

Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: www.elsevier.com/locate/conctc

Understanding practice-based research participation: The differing motivations of engaged vs. non-engaged clinicians in pragmatic clinical trials

Donna A. Messner^{a,*}, Rachael Moloney^a, Amy H. Warriner^b, Nicole C. Wright^c, Phillip J. Foster^d, Kenneth G. Saag^d^a Center for Medical Technology Policy, Baltimore, MD, USA^b Division of Endocrinology, Diabetes and Metabolism, University of Alabama at Birmingham, USA^c Department of Epidemiology, University of Alabama at Birmingham, USA^d Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, USA

ARTICLE INFO

Article history:

Received 3 June 2016

Received in revised form

15 August 2016

Accepted 22 August 2016

Available online 23 August 2016

Keywords:

Pragmatic clinical trials

Practice-based research

Clinician engagement

Learning health care system

ABSTRACT

Background/Aims: Pragmatic clinical trials (PCTs) represent an increasingly used strategy for “real-world” trials. Successful PCTs typically require participation of community-based practices. However, community clinicians often have limited interest or experience in clinical research. Many barriers to practice-based research have been described, but possible motivations to participate among community practices not active in research have not been well explored. The tendency is for researchers to assume similar motivations and priorities across all candidate practices. This is not necessarily the case. A better understanding of the range of reasons clinicians might see for participating in pragmatic trials could be key to promoting this type of practice-based research.

Methods: Semi-structured interviews were conducted with 30 clinicians and staff members. Half of the interviewees had experience doing practice-based clinical trials and half did not. Individuals in these two groups were also diversified in terms of their practice size and location. Participants were asked about motivations and barriers to doing practice-based research in the context of a planned osteoporosis pragmatic clinical trial. Interviews were transcribed, coded, and analyzed.

Results: Barriers identified for both experienced and not-experienced clinicians and staff members included: a lack of time, increased paperwork, disruption to work flows, and concern over practice finances. Similar findings have been reported in the US, UK, Europe, and Australia. However, regarding positive motivations of practices to participate, we found systematic differences in attitude between research-engaged and research-naïve practices that have not been previously reported. The research-experienced group offered a greater number and variety of reasons to take part than the not-experienced group. While both groups expressed motivations related to patient care, clinicians and staff members experienced in practice-based clinical trials were much more likely to cite intellectual, professional, and societal benefits not envisioned by the other group.

Conclusions: We conclude that clinicians not already participating in practice-based trials may have a narrower range of motivations than those already participating. The lack of a broader view of possible benefits to participation may also translate into more obdurate recruiting challenges. These results point to the need for recruitment, engagement, and messaging approaches differentially tailored to the needs and interests of non-participating practices.

© 2016 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Traditional randomized controlled trials (RCTs) often lack generalizability to routine care settings and fail to account for heterogeneity in patient characteristics and preferences. [1–4] One

* Corresponding author. Center for Medical Technology Policy, World Trade Center Baltimore, 401 East Pratt Street, Suite 631, Baltimore, MD 21202, USA.

E-mail address: donna.messner@cmtpnnet.org (D.A. Messner).

strategy to enhance trial relevance is to use pragmatic clinical trials (PCTs) [1,5,6]. PCTs are large RCTs designed to admit variations more representative of real-life conditions of care than traditional “explanatory” RCTs in which patient population characteristics, care setting, care administration, and follow-up are tightly controlled [7–9]. To capture variations across broad populations and care settings, PCTs should ideally be conducted across a range of practice settings, including community-based practices not typically involved in RCTs.

PCTs have increasingly gained purchase. Programs such as the NIH Collaboratory (a pilot program to conduct PCTs through a network of health systems) [10] and the Agency for Healthcare Research and Quality’s Practice-based Research Networks (PBRNs) [11] have helped to establish the infrastructure and best practices needed for successful community-based trials. Nevertheless, important challenges remain. Broad-based participation by many practices not routinely engaged in research is required for a robust clinical research enterprise capable of exploring less common conditions or adverse events across varied community settings. Yet 85% of physicians who participate in clinical trials do not repeat the experience [2], pointing to a significant disconnect between the expectations of novice clinician-researchers and the current reality of doing trials.

