Author's response to reviews

Title: Bridging the Gap between Basic Science and Clinical Practice: A Role for Community Clinicians

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Author's response to reviews: see over
July 20, 2010

Gregory Aarons, MD
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Re: Response to Reviewers for 3 Linked Manuscripts:
1. Kahn, et. al., Bridging the Gap between Basic Science and Clinical Practice: A Role for Community Clinicians (MS ID: 8993275072034627)
2. Beckett, et. al., Bridging the Gap between Basic Science and Clinical Practice: The Role of Organizations in Addressing Clinician Barriers (MS ID: 3357063182034652)
3. Ryan, et. al., Reengineering the Clinical Research Enterprise to Involve More Community Clinicians (MS ID: 6016189052034664)

Dear Dr. Aarons:

I. OVERVIEW OF RESPONSE TO THE EDITOR

I.1. Overall Comment from Editor
Thank you for the recent revisions on your manuscript and the other two manuscripts in this series. I have carefully read each of the revised manuscripts and responses to editor and reviewer recommendations. The manuscripts are improved, however there are some issue to be addressed prior to sending them out for re-review.

Thank you for sending this additional note. I am very appreciative of your interest in these three manuscripts we have submitted. We are eager for Implementation Science to publish the three linked manuscripts under review. As you know, there have been extenuating circumstances related to my team completing reviews. I believe all of the queries made to the research team are now addressed. However, I would like to arrange a phone call so that we can be sure any outstanding issues are promptly addressed.

Attached please find our responses to the helpful comments you have made. Each of these comments has been addressed in a revised manuscript. This document services as the cover letter including a point-by-point response to the concerns listed. Within this cover letter, I highlight the Editors’ comments in bold, the Authors’ responses in not bold text, and text extracted from the revised manuscript in italics.
1.2. Overview from Editor

The resubmissions are responsive to reviewer concerns. However, there was an additional correspondence to you dated August 19, 2008 with detailed editor comments that appear not to have been addressed in this set of revisions for the three manuscripts. That correspondence referred to the manuscript in which Gery Ryan was the lead author because I believed that that was to be the first in the series. However, your response (August 19, 2008) stated that the manuscript for which you are the first author was to be first, Beckett second, and Ryan third. Thus, a highly detailed methods section should be provided in the first (Kahn, et al) manuscript so that the Beckett and Ryan papers can refer to that manuscript with information about the particular sample characteristics for each paper.

I appreciate your calling this detailed set of comments to my attention. I did not recognize from the August 19, 2008 correspondence the level of detail you hoped to see as documented in a subsequent correspondence. I believe I now understand what you are requesting. The pages that follow in this text document the authors understanding of changes you are recommending for the manuscripts and document our responses. I believe all of the comments you have made are now addressed.

To further set the stage for linking the three manuscripts, we have newly introduced this sixth (next-to-last) paragraph in the Introduction Section of the manuscript. Within the Methods and Results section that follows, we then provide additional details regarding methods and response rates.

As a component of the NIH Roadmap, consideration was given to the development of a sustained cadre of large numbers of practicing clinicians who could participate in clinical research in the context of their community practice. We were funded by NIH to help develop a conceptual framework as a model for a system that would allow a large number of clinicians to participate in clinical research while they care for patients in their office settings. To assist NIH in the development of a conceptual framework as a model for this new type of infrastructure for translating research into practice and back, we conducted a classic formative evaluation. We have edited the second sentence of the last paragraph of the Introduction Section.

This manuscript addresses the challenges that must be addressed to motivate community clinicians to commit to a sustained engagement in research in the settings in which they deliver clinical care. As part of the effort supported by the NIH Roadmap, we conducted a study to identify the feasibility of a new national cadre of practicing clinicians who could participate in clinical research in the context of their community practices by focusing on barriers to research participation and strategies to overcome them. This paper describes the barriers reported by community clinicians and proposes potential strategies for avoiding them.

Within the fifth paragraph of the Introduction, we have also updated website references and specifically updated the number of CTSA awards that have been funded to date.
I.3. Comments across the three manuscripts
This is also consistent with reviewer comments. However, some of the recommendations below also apply to the other two manuscripts. Thus as you are lead author on the series, I am requesting that you ask the other manuscript lead authors (Beckett, Ryan) to also revise according to the recommendations below.

This has been done.

We are asking for the detailed methods section, however, in only the lead manuscript.

This is described in Section II below.

The most pressing concern for the two follow-up manuscripts is separating results from discussion (i.e., speculation about the meaning of qualitative results should appear in the discussion sections).

This is described in Section III below.

