ADAPTABLE Supplement Roundtable Meeting:
Integrating Patient-Reported Health Data and
Electronic Health Record Data for Pragmatic Health Research

Summary of the Meeting Held September 14, 2017 at the NIH National Center for
Complementary and Integrative Health

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Executive Summary:
Researchers today face an abundance of riches when it comes to available data, but they also face a dilemma of determining which sources are correct, which are incorrect, and when the truth might lie somewhere in between different sources. For example, a researcher analyzing data on heart attacks may find that while electronic health records may show a certain number of myocardial infarctions, survey data sources from patients do not reflect the same number of events. Which source is correct?

A shift at the national level toward putting patients at the center of healthcare research and care delivery means that people are collecting and contributing their own data through a variety of sources. This shift presents both a challenge and an opportunity for researchers to harness the power of patient reported data to improve research and ultimately, healthcare. This is an especially important opportunity for pragmatic studies and trials which are designed to reflect "real-world" medical care by recruiting broad populations of patients, embedding questions into the usual healthcare setting, and leveraging data from health systems to produce results that can be readily used to improve patient care.

Recognizing this challenge, the Office of the Assistant Secretary for Planning and Evaluation (ASPE) at the U.S. Department of Health and Human Services (HHS) provided the National Institutes of Health (NIH) Collaboratory Coordinating Center with funding to convene an expert roundtable discussion to explore ideas and recommendations for best practices, key challenges, information gaps, and future research needs for promoting best practices in the use of patient-reported health (PRH) data in pragmatic studies.

This roundtable exercise emerged from the challenges faced by ADAPTABLE (Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-Term Effectiveness), a three-year pragmatic clinical trial comparing the effectiveness of two different daily doses of aspirin widely used to prevent heart attacks and strokes in individuals living with heart disease.

Eighteen experts from eight institutions attended the roundtable. Experts came from a wide variety of backgrounds including biostatistics, epidemiology, oncology, nursing, psychiatry, health policy, and regulation, bringing a diverse set of ideas and experiences to bear on the problem.

The discussions were grounded in the recognition that clinicians must defer to patients as the "unique and privileged reporters" for certain data variables such as fatigue and pain. However, for the purposes of this roundtable, participants were asked to consider sources of data in which patients are not privileged and unique reporters, but rather can supplement, contradict or agree with the different sources of the same information (for example, how often has a patient been hospitalized?) The "true" answer to a question could come from the electronic health record, or a physician's note, or from a patient's recollection. Participants agreed that many sources are feasible and none has the clear privilege of "truth." It is important to look for corroborations among variables that lead toward the "totality of evidence."

All agreed that finding ways to generate PRH data and analyze it alongside electronic health records, claims data, and other sources holds the potential to help researchers greatly enhance healthcare research.

Roundtable attendees broke into discussion groups where they focused on two primary unanswered questions:

1. What are the best practices for capturing PRH data in pragmatic studies?

2. Once captured, what are the optimal analytic approaches for integrating this information with other data collected as part of a study, including data from the EHR?

Attendees agreed that white paper publications are the aim of the roundtable exercise. Papers will need to be structured around the multiple scenarios that might occur to give readers guidance on questions to consider depending on the purpose of their research. When debating how to "boil the ocean" and what exactly to focus on, participants agreed that answering these questions within the context of pragmatic trials is a good place to start.

In short, the group agreed that there is no single or easy answer, but rather a wide-ranging literature that could be applied against specific circumstances. What is absent and often urgently needed is a set of recommendations that can help researchers better understand the sets of circumstances and considerations that could guide when and how to gather and integrate PRH data with other data sources. This roundtable was intended to serve as a springboard toward advancing the literature through resulting white papers.

Meeting Background:

Electronic health record (EHR) data are not always complete with respect to a patient's medical history, clinical events, or treatment. Patient-reported health (PRH) information (and in some cases caregiver-reported health information) may augment capture of these data points in the setting of pragmatic studies, but key questions remain about the fitness-for-use of such data in research. Discussions at the ADAPTABLE Supplement Roundtable focused on the capture of PRH data and EHR derived data and how PRH data can be integrated with other data sources to improve the conduct of pragmatic health research. The roundtable discussion was expected to produce at least one jointly authored white paper publication on available resources for best practices, key challenges, information gaps, and future research needs for promoting best practices in the use of PRH data in pragmatic studies. Participants identified two papers they would like to write.