Further, many practicing clinicians have little interest in research. While many barriers to involvement have been described in the literature, the possible motivations to participate among those not currently active in PCTs have not been well explored. The tendency is for researchers to assume similar motivations for prospective practices to participate. This is not necessarily the case. A better understanding of the range of reasons clinicians might see for participating in pragmatic trials could be key to promoting this type of practice-based research.

Below we describe a set of interviews in which we asked physicians and staff members in community practices about barriers to participating in PCTs and reasons to do so. We found notable differences, especially in the motivations to participate in PCTs, between those who already participate and those who do not. These results may provide insight into how PCTs can be better planned, communicated, and implemented for enhanced relevance to, and recruitment of, community-based practices.

2. Methodology

A total of 30 semi-structured interviews were conducted with 24 physicians and 6 staff members. The interview guide was designed to inform the development of an iPad-based informed consent tool in a planned osteoporosis PCT. If successful, the project would address a key barrier to doing community-based PCTs—work flow disruption associated with informed consent—to make practice-based PCTs more practicable. To understand the relative importance of this one barrier to clinicians and staff (both those already participating in practice-based trials and those who are not), the interview guide included questions on the barriers to, and chief reasons to participate in, clinical trials that use their practices as sites for recruiting, implementation, and data collection (“practice-based trials”).

Interviewees were recruited through email listservs of the Alabama Practice Based Research Network (APBRN) and the American Academy of Family Physicians (AAFP). Participating physicians received \$100 and staff members received \$50 as honorarium for the 30- to 60- minute interview. Not-experienced prospective interviewees proved resistant to recruitment. After multiple failed email appeals, we ultimately identified and recruited not-experienced physicians by having network directors specifically reach out to colleagues in the network known to lack practice-based trial experience.

The initial recruitment target was 12 experienced and 12 non-experienced practice members for a total of 24. Among each subgroup of 12, 6 would ideally be rurally located while another 6 would operate in suburban or urban settings. Differing practice sizes were also desired across these subgroups. Since we were soliciting volunteers through a listserv and recruitment was relatively slow, we would not have been able to select specifically for practice size or other characteristics without significantly increasing the size and duration of the investigation. For the purposes of the project, this was deemed unnecessary. However, experienced practice members were initially oversampled in an effort to encounter volunteers who were non-experienced (before network directors were asked to assist with recruitment). This resulted in 30 total interviewees of the composition shown in Table 1. A first set of 9 interviews were accomplished to pilot test the interview guide and assure that all key topics of interest were being covered. Then the remainder of the interviews were completed.

We defined “experienced” clinicians and staff as those who, at a minimum, had participated in patient recruitment and consent procedures for clinical trials (whether of pragmatic or explanatory design). Those having only quality improvement research experience or experience with observational studies were considered to be “not-experienced” for the purposes of this study.

Experience status, practice size, and location were determined through self-identification by key informants. Initial identification of experience status for screening purposes was accomplished through self-identification in an electronic response form. The first 9 (pilot) interviewees were purposively sampled (i.e., specifically selected for interviews [12]) consistent with the criteria used for the larger group, with practice size and location confirmed through online research.

Interviews were recorded, transcribed, and coded for analysis. Development and refinement of codes was accomplished through collaborative team-based coding (using two coders) and facilitated by NVivo software [13].

3. Results

3.1. Challenges to participating in clinical trials

For our interviewees, chief among the concerns regarding practice-based PCTs was a possible strain on practice resources. Half of all interviewees (15, 8 of whom had clinical research experience as defined above) indicated that finding time for clinical

Table 1
Characteristics of Interviewees and their practices.

Characteristic	% of informants (N = 30)
Interviewee Characteristics	
Male	53%
Female	47%
Clinician	70%
Staff Member	30%
Has experience with clinical trials	53%
Has no experience with clinical trials	47%
Practice Characteristics Associated with Each Interviewee	
<i>Practice Location</i>	
Urban	37%
Suburban	33%
Rural	30%
<i>Practice size</i>	
Solo (1 attending physician)	20%
Has 2 to 4 attending physicians	37%
Has 5 to 7 attending physicians	37%
Has more than 7 attending physicians	7%

trial procedures between the daily routines of clinical practice was (or was anticipated to be) challenging. Many informants indicated that they lacked staff or wished they could hire additional staff to cover the extra duties for clinical trials. Six out of the 7 interviewees who specifically cited inadequate staffing were not experienced with clinical research. Five of these informants said that they would want the sponsor to help with trial coordination, either through sharing a “roaming research coordinator” with other trial sites, or providing resources to hire a part-time coordinator.