I.4. Concluding Notes
We appreciate the work of your team on these important manuscripts and look forward to your further revisions. I provide additional detail on revision of the methods and results sections below. Please revise according to these comments and resubmit the manuscripts.

Once again, I want to extend the appreciation of our authorship team towards Implementation Science for extending the deadline for this series of manuscripts. The NIH project which supported this effort was extremely ambitious. The NIH Roadmap and its far reaching recommendations are now beginning to be realized throughout many sectors of the research and clinical communities. The conceptual framework and feasibility studies associated with the concept that NIH could support clinical research within a stable cohort of community clinical practices has touched CTSA, clinical trials networks and the nature of NIH funding streams. We appreciate your consideration of this set of papers documenting one important component of this work.

After so many years of work on the project and on the manuscripts, and a nasty illness, it’s great to be back and help to launch these papers. Hopefully, their dissemination will inform others and stimulate debates that ultimately will improve the implementation of our nation’s science. In this way, we hope population health will be improved.

II. EDITS TO METHODS AND RESULTS SECTION OF MANUSCRIPT 1 (Kahn, et al)

II.1. “Methods Section”. The description of the research methods lacks detail in almost all areas
We agree the methods section was somewhat terse. It was initially designed to be brief to limit word count. In response to your request for a more developed description of the research methods, substantial additional information has now been added to the “Methods Section”.

Since the number of completed interviews, the response rate, and the description of the interview participants are “results”, we have included substantially more information on that topic in the “Results” section. Below is a listing of edits to the manuscript that we have made in response to your very useful queries.

We revised the overview (first) paragraph within the “Methods section”.

Overview. We used an iterative process to focus the content of interviews to best assess the perspective of clinicians and other key stakeholders regarding the feasibility of ongoing research participation by community clinicians in their own practice settings. We began with an environmental scan of academic and trade journals, the internet, and public- and private sector reports of clinical and community-engaged research. The results of this review were used to develop semi-structured interview protocols that varied somewhat according to the interviewees’ experience with clinical research. The protocols served as a general guide with example probes rather than as a set of specific questions to be asked of every respondent.

We interviewed key informants who could provide information about the realities of clinical research and clinical practice in terms of opportunities, costs, and liabilities based upon informant’s clinical, research, and/or administrative and leadership experiences. From September 2004 through August 2005, the evaluation team conducted key informant interviews of clinicians and other stakeholders to assess the feasibility of implementing research in the context of ongoing community practices. Clinicians included physicians, dentists, and nurse practitioners. Other stakeholders were defined as individuals who led or coordinated research operations associated with clinical research or clinical practice networks, and representatives of organizations that recruit, train, or support community clinician involvement in clinical trials and/or clinical research networks. Using a two-phase process, we initially developed a preliminary list of candidate organizations and individuals who could potentially provide information about the feasibility of adapting health care delivery systems and clinical practice to support clinical research in community practices. After review of candidate bios, publications, and references pertinent to their clinical, published, or administrative (leadership), for Phase I interviewers, we identified a set of candidate informants to provide information about the feasibility of the program. For Phase II interviews, we then conducted interviews relevant to the feasibility of a program of community-based clinical research overall and within specific urban and rural settings across all regions of the United States.

II.2. Methods Section. For example, the participant sample is not well described

Within the Methods Section, we have revised text within the two subheadings shown below to provide more detail. First we describe “Participant Interview Methods” section (renamed from “Stakeholder Interview Methods”), then the “Identification of Participants and Data Sources” section, and then the “Interview Protocol Development and Use” sections. Within the latter section, we indicated that
examples of major topics addressed in various protocols are shown in Appendix 1 below. We rename the subsection “Stakeholder Interview Methods” to “Participant Interview Methods”.

**Participant Interview Methods.** The initial approach to obtaining stakeholder input began with a focus on four key groups of stakeholders whose representatives we expected could provide unique information regarding the incentives, disincentives, and barriers to clinician enrollment of their patients in clinical research. The four key groups include:

1. Individuals (community clinicians, study leaders, and study coordinators) who already participate in clinical research networks
2. Community clinicians in whose office clinical research could potentially take place, though they have no prior history of participating in research
3. Professionals directing clinical research networks involving research in community practices that could serve as prototypes for research in community settings
4. Representatives of professional societies, pharmaceutical companies, clinical research organizations, and other organizations that have recruited and trained community healthcare providers for clinical trials and clinical research networks and/or have key information regarding clinical research networks.