For the purposes of this meeting summary, the term "PRH data" includes patient- or caregiver-reported health information that may also exist in the EHR, including hospitalizations, co-morbid conditions, and medications, but does not include subjective patient-reported outcomes such as symptoms, functional status, or fatigue.

The full agenda and background literature is available in Appendix A.

Roundtable Objectives:

Roundtable attendees were charged with discussing two unanswered questions:

1. What are the best practices for capturing PRH data in pragmatic studies?

2. Once captured, what are the optimal analytic approaches for integrating this information with other data collected as part of a study, including data from the EHR?

Roundtable attendees broke into two workgroups focused on main expected components of the white paper deliverable, with one workgroup member assigned to lead the discussion of each component.

Introduction & Discussion

Wendy Weber, Branch Chief for research at the National Center for Complementary and Integrative Health (NCCIH) and program officer for the coordinating center of the NIH Collaboratory, welcomed attendees and informed the group that the NIH Collaboratory Coordinating Center received supplementary funding from the Office of the Assistant Secretary for Planning and Evaluation (ASPE) at the U.S. Department of Health and Human Services (HHS) (which is responsible for the Patient Centered Outcomes Reporting (PCOR) Trust Fund) to convene the roundtable and production of the resulting white papers. Dr. Josie Briggs, Director of NCCIH, then told the group how important this roundtable will be in changing the landscape

of clinical research, saying that as a physician, she needs layers of good quality evidence. While the ways of generating evidence used currently are "OK," they do not fully give clinicians the information they need to make evidence-based decisions. This roundtable, which explores the critical and often untapped use of PRH information, is intended to further the body of knowledge that moves evidence generation forward.

Attendees then introduced themselves and expressed their own interests in this topic (see Appendix B for full affiliations and biographical details.)

Emily O'Brien thanked the group for convening and for suggesting background readings to ground the day's discussions and the future papers. She offered an update on supplement work that is funding the roundtable. Many of the attendees are actively working on the topics of the roundtable and are already familiar with the problem: PHR information (and in some cases caregiver reported health information) may augment capture of theme data points in the setting of pragmatic studies. Key questions remain about the fitness for use (quality) of such data in research. EHR data are not always complete with respect to a patients' medical history clinical events or treatment, Dr. O'Brien said, adding that Dr. Rockhold, when asked to participate in this group, said that the idea that EHR data is incomplete is the "understatement of the decade." Dr. O'Brien said that she did not expect the group to solve the entire problem in one day but that the publications resulting from the discussions will be a good contribution to the literature.

Despite increasing use of PRH data in pragmatic research, fitness for use has not been that well defined, particularly in the setting of contemporary pragmatic clinical trials. In planning, how best to use the time of the roundtable attendees, meeting organizers arrived at two main goals of the meeting which also inform the division of the two breakout groups:

1) Discuss how to capture PRH data and EHR-derived data and think how existing best practices that work well from efforts such as survey research could be applied to produce the most valid and robust source of information for the conduct of pragmatic trials.
2) Once the data is available, what do we do with it? This data can be especially useful for patient reported information such as fatigue, depression, or functional status, but particularly in instances where elements might exist both in a patient reported data source as well as in an EHR source or claims data source, how do we integrate sources and analyze those sources, particularly in instances where there maybe conflicting information or missing information from one of the sources? This involves thinking about the back-end analytic piece of this problem and how we can apply best practices once all those data are captured.