Resource-related subthemes included: concern that clinical trial procedures were disruptive to work flow (3 informants, 2 experienced); possible backlogs in the waiting room (2 informants); and insufficient office space for recruitment and consent (4 informants); and paperwork burdens (7 informants, 4 experienced).

Finances were a concern for 11 informants (6 experienced); of these, 8 expressed concern that compensation received for doing clinical trials is insufficient to cover the additional workload incurred. Another 3 informants said doing clinical trials depletes revenue because research activities deprive them of time they could spend with the routine patients who account for the bulk of their compensation.

Despite these financial concerns, some informants saw trial-based money-making opportunities as ethically suspect, particularly industry-sponsored trials. Although many PCTs are not industry-funded, industry does sometimes recruit community practices for trials. One interviewee asked, “Will patients feel like we’re just using them to earn financially?”. For this physician, the answer was doing studies “that benefit the practice, patients, and staff in some way other than financially.” Four other physicians also voiced a wish to guard against “commercial bias”.

Another ethical concern was conflict-of-interest, as noted by 6 interviewees (4 having clinical trial experience). Two informants were concerned about coercion of patients to participate in studies; 1 said research “interferes” with patient care. One rural non-experienced clinician said, “I wonder if it hurts my credibility, in the long run, trying to sell them or trying to offer them to be part of a study.” The theme of conflicting clinician/researcher roles was articulated most forcefully by an experienced physician in an urban practice setting. He previously participated in drug and other intervention trials but discontinued involvement because the message of the clinical trial recruiter, he said, “is not consistent with why I want to see them in my office. It’s not consistent with better diabetic control, better hypertension control. They’re an entirely different message.”

Practitioner disinterest was a frequent theme in these conversations. A third of all interviewees indicated that the interest level of colleagues or staff was insufficient or required special incentives. Although 2 physicians said that clinical trials provided an opportunity for the staff’s professional growth, 4 indicated that their staff would only see it as an extra burden. “Their needs are more emergent,” said one clinician, noting that pay incentives could be helpful. Another clinician said selecting topics relevant to care was key to motivating his staff. “... for the postpartum study, the nurses jumped right in because it looked like they were really helping people, and it was part of care.”

Research relevance, while important to many, was sometimes insufficient to overcome barriers. Three experienced clinicians indicated that they participated in studies their colleagues ignored. For one non-participating clinician, research was “always just too much time and effort with a busy practice.” This interviewee, who was a rural family practice physician, added that the state university’s medical school was enlisting rural physicians for clinical trials. He saw this outreach as intrusive and assumed the motivation for trials to be primarily financial. “I know it brings money into the college that wouldn’t exist otherwise, so that seems to be the primary carrot.”

Four out of the 9 physicians without experience in clinical trials noted that they would need support and buy-in from others to participate in clinical trials; colleagues, administrators, “corporate hierarchy”, department chiefs, and practice leadership were all noted as individuals or entities in need of convincing. The concerns were both financial (“my partners [are] strictly looking at the bottom line”) and organizational (“bringing everyone together to see how ... we can modify our schedules”). One informant added that he needed assistance understanding how to get started, and to educate administrators on what would be required and why it was worth doing: “... good help, good education can definitely help us incorporate this into our practice.”

3.2. Motivations for participating in clinical trials

The most common motives to participate in practice-based trials cited by our interviewees revolved around patient-centered or humanitarian goals. Eight informants indicated that they hoped to provide direct benefits to the patients through trials and 8 said that they wanted to create knowledge that was specifically relevant for patient care. Other benefits to patients included free access to care, early access to new therapies, finding solutions to difficult health problems, and getting patients more involved in their own care. Seven interviewees saw conducting clinical trials as a public good because it created knowledge “for the betterment of society” and the community.

Professional development—the opportunity to learn something new, provide educational opportunities for staff, students, residents, and interns—was cited as a motivation by 6 informants. Others said clinical studies “keep things interesting” and provide an opportunity to be “a part of something bigger than your day-to-day thing.” Three interviewees also indicated that they believed clinical trial participation would reflect positively on their practices, providing a competitive edge. It would “show the patients we’re on more of a cutting edge.”