Our expectation was that these representatives could provide unique information regarding the incentives, disincentives, and barriers to clinicians’ enrollment of their patients in clinical research. We considered each representative to be a key stakeholder whose input into and support of various facets of a clinical research program within community would contribute to its success.

**Identification of Participants and Data Sources.** We sought not only to identify a reasonable number of informants in each major category (e.g., providers) and subcategories (e.g., primary-care–based research networks) but also to ensure that the sample was diverse with respect to geography, informant demographics, knowledge, and experience base. We also focused on those informants who could provide data on specific costs of conducting clinical research.

We used key contacts supplemented by “snowball” sampling in which we asked each informant to identify additional individuals we should interview from selected categories. This snowballing was an iterative process in which new leads from interviews and continuing feedback from the NIH project officer continually expanded the number and types of informants identified. At the same time, our targeting of specific individuals to interview was informed by emerging themes and issues for which we believed additional interviews with representatives from a given stakeholder group would be helpful.

**Interview Protocol Development and Use.** We developed interview protocols to learn informants’ views about the feasibility of various design strategies for supporting research in clinical practice in community settings. Interview protocols served as a general guide with example probes rather than as a set of specific questions that was asked of every respondent. Examples of major topics addressed in various protocols are shown in Appendix Table 1.
Appendix 1: Major Topics Addressed in Interview Protocols for Interview Phases 1 and 2

<table>
<thead>
<tr>
<th>Phase 1</th>
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<td>Methods of clinician recruitment</td>
<td>Incentives and disincentives for clinician participation</td>
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<td>Motivations for clinician participation</td>
<td>Options for clinician participation</td>
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<td>Methods for clinician retention</td>
<td>Organizational barriers to clinician participation</td>
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<tr>
<td>Strategies for clinician retention</td>
<td>Advantages and limitations of different types of research networks/organizations</td>
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<td>Potential role of emerging information systems</td>
<td>Addressing privacy, HIPAA* and institutional review board issues</td>
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<td>Specific recommendations to NIH on practice design to support research within community practices</td>
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<td>Phase 2</td>
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<td>Testing reactions to proposed research models within community practices</td>
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<td>Issues related to partnering</td>
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<td>Infrastructure organizations to complement clinician organizations to support clinical research within practices</td>
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<td>Optimal configuration for different types of research studies</td>
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<td>Governance, oversight, and quality control for research conducted within clinical practice</td>
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<td>Ethical and professional issues</td>
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<td>Political and liability issues</td>
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<td>Costs associated with conducting various types of clinical research studies</td>
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<tr>
<td>* HIPAA: Health Insurance Portability and Accountability Act</td>
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II.3. There is no information about response rates (i.e., how many potential respondents were contacted and how many agreed to participate and how many declined and why)

Although related to methods, we conceptualize the number of participants and response rates as Results. Thus, we have added a new section, “Interview Participants” at the beginning of the Results section as documented below (Subsection “Interview Participants”).

Interview Participants. Between September 2004 and September 2005, a total of 243 informants representing affiliations from a broad collection of settings that varied with respect to practice type, size, ownership, and access to technologies such as electronic medical records and web-based research tools, were interviewed. Interview participants were diverse by advanced degree (MD 70%, PhD 10%, DDS 6%, MD PhD 4%, RN Nurse Practitioner 3%, Master’s degree 3%, and unknown 3%). Thirty percent of participants were female. Participants came from 35 different states.

Between September 2004 and September 2005, a total of 243 informants representing affiliations from a broad collection of settings that varied with respect to practice type, size, ownership, and access to technologies such as electronic medical records and web-based research tools, were interviewed.
For Phase I interviews, we identified 106 potential informants and attempted interviews with 97. Amongst those attempted, we completed 73 (response rate 73/97=75%). Of those not interviewed, six declined to participate, one was unavailable, and 17 did not respond. Appendix 2 shows the different categories of informants and the number of each type interviewed during Phase I. In many cases, respondents could be placed in more than one category but for the purposes of this report we list only their primary role.

For Phase 2 interviews, we identified 237 potential informants and attempted interviews with 204. Amongst those attempted, we completed 170 (response rate 170/204=83%) including interviews with 112 active clinicians. Fifteen informants participated in more than one interview. Of those who invited to participate, 16 of 33 community providers referred to the research team by a PBRN contact specifically for interview, declined because of their busy schedules. Additionally, four other invited participants were unavailable, and 19 did not respond. Appendix 3 shows the different categories of informants and the number of each type interviewed during Phase II.

