred methods for notification and consent. Interviewees were also prompted to discuss potential effects of the research on the clinician–patient relationships and physician workflow, as well as institutional expectations and strategies for engaging clinicians.

Recruitment & interviews

To capture views across a range of practice settings, recruitment targeted hospitalist and outpatient clinicians in four types of healthcare systems (integrated for-profit, integrated not-for-profit, nonintegrated for-profit and nonintegrated not-for-profit) [14]. We identified geographically diverse institutions in each of these four categories and recruited individuals using institutional physician directories.

Given difficulty in recruiting participants by direct mail and email we expanded our recruitment methods to include: in-person recruitment at professional society meetings (i.e., Society of General Internal Medicine and American College of Physicians); snowball recruitment (where an interviewee helps to identify additional interviewees); and follow-up contact via email, phone and fax. Interviewees received US$100 as compensation for their time.

In total, 20 telephone interviews were conducted between March and September 2015. Physicians provided oral consent to participate. Interviews lasted 45–60 min and were audio-recorded. The recordings were transcribed, stripped of personal identifiers and reviewed for accuracy by a study coordinator.

Analysis

Using a grounded theory approach, the interviewers and coders developed thematic codes based on the interview guide and initial interview transcripts [15,16]. Codes were iteratively revised and refined by the study team over the course of coding the initial interviews. Each transcript was independently coded by at least two team members who met to compare codes and resolve disagreements [17,18]. All transcripts were then entered into NVivo 10 software (QSR International Pty Ltd, Cambridge, MA, USA).

Coders tracked the appearance of new themes in sets of five interviews; four new themes were coded in the second set of interviews, one new theme in the third set, and no new themes in the final set [19]. Thus, it was

Table 1. Hypothetical study descriptions

Type	Practice setting	Description
CER (n = 14)	Outpatient (n = 9)	Individual patients are randomly assigned to receive one of two drugs commonly used to treat a urinary tract infection. The drugs being compared were described as safe and effective, US FDA-approved and routinely used. The hypothetical study sought to determine which drug was more effective at treating the condition
	Hospitalist (n = 5)	Individual patients are randomly assigned to receive one of two drugs commonly used to treat deep vein thrombosis. The drugs being compared were described as safe and effective, FDA-approved and routinely used. The hypothetical study sought to determine which drug was more effective at treating the condition
Medical center operations (n = 13)	Outpatient (n = 8)	Entire clinics are randomly assigned to use either a hand sanitizing gel with a moisturizing component or a sanitizing gel without a moisturizing component. In the hypothetical study, both gels are commonly used by institutions around the country and are being compared with determine if one is associated with lower infection rates
	Hospitalist (n = 5)	Entire hospitals are randomly assigned to use either a hand sanitizing gel with a moisturizing component or a sanitizing gel without a moisturizing component. In the hypothetical study, both gels are commonly used by institutions around the country and are being compared with determine if one is associated with lower infection rates
Physician education/support (n = 13)	Outpatient (n = 9) Hospitalist (n = 4)	Individual physicians are randomly assigned to receive or not receive a computerized pop-up alert designed to notify physicians of adverse drug interactions. The study compared the rate of adverse drug interactions between physicians in the two study arms[†]

[†]In initial interviews, many participants familiar with pop-up alerts voiced ethical objections to a study in which some physicians did not receive an alert. After nine interviews the scenario was revised to individually randomize physicians to receive a simple pop-up or a pop-up requiring documentation of the possible interaction in patients' medical records.
CER: Comparative effectiveness research.

determined that saturation had been reached after 20 interviews.

Results

Respondents' demographic characteristics are reported in Table 2. Major themes in the interviews included: familiarity with PCTs; research experience; physician preferences regarding notification and consent for PCTs; balancing concerns about study risks and burdens with study benefits; and physician engagement in research. We did not identify any substantial differences among respondents based on demographic characteristics or practice setting. Consequently, results are reported in aggregate, but attributions include information about gender and practice setting. A list of codes with representative quotes is provided in Supplementary Table 1.