Dr. O'Brien said that in thinking about PRH data and looking at the landscape of existing literature, one topic that frequently comes up is "Conventional Patient Reported Outcomes" – that is, subjective information that is not typically in the EHR, such as fatigue, sexual function, and functional status. These types of information are not typically interpreted by a clinician but

are increasingly important as we think of the risks and benefits of therapies and outcomes. The focus of this group, however, is intended to be on the sorts of patient reported data that might also exist in EHRs or claims data (such as hospitalized events, medications, comorbidities) and that is thought of as verifiable information that may or not be present given the limitations of both data sources. The hope is that both sources of data could inform one another. For the purposes of the roundtable discussions, it is important to distinguish between patient reported outcomes and patient reported health information that could supplement less than perfect clinical data sources. We want to make distinctions between outcomes, and our focus, which is information that can supplement less than perfect data sources, she said.

Dr. O'Brien offered a working definition for consideration:

"PRH data includes patient or caregiver reported information that may also exist in the EHR, including hospitalizations, comorbid conditions and medications a but does not include subjective patient reported outcomes such symptoms, functional status or fatigue.
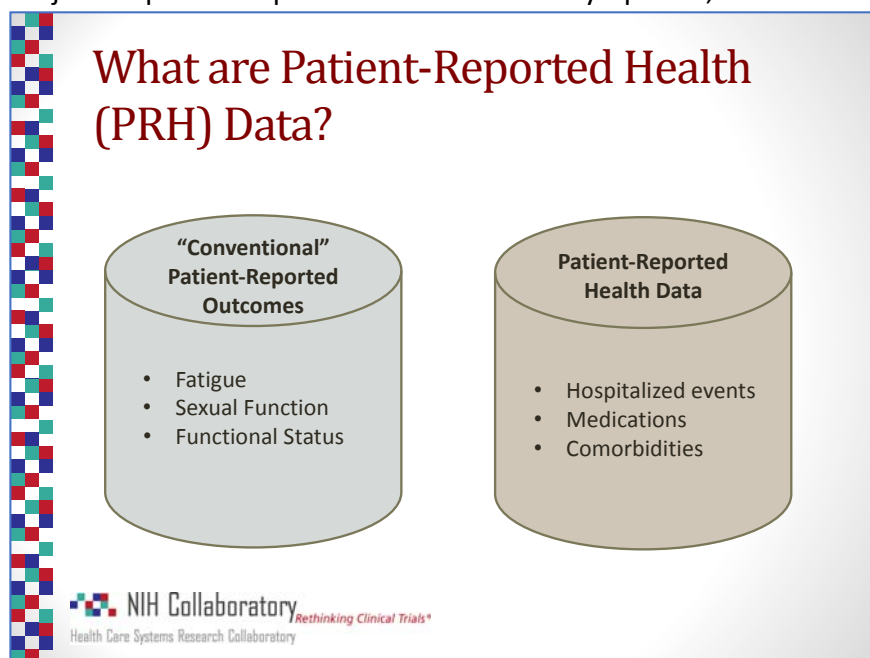
Participants at the roundtable debated this framing and asked a number of clarifying questions:

- One participant asked if data from wearable devices is included in the discussion. Dr. O'Brien said that the focus of the roundtable has been grounded in the structure and design of the ADAPTABLE Trial in which patients are reporting information on their medications and hospitalizations.

- Another question was posed about the distinction between patient-reported and caregiver-reported information and it was noted that, from a regulatory perspective, this was an important consideration. The group was asked to consider adding caregiver

data to multiple sources of data rather than grouping it in with patient reported data. Talking about both sources is crucial, but they should be separate. For example, adolescents may be taking medications of which parents may be unaware.

- One attendee asked why not include quality of life data into these discussions which may already be included in the EMR. Dr. Weinfurt answered by saying that what gave rise to the framing for this roundtable was the recognition that there are variables of data for which patients are "unique and privileged reporters" of information and clinicians cannot answer this information, for example, fatigue or pain. For the purposes of this roundtable, participants are being asked to consider the sources of data in which patients are not privileged and unique reporters, but rather can supplement, contradict or agree with the different sources of the same information, for example, how often a patient has been hospitalized. Dr. Briggs said that when the supplement for this roundtable was written, the idea behind it was partly that medication data reported by patients might be a more accurate reflection of what they were actually taking than medication data in the EHR. The question of verifiability is an important variable but it won't always be possible to make a completely bright line in our discussions.