Six informants said that the business model would have to work to accommodate clinical trials. For 3 of these interviewees, financial gain was a motivator: “... it’s financially rewarding if you do it right and do enough of it.”

Notably, most of the physicians who talked about benefits beyond patient care or finances were already participating in clinical trials. While direct benefits to patients were important for this group, they were also motivated by creating knowledge for society or community (6 of 7), or intellectual stimulation (7 of 7), or professional development (5 of 6). By contrast, physicians not already participating in trials were less likely to cite these—or any—positive motivations for participation. There were 45 mentions of positive reasons to participate in research from the experienced group vs. only 16 mentions by non-experienced participants (Table 2). When interviewees who lacked clinical trial experience did cite reasons to participate, they tended to focus on direct patient benefits rather than on intellectual or societal benefits.

4. Discussion

Consistent with our findings, studies of physician participation in research in the US, UK, Europe, and Australia identified lack of time and unwillingness to take on additional work as primary barriers. Clinicians say they are overworked or have too much paperwork [14–21], have limited staff support [20], and need “protected time” to conduct research [22]. Physicians often said that clinical research will create extra expenses or labor hours in need of compensation [14,16,20,22,23]. They noted their lack of research training [16]

Table 2

Reasons to participate in pragmatic clinical trials as offered by experienced vs. non-experienced clinicians and staff members.

Reasons cited	Experienced (15 informants)	Not-experienced (15 informants)
Benefits oriented to patient care		
Offer free medicine/care	2	0
Offer care they need anyway as part of study	2	1
Affords more care time with patients who want it	1	0
Early access to new treatments	3	0
Create knowledge for patient care	6	3
Solutions to difficult patient problems	2	1
Real-world patients in clinical trials	1	2
Get patients involved in own care	2	2
Quality improvement	0	1
Benefits not oriented to patient care		
Gain competitive edge in practice	4	1
Financial benefits	4	2
Intellectual stimulation in practice	7	1
Knowledge for benefit of society or community	6	1
Professional development	5	1
Total reasons cited	45	16

and said the research question must be relevant to clinical practice [24].

The literature also reflects a concern for some clinicians that research is incompatible with patient care, either due to a perceived conflict in goals [25,26], fear of undermining the doctor-patient relationship [25], or a sense that the doctor's "primary allegiance is to the individual patient, with less inclination to participate in RCTs when there is uncertainty about the best treatment" [27]. These concerns pose a barrier not only to practice-based trials, but more generally to creation of a "learning healthcare system" in which systematic learning during patient-clinician encounters would be routine [28–30].

In response to the barriers noted above, the literature offers strategies for mitigation, e.g., assuring relevance to clinical practice, regular feedback to clinicians by study leaders, minimizing impact on usual clinical care, and compensating clinicians who participate in research [14,24]. However, our study suggests that it may not be enough to identify the barriers to practice-based research and design strategies to mitigate them. Little effort has been made to see if positive motivations for research participation differ in any systematic way between clinicians already engaged and those who are not. Our research suggests they do.

This was a small qualitative study not designed to explore these attitudes in depth. As noted in the methods section, systematic sampling for specific subgroup characteristics was not done. So, for example, the study was not designed to assess quantitatively whether non-experienced practice clinicians and staff were systematically different in some other way (e.g., age, specialty, or training) between the two groups. Nevertheless, the observed difference between experienced and non-experienced practices appears to persist across a range of practice settings and sizes. If this result holds true more generally, it would suggest that the communication and recruiting strategies needed to attract participants to community-based research differ according to the target audience. Unlike the idealistic colleagues who believe (as one experienced interviewee said) "you just have to make it work" because it is worthwhile, non-participating practices may need a more compelling argument for direct benefit to patients—not only future patients who benefit from knowledge generated, but current patients who can benefit from enhanced access to care, better quality of care, more interest in their own care, or other factors.

In addition, more effective engagement strategies are likely

needed. As noted above, in this study not-experienced physicians ignored repeated recruitment appeals through PBRN listservs. Personal appeals from network directors were ultimately required to recruit these interviewees, and most of them sat for interviews as personal favors. Participants such as these are not looking for research opportunities. It will take more targeted efforts to contact such practices and achieve meaningful communication on planned research endeavors. Engaging non-experienced clinicians early in design and throughout the research process may help to assure practice-based studies are meaningful to these prospective participants [31,32]. It may also help to create strategies for communicating with these clinician-stakeholders not only in recruiting, but throughout research and dissemination of results.