Familiarity & research experience

The majority of physicians who discussed the CER (drug comparison) and operations (hand gel) studies (13/14 and 10/13, respectively) indicated that they were familiar with these types of PCTs, whereas approximately half (7/13) who discussed the physician support (pop-up alert) scenarios were accustomed to such interventions, but were not familiar with this type of physician-focused PCT. Only two interviewees had knowingly participated in PCTs either as subjects or investigators; about half (9/20) were not actively involved in research.

Notification & consent

As described below, physicians' views about the need to notify or obtain consent from physicians and patients differed according to the type of PCT being considered. Discussions about notification and consent focused predominately on patients for the CER scenarios, and on both patients and clinicians for the other two types of PCTs, for which interviewees more clearly identified physicians as study participants.

Comparative effectiveness research (drug comparison)

All respondents who discussed the CER scenarios (14/14) believed that patient consent was required. Many (10/14) highlighted the study's direct effects on patients as the predominant reason to obtain con-

Table 2. Participant characteristics.

Characteristic	n (%)
Gender:	
– Male	10 (50)
– Female	10 (50)
Specialty:	
– Outpatient	13 (65)
– Inpatient	7 (35)
Practice setting:	
– Integrated	12 (60)
– Non-integrated	8 (40)
– For profit	7 (35)
– Not for profit	13 (65)

sent. One physician explained: "…for a head-to-head drug trial of seemingly equivalent drugs, who directly or indirectly we think are equivalent, nevertheless has this looming sense that they might be different in substantive ways that are so sort of. because they are going to be delivered in the body of the patient, that there's something about the body that's important and respect-deserving, right?" (outpatient setting, male, integrated, not-for-profit).

For some (5/14), randomization triggered the need for consent because it is a departure from clinical care. Others (5/14) believed that any research involving patients requires consent; and some (7/14) assumed that PCTs are subject to the same regulatory requirements as traditional clinical trials. Half of the physicians thought consent should be obtained because of an ethical obligation to inform patients about the study and how it would affect their care.

One interviewee argued that consent might not be necessary as a regulatory matter but could be beneficial for institutionally focused reasons, stating, "I don't think the consent is sort of a necessary threshold element, unless it's part of some broader institutional need for kind of legitimacy and consistency and everything else ... not because of the research itself, but for some other political purpose" (outpatient setting, male, integrated, not-for-profit).

Medical center operations (hand gel)

Most (12/13) interviewees who discussed a medical center operation scenario thought that some type of notification was necessary, but because they viewed this type of study as extremely low risk, most (10/13) did not necessarily think that this needed to be accomplished by obtaining explicit consent. One explained, "… it has extremely low impact and low risk on one patient and it's never going to get done if you require consent from every patient for something so tiny" (hospitalist, female, non-integrated, for-profit). Physicians drew comparisons between the study and typical clinical practice when explaining why they thought consent was unnecessary – because patients and clinicians are typically unaware of specific products an institution uses, they would not need to give consent for a study comparing two commonly used, US FDA-approved products. Alternatively, a few (3/13) interviewees thought consent was a regulatory requirement or should be obtained to respect patients' preferences. One explained, "I think it's fair that the patients know they're being involved, giving them the option to decline ... some patients don't want to be involved in any type of study" (outpatient, male, integrated, not-for-profit).

However, even when explicit informed consent was viewed as largely unnecessary, most interviewees (11/13) thought that patients, physicians, and all staff at an institution should be notified about the study to promote transparency. A few pointed out that this could reflect well on institutions. One physician explained, "why not tell everyone? … I think that brings pride for the institution to know that people are like looking into this" (hospitalist, female, non-integrated, for-profit).