- A clinician pointed out that "medical history" might make more sense to talk about as that is specific to events and comorbidities. "Health data" can be an overly broad term.

- Another attendee pointed out that, especially in randomized controlled trials, researchers may look to PHR data to be predictive and an important question was how reliable patient data might be in making future decisions in the context of clinical trials. Dr. Briggs said that many working in this space had hoped that EHR data would give researchers the ability to extract data in real time, but it seems that is not possible. In the NIH Collaboratory experience, researchers have found significant lag times. Targeted questions, however, might have the ability to generate closer to real-time answers.

- For the white papers, perhaps in addition to the two "buckets" of information (i.e., privileged vs. verifiable), one participant suggested that another bucket be added for variables such as claims, wearable devices, etc. to highlight that there is a wide range of sources to consider. It may be best to represent variables, another participant said, as a continuum rather than buckets as there will always be gray areas.

- Dr. O'Brien said that when we discuss "fitness for use" we need to define use. For the purposes of this supplement, we are interested in doing work to validate what we are finding in ADAPTABLE and the National Patient-Centered Clinical Research Network, PCORnet. As part of the white paper development process, we need to think about whether we want to focus it on this use case or as something broader.

- Another participant asked whether the group should clarify whether we are trying to answer questions posed by a prospective study design versus retrospective and whether

we should be looking at data that is already being captured versus data that should be captured (missing data versus measured data.) Others indicated that for the purposes of the ADAPTABLE supplement, the problem is that different sources of data are addressing similar events. But it might be appropriate to highlight other uses as well. Perhaps we need to produce guidance on how to gather considerations for when we collect data and reasons and rationales for doing it.

- One participant suggested that "verification" is a tricky term and that "concordance" might be a better word. For example, if the EHR reports that the patient was admitted for chest pain and the patient reported a "heart attack" that is a close agreement to what happened. Whereas if the EHR says a patient was admitted for a myocardial infarction and the patient says nothing happened, that indicates a "different magnitude" of problem. "Verification" might sound like an IRS audit.

- One participant asked: Is the primary question about quality of data or about getting more information and reducing bias in our scientific question? Another participant framed that question around the issue of prescribing data which might have missing data and it might be that there are higher quality sources to draw from. How can we design data collection to reduce discrepancy and bias?

- Another participant asked if this effort should consider questions about adjudication. For example, a patient with a 23-hour stay might say he was hospitalized, but the record might not say that he was "admitted." In ADAPTABLE, adjudication happens at the call center level where a patient reports a hospitalization and then the call center obtains the medical records to verify. The problem arrives when the EHR shows an event that the patient doesn't report.

Dr. Weinfurt, in summarizing the discussion said he heard three categories of variables: 1) Subjective experiences such as symptoms and daily functioning, things that only the patient can report on and is the privileged source of information, 2) Outcomes from procedures or tests, such as functional assessments, in which, if the procedure was administered correctly, the outcome is the most accurate source of information, and 3) Events, treatments and diagnoses for which it is unclear what the privileged source of truth might be. The "truth" of this last category could come from the EHR, it could come from a physician's note or from a patient's recollection. We are interested in studying the last category because many sources are feasible and none has the clear privilege of "truth." We are only looking for corroborations among variables that lead toward the "totality of evidence."

Another participant suggested the white paper be structured around the multiple scenarios that might occur to give readers guidance on questions to consider depending on the purpose of their research. When debating how to "boil the ocean" and what exactly to focus on in resulting white papers, participants agreed that focusing on answering these questions within the context of pragmatic trials might be a good place to start.

Participants then broke into two working groups.

Eliciting PHR Data in Pragmatic Studies: Workgroup #1

Participants in this working group explored how best to integrate PHR into pragmatic studies with a specific focus on leveraging survey methodology and collection opportunities via mobile technologies.

Discussion & Major Themes
In the first part of this discussion, Antonia Bennett led a discussion of how to leverage survey methodology for PRH data capture in pragmatic trials. Bennett began the workgroup discussion with a framework for solving a practical problem: Aware of limitations from EHR and claims data, can we provide guidance to researchers to define endpoints suitable from PRH data sources?