Notably, informants often made no distinction between pragmatic and explanatory trial designs in their responses. While this can be seen as a limitation of the study, it also provides insight into another potentially important aspect of clinician engagement: education on how a specific proposed clinical trial may differ from clinicians' preconceptions of what a "typical" clinical trial entails.

5. Conclusions

For an expanding assortment of large, well-designed PCTs to be done, the numbers of participating practices must grow. We conclude that clinicians not already participating in practice-based trials may have a narrower range of motivations than those already participating. The lack of a broader view of possible benefits to participation may translate into more obdurate recruiting challenges. These results point to the need for recruitment, engagement, and messaging approaches differentially tailored to the needs and interests of non-participating practices. Even with these measures, many practices will choose not to participate. However, as noted earlier, open and transparent engagement can serve to bolster the confidence of non-participating practices in the legitimacy and relevance to patients of the proposed research.

Funding

This research was funded by Agency for Healthcare Research and Quality (AHRQ) grant U19 HS21110.

Declaration of conflicting interests

The Authors declare that there is no conflict of interest.

References

- [1] S.R. Tunis, D.B. Stryer, C.M. Clancy, Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy, *JAMA* 290 (12) (2003) 1624–1632.
- [2] R.A. English, Y. Lebovitz, R.B. Giffin, Institute of medicine (U.S.), National academies press (U.S.), in: *Transforming Clinical Research in the United States: Challenges and Opportunities: Workshop Summary*, National Academies Press, Washington, D.C., 2010.
- [3] J.H. Ware, M.B. Hamel, Pragmatic trials — guides to better patient care? *N. Engl. J. Med.* 364 (18) (2011) 1685–1687.
- [4] R.M. Califf, Characteristics of clinical trials registered in, 2007–2010, *JAMA* 307 (17) (2012) 1838.
- [5] B.R. Luce, Rethinking randomized clinical trials for comparative effectiveness research: the need for transformational change, *Ann. Intern. Med.* 151 (3) (2009) 206.
- [6] M. Helfand, S. Tunis, E.P. Whitlock, et al., A CTSA agenda to advance methods for comparative effectiveness research, *Clin. Transl. Sci.* 4 (3) (2011) 188–198.
- [7] K.E. Thorpe, M. Zwarenstein, A.D. Oxman, et al., A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers, *Can. Med. Assoc. J.* 180 (10) (2009) E47–E57.
- [8] K. Loudon, M. Zwarenstein, F. Sullivan, P. Donnan, S. Treweek, Making clinical trials more relevant: improving and validating the PRECIS tool for matching trial design decisions to trial purpose, *Trials* 14 (1) (2013) 115.