Physician support interventions (pop-up alert)

For the pop-up alert study, some (5/13) respondents thought that physician consent was needed and only one thought patient consent was needed. Those in favor of obtaining physician consent reasoned that because the study directly affects physicians and their workflow, they should be asked to give consent. One interviewee explained, "…if you're altering their (physicians') process, you're saying, 'I'm going to require that you do this extra step, or I'm not going to require that you do this extra step, I can't tell you ahead of time which group you're in,' and (we should) really ask people's permission before we do things like that" (outpatient, male, integrated, not-for-profit). Conversely, those who thought physician consent was unnecessary (5/8) did so because they believed the study would not significantly deviate from clinical care. Two interviewees held that participating in studies like this is an inherent aspect of medical practice for which physicians essentially give consent when they begin practicing. One participant observed, "there's some potential – what you might call harm to providers in terms of their efficiency and learning something new, but I think that falls within the professional duty of the job" (outpatient setting, female, integrated, not-for-profit).

The physician who was in favor of obtaining patient consent believed it was a regulatory requirement. Others (5/13) argued that consent from patients should not

be required because patients would be only indirectly affected and their clinical care would remain unchanged. Two drew comparisons between the study and typical clinical practice to argue against the need for additional consent. One interviewee said: "patients in the hospital are taking a lot of medications without giving consent. They usually give consent that they're going to get treatment. So you're basically ... not really giving them a new medication. So I don't think that would require consent. I don't think it would be considered unethical to do this study without a patient consent" (hospitalist, male, non-integrated, not-for-profit). In addition, one physician doubted the utility of obtaining consent, explaining, "well let's get to the point of it. Are patients somehow entitled to knowledge that their doctor was randomized? ... I don't know how much work consent does for us in that situation. I think they make us feel better, but I'm not sure how much sort of substantive work they're doing" (outpatient setting, male, integrated, not-for-profit). Another expressed a desire to be transparent but thought consent might make the study seem overly complicated and worry patients. One physician believed that patient consent for physician support studies would be necessary only in circumstances where a patient is usually required to give explicit written consent in their clinical care (e.g., for surgery).

Balancing concerns & potential benefits

Interviewees were generally supportive of pragmatic research on usual medical practices in terms of their willingness to participate in such a study, but some indicated that their support for it would depend on the balance between burdens to physicians and perceived benefits. In particular, most (12/14) were willing to participate in a comparative effectiveness scenario, but a few (three) of these physicians this willingness was predicated on it not being burdensome; most (11/13) were willing to participate in a physician support scenario; and most (11/13) were willing to participate in a medical center operations scenario.

Concerns about physician burdens

In the comparative effectiveness research scenarios in which there was a perceived need for notification or consent among all physicians, nearly all (12/14) expressed concerns about the burden of physicians having to do so. Two respondents anticipated physician opposition to devoting clinical time to discussing a research study for which they were not an investigator. One observed: "so if the researcher's not there and then the onus is on the clinician, I think that there's going to be some resistance to doing that, to having to do … I mean assuming that you're doing a consent, which I think you kind of need to in this scenario, I think it would be hard ... the clinic is really pretty tight, so I think it would really add more stress to have to consent someone in clinic for that" (outpatient setting, female, non-integrated, for profit, CER). Four not only believed that such a scenario would take time and impact work flow, but argued that it is simply not feasible for physicians to spend time discussing the study with patients and/or obtaining consent. Two believed that doing so would be sufficiently burdensome that the research should be conducted without obtaining consent or notifying patients.

In other cases (3/20), physicians assumed that other clinical staff or research staff would assist with research implementation to ease the burden on physicians: "they'd have to. hire someone that would be the one that would go in and explain it all. We as physicians would have. I mean we just don't get that luxury of having the time to sit there and explain what a research study is, let alone all the nuances..." (hospitalist, female, non-integrated, for-profit, CER).

The main burden most (8/13) physicians identified with the pop-up alert study was the risk of fatigue. Each pop-up would require only a few seconds of attention, but the cumulative effort of acknowledging new pop-ups, in addition to any existing pop-ups would be draining. By contrast, interviewees had relatively few concerns about the hand gel study, which they did not believe would affect physician workflow. In general, they viewed the study as an examination of institutional practice rather than a clinical concern for physicians.