Across both phase I and Phase II interviews, there were many cases in which respondents could be placed in more than one participant category. However, we categorize respondents only according to their primary role. For example, in addition to the 44 Phase II providers listed below, 10 more clinicians with active practices were interviewed but are categorized as PBRN leaders, rather than clinicians. Several Academic Medical Center leaders (> 8) also maintain active clinical practices.

Furthermore, we have added Appendices 1 and 2 as suggested by the editor to provide additional information about the interview participants by Interview Phase.

II.4. The terms “clinicians and stakeholders” from “five key stakeholder groups” provides very little information about the respondents

Within the first paragraph of the methods section (sentences 2 and 3), we have specified what we mean by the terms “clinicians” and “other stakeholders”.

Clinicians included physicians, dentists, and nurse practitioners. Other stakeholders were defined as individuals who led or coordinator research operations associated with clinical research or clinical practice networks, and representatives of organizations that recruit, train, or support community clinician involvement in clinical trials and/or clinical research networks.

II.5. Additional details about respondents should be included

The distribution of respondents by degree are listed in the first paragraph of results.

Amongst those invited to participate, the participation rate was quite high. This likely related to the endorsement of NIH who supported this effort. The one exception to this is among PBRN (Primary Care Based Research Network) physicians. This information is presented within the first subsection of “Results”.
Of those who invited to participate, 16 of 33 community providers referred to the research team by a PBRN contact specifically for interview, declined because of their busy schedules.

Appendices 2 and 3 present additional information about the respondents.

II.6 Consent Process
The manuscript states that an oral consent process was discussed. Does this mean that a waiver of written consent was obtained? Please be explicit about the consent process and IRB approval.

Within the “Methods” Section, within the Subsection “Interview Data Collection Process” (paragraph 1), we have expanded the text to more fully document our consent process.

Interview Data Collection Process. All informants prior to being interviewed were sent descriptive materials about the NIH Roadmap initiative and the proposed concept of NIH possibly launching a program to support the conduct of research within community clinical practice, the purpose of the interviews, and a consent protocol. The RAND IRB reviewed these materials and procedures prior to the start of the interviews. The one-page consent protocol that had been mailed to informants in advance of the interviews, was orally read verbatim to interviewees at the beginning of the interview phone call. Informants were asked to agree to participate prior to participating in the body of the interview.

II.7 Interview Guides
In order to facilitate reader understanding of your interview approach, please provide your interview guide as an appendix.

As described in the Methods section (para 1), we used a two-phase process for the interview processes.

We initially developed a preliminary list of candidate organizations and individuals who could potentially provide information about the feasibility of adapting health care delivery systems and clinical practice to support clinical research in community practices. After review of candidate bios, publications, and references pertinent to their clinical, published, or administrative (leadership), for Phase I interviewers, we identified a set of candidate informants to provide information about the feasibility of the program. For Phase II interviews, we then conducted interviews relevant to the feasibility of a program of community-based clinical research overall and within specific urban and rural settings across all regions of the United States.

We used a separate interview guide for Phase I and Phase 2 as described in the text. Phases I and II interview guides have respectively been added as Appendices 4 and 5.

II.8 Please provide a detailed description of your data collection process
Were all interviews recorded? If so how were recordings transcribed? If interviews were not recorded, state why and how field notes were taken and utilized in the analysis process. Were transcriptions checked for accuracy?
Within the “Analysis of Interview Data” subsection of the “Methods Section” (paragraph 2), text reads as follows.

One or more of the investigators on the project conducted each interview, each with an advanced academic degree associated with interview training. In all, seven team members led and/or participated in the interviews. All interviews were audiotaped and transcribed into text. Transcriptions were read and checked for accuracy by the primary interviewer.

II.9. Please provide a detailed description of your data analysis approach and process

We have rewritten this section to provide additional detail in the last section of the “Results”.

Analysis of Interview Data.

All interview transcripts were entered into a text management software program (Atlas/ti). Two or more investigators reviewed all transcripts within two weeks of the interview to identify key themes. Each reviewer compiled an independent list of initial themes. These were then reviewed by the research team (including all interviewers) and a consensus was reached as to which themes to examine more fully. A codebook was then developed and applied to all the transcripts. In this exploratory phase, it was most important to check to ensure that the main themes were endorsed by our informants. To this end, we check with almost one-quarter of the Phase I informants during a follow-up interview where we confirmed that our selected themes were indeed salient to our informants.22 This attention to detail resulted in a key issues content change between the early and the late interviews which is specified in Table 2.

The interview findings and the literature review informed the development of a model for a program to recruit and train a stable group of community clinicians for participation in research. Based on these findings, we proposed a set of tactics and strategies to address the barriers which the community clinicians identified and further refined the model.