The initial questions for the researcher to explore might be:

- What are your endpoints?
- What are your data sources?
- What is your data validation plan?
- How do you bring data sources together?
- Does the data exist or do tools need to be developed to elicit the PRH?
- Researchers need to understand level and types of data, such as data coming from the "All of Us Research" program. Will researchers use PRH data?

Main points expressed during the discussion included:

- PRH comes from different sources including the patient, EHR, and claims data and while on its own, each source is incomplete and includes errors, each source can complement the others.
- EHR is not the complete capture of comorbidities or medications—for example, it often does not include over-the-counter medications.
- When developing tools to elicit PRH, the group recommended drawing from the patient reported outcomes (PRO) literature. However, the question was raised, how confident can we be that the principles of PRO surveys apply to PHR? The group suggested that the white paper resulting from this discussion include an appendix of suggested articles. Authors would not "authorize" articles but provide them as a resource only.

The group then turned to the topic of identifying the best practices when developing tools to elicit patient reported heath data? Questions posed included:

- How can we get the highest quality data?

- What are the best practices for eliciting different types of information such as comorbidities, medication use, and utilization?

This workgroup agreed that tools should be designed for both—existing data and elicited data. Questions raised included:

- What data could be asked of patients that can be validated?
- How do we elicit patient reported health data?
- How do evaluate quality of the data?
- What are use-case examples that we can share? Examples from ADAPTABLE include medications, medical history, utilization, and outcomes.

The guiding principle is to draw from patient reported outcome writing survey methodology. The group explored the following methods used to elicit data:

Recall method
- **Comorbidities**—recall may not apply.
- **Symptoms**—a one week timeline was suggested.
- **Medications**—recall may work; however, answers from patients may depend on location—where is the patient completing the survey. If at home, patients may check their pill box or medicine cabinet to confirm answers.
- **Chronic conditions**—patients may not be able to accurately distinguish acute from chronic conditions.

The group recommended a literature search of what is known and unknown with use of recall domains.

Language: The work group agreed that there are multiple ways to ask questions that may elicit different responses. Wording of questions matter.

For example, when asking about medication use, you can ask: 1) Do you have a prescription for X drug? 2) Have you filled your prescription for X drug? 3) Do you take X drug? 4) Have you been told to take X drug?

Format of Questions: The group discussed the best format (multiple choice, list, free text) for responses, suggesting that one format does not fit all. For example, medications are typically answered using a list or index; whereas, questions on comorbidities are more suitable for a multiple-choice response. Medication databases are available that can be accessed to facilitate data reporting. In addition, applications to capture a photo of medicines also available.

Redundant versus complimentary data: Redundant data is data that is additional and permits correction of errors in stored or transmitted data (all scripts and claims.) Complementary data is asking the patient for additional information and looking claims data. When intentionally

collecting complementary data—recognize that there are many things one can ask a patient that can never be found somewhere else. The patient is the only source for that information.

Also, be clear when data originates from different sources. From the Food and Drug Association (FDA) perspective, researchers need to be able to trace the origination of the data source. Data from patients can be seen as a weakness if you don't propose a means to validate the data. It is important to educate researchers, reviewers, and regulators how to recognize and elicit high-quality data from patients. Participants also discussed the importance of creating a combined endpoint. Is it more useful to estimate a latent trait or more valuable to have a combined endpoint?