Weighing potential benefits and burdens

While interviewees discussed a number of study-related burdens, these were not necessarily prohibitive barriers to the research. A slight majority (13/20) of interviewees said they would be willing to take on additional burdens given the anticipated benefits. For example, in discussing the pop-up alert study a respondent explained: "…every time we see an alert about a medication we just don't like it because we have to document something. It's going to take more time ... but overall, I think the potential benefit from it would make everybody willing to participate" (hospitalist, male, non-integrated, not-for-profit, pop-up).

In summary, nearly all interviewees said they would be willing to participate in each hypothetical study they discussed, or a similar type of study, with the conditions that they be clinically relevant and minimally affect workflow.

Physician engagement

Preferences regarding physician engagement (i.e., how, when, and why physicians might desire to be involved

in the design and implementation of particular PCTs) varied widely. Many (7/20) said they would not want to be involved in designing studies because of practical constraints (e.g., time), lack of research experience or lack of interest in study topics. In general, interviewees preferred to be notified about studies after they had been designed and just prior to implementation.

Those respondents who wished to be involved in the design process (8/20) were typically motivated by an interest in a particular topic or wanted to ensure that the study was clinically relevant, especially if it would directly affect their practice or patients: "I think it's all kind of about relevancy to what you do. So if it was something that was clearly relevant to the work that I did, or something that I was actively trying to improve or look at, I think it would be fun to be involved" (outpatient, female, integrated, not-for-profit).

One quarter of the interviewees (5/20) saw a need to include physician representatives in study design to incorporate clinical perspectives and appropriately manage the burdens of study implementation on physicians. Representatives could also help ensure that studies address important clinical concerns, leading to better buy-in among physicians. One interviewee explained, "so I think unless the researchers are involved in the actual day-to-day running of the … if they're not intimately familiar with the actual clinical process they may not get a good answer because people won't do it or they didn't ask the right question" (outpatient setting, male, integrated, not-for-profit).

Discussion

The physicians we interviewed articulated a wide range of opinions about pragmatic studies, whether these studies require notification or consent, and the roles they would want to play in their implementation. Accordingly, our data can help to inform the design and implementation of these types of studies and approaches for physician engagement in them, as well as suggest avenues for future research.

Our data document a broad spectrum of beliefs and preferences regarding notification and consent for pragmatic research studies that differ according to particular types of studies. In general, physicians generally thought patient consent was necessary for the comparative effectiveness scenarios and unnecessary for the operations (hand gel) scenarios, while voicing mixed opinions about the physician support (pop-up) scenario. However, these opinions varied within study types, perhaps reflecting unsettled beliefs regarding the need for and type of consent for PCTs in general [20]. Despite lack of consensus regarding consent requirements for various types of PCTs, physicians consistently expressed a strong desire to protect their patients' rights and interests. In assessing the need for patient consent or notification, the immediacy of study effects on patients was salient (i.e., the more immediate the effects, the greater perceived need for consent). In addition, the desire to give patients information about pragmatic research was driven by a belief that patients deserved to know or for the sake of transparency. These are important values that should be considered in determining the appropriateness of proposed approaches to notification and consent for particular pragmatic research studies.

While only a few (3/20) physicians discussed notification and consent in the context of particular clinical settings, those who did highlighted the importance of tailoring approaches based on the needs of specific clinical contexts or patient populations. For example, a patient visiting her primary care physician for a routine checkup might wish to have an in-depth discussion about study risks and benefits, whereas a severely ill hospitalized patient may be unable to have such a conversation. Even if consent were not strictly necessary from a regulatory perspective, in some circumstances (e.g., when vulnerable populations are involved), consent could serve the purpose of cultivating institutional trust or demonstrating respect. As some interviewees described, different approaches may be needed in different circumstances.