III. EDITS TO RESULTS SECTION OF ALL THREE MANUSCRIPTS

III.1. There is much speculation that appears to come from the authors rather than interviewees in the results section that would be better placed in the discussion section. Please separate results from discussion and include appropriate quotes from your interviews to support the results

III.1. Manuscript 1 (Kahn, et al)
Within the Results section of the Kahn manuscript, the section titled, “Interview Themes”, is organized around three key factors that impede physician participation in community-based research. Within each of these three sections, there is a subsection describing important themes that emerged from analysis of interviews.

We have incorporated one quote for each of the three sections they categorize the key factors that impede physician participation in community-based research.
To clearly separate results from discussion, we have included a Commentary section within the discussion of each theme. For example, for the theme, Addressing Community Practice Concerns, we divide the text between the clinician reported themes, and the commentary. We follow this pattern across the reporting of all of the themes.

Addressing Community Practice Concerns. Clinicians as a group repeatedly expressed the belief that without acknowledgement of their potential contribution (via non-fiscal or fiscal recognition), they have little stake in clinical research and will not contribute in a sustained manner. When clinicians believe their voices are heard and responded to, they have more of a stake in clinical research and are more willing to respond to the inevitable challenges that arise.

Commentary: Some of the mechanisms that were suggested by respondents to engage clinicians included: reframing research questions and study designs to increase meaning for community clinicians; attending to the complexities of the relationships between community and academics, which can become magnified in research studies; and addressing clinician and patient distrust of research.


This manuscript edited the Methods Section including addition of two new paragraphs at the end of Methods.

A previous article described the barriers we identified for clinician participation in research within the context of their own community practices and proposed a number of innovations to remove them (6). In the Results section of this article, we expand upon concerns reported by clinicians when deciding whether or not to incorporate clinical research into the context of their community practices. We organize this discussion around a model selected and adapted by the research team to account for decision-making about participation in clinical research as reported by clinicians themselves. (13) Recognizing the importance of partnerships and infrastructure in supporting complex activities such as sustained research activities within the context of ongoing clinical practice, we then present strategies that healthcare organizations can use to address clinician concerns. These strategies should increase the likelihood that clinicians will choose in a sustained way, to incorporate into their practices research that could inform clinical questions, methods, analyses, and clinical recommendations built upon their own patients and others like them.

These strategies are derived from the research team’s synthesis of clinician self-reports, literature review, and internal discussions. Where relevant, we apply potential strategies to specific barriers or issues identified through clinician self-report interviews.

III.3. Manuscript 3 (Ryan, et al)

This Manuscript draws heavily on what we learned about the problems community clinicians face in participating in research (Manuscript 1) and what might be done to engage more community clinicians in research at the practice level (Manuscript 2). The focus of this manuscript, however, shifts to a much larger scale and addresses how we might engage a large cadre of community clinicians (i.e., 40,000 – 80,000) over time at a national level. we clearly recognized that a national system must address the same issues described at the practice level, including: research design, protocol development, recruitment of clinicians, general and study-specific training, on-going support, quality assurance, clinician feedback, and use of study results (all covered in Manuscripts 1 and 2).
The challenge we faced was how to conceptualize and design a national system of researchers of this scope and magnitude when there are no examples to study. We treated this part of our research as a formative evaluation problem. As we note in our methods section on Page 4 (Manuscript 3, Ryan et al):

As a methodological approach, formative analysis consists of an iterative and goal-directed research process by which investigators: (a) identify key issues and potential solutions through interviews, observations of panel discussions and literature reviews; (b) engage in lengthy and ongoing team discussions to prioritize issues, articulate advantages and disadvantages of each type of solutions, and develop multifaceted and integrated responses; (c) use key stakeholders as sounding boards to test and adjust the proposed system of responses as necessary; and (d) repeat as necessary. It is important to note that this process relies on a combination of both empirical evidence (i.e., steps a and c) and the experience and problem-solving ability of team members.

We have also tried to be clear that the purpose of this formative analysis is not to come to a conclusion on what is the “best” model, but rather helps focus the discussion on key issues that will need to be addressed. As we note right before our result section:

Below we present an outline for a national system to engage and support large numbers of community clinicians in clinical research. In presenting this model, we have been careful to describe what we believe are key components and elements that should be included in any large-scale system of this type. In no way should this outline be considered a final model. Instead we see this as a starting point for a larger discussion on how we might think about re-engineering the research enterprise.

If you have any questions, please call me at (310) 794-2287 or email me at kahn@rand.org.

Sincerely,

Katherine L. Kahn
Senior Natural Scientist