The group then discussed how to elicit the highest quality information from a patient. When looking for the "truth" of an event, diagnosis or medication history, from the perspective of the patient, do patients:

- Accurately remember?
- Understand the question being asked of them?
- Understand their medical situation?
- Respond honestly? Some patients may knowingly not respond truthfully for fear of disappointing healthcare providers, caregivers, family members, etc.
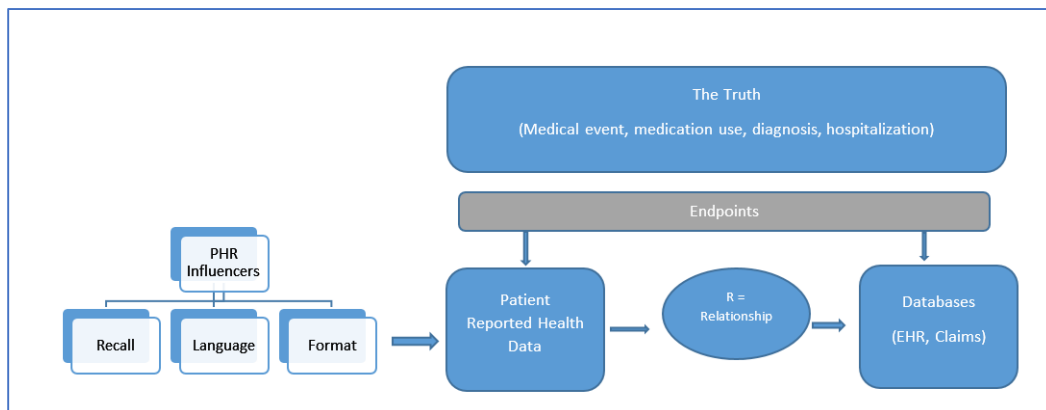
PHR Data Collection via Mobile Technologies: Opportunities and Best Practices

The group then shifted the conversation toward digital platforms (e.g., mobile, web based) to collect PHR. Mattias Jonsson lead the discussion and referred the group to the comprehensive paper by Coons, et al paper, *Capturing Patient-Reported Outcome (PRO) Data Electronically: The Past, Present, and Promise of ePRO Measurement in Clinical Trials*. Considerations discussed included which technologies work best for which populations:

Phones
- Almost everyone has a phone, including underserved populations.
- Android is more popular worldwide.

Tablets
- Tablets are more popular with older populations (65+).

Laptops and Integrated Voice Technologies
- These technologies have limitations with the general public and were not discussed in this working group.

Bring your own device (BYOD)
- The group agreed that the best approach is for patients to use their own device instead of the study providing patients with a device.
- Benefits of a study-provided device include control, encryption, and lock-down access.
- Benefits of BYOD for the study include less expense and no bottleneck with purchasing and distributing the devices.

Limitations discussed and outlined in the article include:
- User technical skill level
- Internet access and network connections
- Web browsers
- Lack of control over the app on the patient's device; patients can disable study notifications
- Distractions with patient's social media, e-mail, texts, etc.

The group then discussed how to give patients' access to the PHR instruments/tools:
- With web-enabled devices such as smart phones, patients can access the instruments on their Web browser instead of a separate app. The advantage to web-based data collection is that it is easy to implement and control what the user will see. The downside to web-based data collection is that it requires a persistent Internet connection.

- With native apps (installed on a device), the research participant downloads a small piece of software onto their smartphone that displays the PHR instruments. The advantage to apps are that patients can access instruments and enter information when they don't have Internet access, for later synchronization. The downside to apps is that it is more complex to implement and maintain, and some features can be disabled by the user.
- With Progressive Web Apps (PWA), where a website can be made to look and function like a native app, and can be used offline. (Emerging technology—will be fully supported ~Q3 2018.)

Other items discussed that need to be considered in the paper, include:

- Willingness – are patients willing to disclose data on different modes (paper versus electronic)?
- Implementation—for example, is the user interface intuitive, and does the tool fit on one screen?
- Application—is it easy to navigate or cumbersome to use?
- Patient training should be provided and embedded in the application.
- Review FDA's guidance on on medical devices and interoperability.
- Is the device/app/system compliant with FDA CFR - Code of Federal Regulations Title 21, Part 11? These regulations specify controls for electronic health records.
- Quality of the software—is there a possibility of losing data?

Finally, the group discussed monitoring compliance. If no one is looking at data at regular interval, then noncompliance can be missed. There is more time to act if someone is looking at data as it is being reported. Regular interval may be hourly, daily, weekly, or some other interval depending on the data collection protocol, to allow time for following up with participants before it's too late.