The need for physician notification and consent was especially salient to interviewees when the research was expected to most directly affect their workflow. The pop-up alert study in particular, which would affect clinicians' everyday practice, elicited a wide range of opinions in comparison to the other two studies, highlighting the importance of engaging clinicians during research design and implementation about research being conducted in their practices. After all, clinicians are important gatekeepers for such research efforts [21]. Engaging physicians in study design and implementation could help identify and minimize study burdens while also helping to ensure the clinical relevance of studies. Physicians appear inclined to support this type of research, but willingness to participate was generally contingent upon the study not imposing unreasonable burdens on clinical care.

Our data also reveal a diversity of physician opinions about PCTs, which will require further research to unpack. For instance, while interviewees expressed a wide range of opinions about the pop-up alert study, our small sample size and the exploratory nature of these interviews prevent us from drawing definitive conclusions as to why this is the case. Physicians may simply have varying preferences about when and how to inform stakeholders about physician support studies. In addition, further examination may reveal asso-

ciations between physicians' practice settings or patient populations and preferred approaches for notification and consent. Alternatively, as PCTs on clinician practices are a relatively new approach, many of the physicians we spoke with have not had the opportunity to participate in them or deliberate about the associated ethical and regulatory issues. Greater familiarity with PCTs on clinician practices may have led the physicians to express different or more developed attitudes towards notification and consent. Future studies should systematically assess the views of physicians who have participated in pragmatic research, ideally concurrent with such research efforts.

Our study had several potential limitations which should be considered when interpreting our findings. First, we spoke with a relatively small number of physicians who were difficult to recruit, which may limit the applicability of our findings beyond the sample studied. Nevertheless, the sample size was sufficient to reach thematic saturation. Second, the broad scope of our interviews did not always allow for detailed comparisons between study types. Third, physicians were responding to hypothetical study scenarios which may not have accurately reflected the true nature of a pragmatic study. However, hypothetical scenarios are well-suited within our qualitative approach to elicit attitudes and beliefs about such studies.

Despite these limitations, our findings suggest that PCTs on usual medical practices can best be carried out if physicians are properly engaged as stakeholders. In addition, while determining whether consent or notification is required for a particular research endeavor is a normative question, our data suggest the importance of considering how such mechanisms could be operationalized. This clearly includes consideration of what, if any, role physicians will be expected to play when they may not be otherwise meaningfully engaged in the research itself. Clinicians likely also have preferences regarding the methods by which they are notified of research studies and/or are asked to participate in them. For instance, it is unclear whether they prefer robust engagement; brief, streamlined communications; or something between such extremes. Having documented a range of important perspectives, future work should investigate physicians' opinions and preferences in a more generalizable sample across multiple variables (e.g., inpatient/outpatient setting, type of institution, among others). Additional research in these areas will enable us to better assess the tradeoffs physicians are willing to make to incorporate pragmatic research on usual medical practices into their everyday work and complement our approaches to ensuring appropriate ethical and regulatory oversight of PCTs, which are described in detail elsewhere [3]. Furthermore, such data will hopefully facilitate physicians' ability to meet their ethical obligations to both their current and future patients.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/full/10.2217/cer-2016-0024

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Disclaimer

The views presented here are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.

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Executive summary

- Physicians are inevitably involved in pragmatic clinical trials (PCTs), which can affect patient care so it is essential to understand their perspectives on such trials.
- Since little is known about physicians' perspectives on PCTs, we conducted interviews with US physicians.
- Physicians are generally supportive of PCTs, but this support is dependent on a variety of factors.
- In regard to PCTs, physicians consider factors such as the expected benefits of the research, minimization of time and workflow burdens, and physician engagement.
- Our data document a broad spectrum of beliefs and preferences regarding notification and consent for pragmatic research studies that differ according to particular types of studies.
- Physicians communicated a desire to respect patients' rights and interests while maintaining a high level of care.
- Future work is needed to systematically assess the impact of PCTs on clinicians in meeting their ethical obligations to patients and the burdens they are willing to accept in exchange for potential benefits.

are directly related to the work described in this manuscript. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

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Papers of special note have been highlighted as:
• of interest; •• of considerable interest

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•• **Provides background information on the context of pragmatic clinical trials, which is helpful in understanding the need for the data described in this manuscript.**

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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