- [9] K. Loudon, S. Treweek, F. Sullivan, P. Donnan, K.E. Thorpe, M. Zwarenstein, The PRECIS-2 tool: designing trials that are fit for purpose, *BMJ* 350 (2015) h2147.
- [10] NIH Collaboratory. <https://www.nihcollaboratory.org/Pages/default.aspx>. Accessed December 28, 2015.
- [11] Home | Practice-Based Research Networks | Agency for Healthcare Research and Quality. <https://www.pbrn.ahrq.gov/>. Accessed December 28, 2015.
- [12] A. Bryman, *Social Research Methods*, fourth ed., Oxford University Press, Oxford; New York, 2012.
- [13] G. Guest, K.M. MacQueen (Eds.), *Handbook for Team-based Qualitative Research*, Altamira, Lanham, 2008, pp. 418–423.
- [14] L.L. Albers, K.D. Sedler, Clinician perspectives on participation in research, *J. Midwifery Womens Health* 49 (1) (2004) 47–50.
- [15] S. Asch, S.E. Connor, E.G. Hamilton, S.A. Fox, Problems in recruiting community-based physicians for health services research, *J. Gen. Intern Med.* 15 (8) (2000) 591–599.
- [16] S.M. Jowett, J. Macleod, S. Wilson, F.D. Hobbs, Research in primary care: extent of involvement and perceived determinants among practitioners from one English region, *Br. J. Gen. Pract. J. R. Coll. Gen. Pract.* 50 (454) (2000) 387–389.
- [17] A. Jones, T.A. Burgess, E.A. Farmer, et al., Building research capacity. An exploratory model of GPs' training needs and barriers to research involvement, *Aust. Fam. Physician* 32 (11) (2003) 957–960.
- [18] S. McIntosh, D.J. Ossip-Klein, L. Hazel-Fernandez, J. Spada, P.W. McDonald, J.D. Klein, Recruitment of physician offices for an office-based adolescent smoking cessation study, *Nicotine Tob. Res. Off. J. Soc. Res. Nicotine Tob.* 7 (3) (2005) 405–412.
- [19] S. Ross, A. Grant, C. Counsell, W. Gillespie, I. Russell, R. Prescott, Barriers to participation in randomised controlled trials: a systematic review, *J. Clin. Epidemiol.* 52 (12) (1999) 1143–1156.
- [20] K. Ried, E.A. Farmer, K.M. Weston, Bursaries, writing grants and fellowships: a strategy to develop research capacity in primary health care, *BMC Fam. Pract.* 8 (1) (2007) 19.
- [21] T. Rosemann, J. Szecsenyi, General practitioners' attitudes towards research in primary care: qualitative results of a cross sectional study, *BMC Fam. Pract.* 5 (1) (2004) 31.
- [22] G. Robinson, M. Gould, What are the attitudes of general practitioners towards research? *Br. J. Gen. Pract. J. R. Coll. Gen. Pract.* 50 (454) (2000) 390–392.
- [23] D.A. Askew, A.M. Clavarino, P.P. Glasziou, C.B. Del Mar, General practice research: attitudes and involvement of Queensland general practitioners, *Med. J. Aust.* 177 (2) (2002) 74–77.
- [24] D.A. van der Windt, B.W. Koes, M. van Aarst, M.A. Heemskerk, L.M. Bouter, Practical aspects of conducting a pragmatic randomised trial in primary care: patient recruitment and outcome assessment, *Br. J. Gen. Pract. J. R. Coll. Gen. Pract.* 50 (454) (2000) 371–374.
- [25] V. Mason, A. Shaw, N. Wiles, et al., GPs' experiences of primary care mental health research: a qualitative study of the barriers to recruitment, *Fam. Pract.* 24 (5) (2007) 518–525.
- [26] E. Hummers-Pradier, C. Scheidt-Nave, H. Martin, S. Heinemann, M.M. Kochen, W. Himmel, Simply no time? Barriers to GPs' participation in primary health care research, *Fam. Pract.* 25 (2) (2008) 105–112.
- [27] P.H.Y. Caldwell, J.C. Craig, P.N. Butow, Barriers to Australian physicians' and paediatricians' involvement in randomised controlled trials, *Med. J. Aust.* 182 (2) (2005) 59–65.
- [28] N.E. Kass, R.R. Faden, S.N. Goodman, P. Pronovost, S. Tunis, T.L. Beauchamp, The research-treatment distinction: a problematic approach for determining which activities should have ethical oversight, *Hastings Cent. Rep.* 43 (s1) (2013) S4–S15.
- [29] R.R. Faden, N.E. Kass, S.N. Goodman, P. Pronovost, S. Tunis, T.L. Beauchamp, An ethics framework for a learning health care system: a departure from traditional research ethics and clinical ethics, *Hastings Cent. Rep.* 43 (s1) (2013) S16–S27.
- [30] R.M. Califf, G.L. Filerman, R.K. Murray, Appendix D, Discussion paper: the clinical trials enterprise in the United States: a call for disruptive innovation, in: *Envisioning a Transformed Clinical Trials Enterprise in the United States: Establishing an Agenda for 2020: Workshop Summary*, National Academies Press, Washington, DC, 2012. <http://www.ncbi.nlm.nih.gov/books/NBK114657/>.
- [31] K.E. Johnson, C. Tachibana, G.D. Coronado, et al., A guide to research partnerships for pragmatic clinical trials, *BMJ* 349 (dec01 7) (2014) g6826–g6826.
- [32] R. Moloney, E. Tambor, S.R. Tunis, Patient and clinician support for the learning healthcare system: recommendations for enhancing value, *J. Comp. Eff. Res* 5 (2) (2016) 123–128.