Analysis of PRH Data in Research Studies: Workgroup #2:

In this workgroup, participants explored issues of PRH data Analysis in Research Studies. Specifically, this group examined analytical approaches for integrating data and approaches to missing data specifically.

Discussion & Major Themes

The group began by framing three types of problems that PRH data might help: 1) gaps in information, 2) measurement errors, and 3) when information is needed in real time.

There are some general truths for each of the three problems, but each will also require more precise consideration. Themes during the discussion included:

- Whether the "real time" problem was similar to the "gaps in information" problem. Others said it would depend on how the information will be used. Participants also questioned how to define "missing" information and whether it is needed for the research question at hand, for adjudication or information later or for future questions.
- Participants asked if the resulting use case discussed in this session should be scoped to be specific to research and not general care and participants agreed. Although discussions will veer into clinical care as data sets are often emerging from those settings.
- Participants pointed out that one consideration for PRH data in research is being careful to not use PRH data to solve the problem of poor study design. If a pragmatic trial asks too much of the clinical setting, for example, adding 17 items to be included in the EHR, the researcher may consider whether the question being asked might not be suited for pragmatic research. It should be stated that pragmatic study designs should be chosen and employed because it is optimal for the question at hand and not just as a cheaper way to get information. The paper resulting from this discussion should refer to the PRECIS 2 tool that offers frameworks on ideal study design.
- Participants in this discussion agreed that they may veer between types of research including traditional research as well as pragmatic trials and that it is hard to disentangle the purpose of the first working group (how to collect PRH data) from the questions of how to analyze PRH data. The best starting point might be assuming common data problems or scenarios that arise in pragmatic research and cause questions about validity and then recommend design strategies to mitigate common problems.
- Another important consideration is the need to integrate sources of data to get unbiased information. An EHR is rarely a single integrated thing, especially for patients who might receive specialty care in one place and primary care somewhere else. In some cases, the patient might be the only integrated source of information.
- The focus should stay on data that is generated as a by-product of routine, standard of care and it is important to recognize that patient reported outcomes data sometimes are collected as part of routine care.
- Much of the work of the NIH Collaboratory could inform this white paper. A recent resource offered high level guidance on how to use an EHR in a highly pragmatic trial. The research question should lead with which data source is used, rather than building the question around the data.
- If we have identified EHR data as a source for inclusion and exclusion data, is it accurate and complete for adverse events? The FDA strongly encourage that the info gets recorded and transmitted to us.
- Participants agreed to focus on 4 specific use cases and then outline considerations for each of the three problems outlined (missing data, measurement errors, real time needs) depending on the question and study design (i.e., how pragmatic is the trial.) The 4 cases would include: 1) Eligibility: Patient data to determine who should be in the study, 2) Exposure, 3) Outcomes, and 4) Study measures: confounders, events

Assumptions moving forward for each case study would include:

- EHR in clinical data is the primary source.
- The research in question is somewhere on the spectrum of "pragmatism."
- The question to explore is whether we need PRH to augment EHR (outcome versus eligibility) and dive into case studies.

Concluding Thoughts

Each workgroup reconvened to share findings and suggested outlines for white papers.

- The group discussed the importance of getting white papers generated from the discussions published in the literature.
- Papers should be ordered sequentially so, although they address different problems and scenarios they will build upon each other. The first paper would lay out background information and arguments that could apply to each paper.
- The working group which focused on gathering PHR data reported that they focused on gathering data that could supplement other sources. They explored different methods that offer principles on how to get the most valid information and raised questions about whether existing methods fit the needs of pragmatic research. They also explored the pros and cons of different modes of gathering information and outlined a suggested research agenda for others.
- The working group tasked with analysis focused on scoping their questions to focus on assumptions about pragmatic design appropriateness and analysis approaches for different purposes (eligibility, outcomes, exposure and study measures.)
- It will be useful to orient readers to specific case studies to explore issues as well as focus on the higher-level questions about PHR.

The first workgroup tasked with capturing PHR for pragmatic trials presented their suggested outline for a white paper.

The working title this group wrote for its outline is "Applying Patient Reported Outcome Methodology to Capture Patient-Reported Health Data." This paper would start with a restatement of the problem and some key assumptions around the issue. The first section of the proposed outline would focus on questionnaire design and some general recommendations and considerations. This section would address defining the population, defining the concept of interest, defining the recall period and issues of comprehension, the response metric length and structure validation and other issues, as part of a general recommendations and considerations section. This section would also point readers to the existing literature on patient-reported outcomes. The next section would explore three types of information and highlight best practices for eliciting co-morbidities, utilization, and medication use. Another section would address the sensitivity of the topic and discuss why researchers might not always

get accurate answers. The paper will also discuss safety reporting and what to do when follow up is required. The second half of the paper would focus on the data collection platforms and approaches and summarize the best available literature. An appendix would point readers to guidelines other leaders and resources to help researchers as they embark on this research.

The second working group tasked with discussing PRH Data Analysis in Research Studies then reported to the group their suggested outline. This group will address how decisions in the design phase can influence the validity of data capture as well as the robustness of the ultimate data set used for analysis. The group revisited key assumptions about pragmatic data and the concept of understanding that in any pragmatic study or project there will always be a range of certainty about the completeness and accuracy of EHR data that is acceptable. That uncertainty level will guide the decision process for which data is collected. This is the first decision to make before deciding to capture patient reported health data. It is also important to determine if the goal is to obtain additional information that reduces bias and to consider the practical trade-offs of additional data collection.

The next step is to determine the purpose for capturing eligibility, exposure, outcomes assessment data. Fitness for use is a relative term and the data may not be appropriate for all purposes. This group will provide examples of when a researcher would use PHR data for eligibility, exposure, or outcomes assessment and when they might not. It is also important to consider the alignment of different sources of data and the global characteristics that can influence whether data is available in one source versus another. Additional factors, such as the timing of when data is captured, the concept that is being measured, and considering the populations that would be likely to have missing data and how to consider those populations in sensitivity analysis to prevent miscalculations.

Finally, this group will offer solutions to achieving concordance and preventing misalignment between two sources, including when to not use patient reported data, when to trust patient reported data, and when and how to find a third way by combining and integrating data. The group envisioned an integrated endpoint similar to a composite in which you might have information on the same clinical outcome from different sources and then, depending on the acceptable levels of false positives and negatives, it might be the right time to use an integrated outcome measurement.

In terms of the solution to misalignment, the group identified a number of dependencies. Again, it is important to consider the number of false positives or false negatives and which are most costly for the purposes of the study. It is also important to consider whether data is missing randomly or not.

The larger group then offered up further considerations for each group:

- It is currently FDA policy to never assume that missing data is not missing at random and will always perform statistical analysis whether or not the sponsor has done so.

- When considering design approaches that would combine data rather than adjudicate a truth from one source or another, consider integrating at the patient level rather than the trial or study level.
- Potential sensitivity analyses should be another consideration for the second group's paper.
- EHR data might change over time, for example, medications or states of health may change and remain in an EHR. It's important to consider whether or not to use time-bound encounter data rather than cumulative data.
- Consider that a single patient may be represented in several EHR systems including primary care, specialty and hospitals. Also, consider that EHRs change over time in how they collect data.

Appendices:

Appendix A: Agenda & Background Information
Appendix B: Biographies

ADAPTABLE Supplement Roundtable Meeting:
Integrating Patient-Reported Health Data and Electronic Health Record Data for Pragmatic Health Research
September 14, 2017
Room TBD, NIH Campus

Purpose: EHR data are not always complete with respect to a patient's medical history, clinical events, or treatment. Patient-reported health (PRH) information (and in some cases caregiver-reported health information) may augment capture of these data points in the setting of pragmatic studies, but key questions remain about the fitness-for-use of such data in research. The ADAPTABLE Supplement Roundtable will focus on the capture of PRH data and electronic health record (EHR)–derived data and how PRH data can be integrated with other data sources to improve the conduct of pragmatic health research.

Note: For the purposes of this meeting, the term "PRH data" includes patient- or caregiver-reported information that may also exist in the EHR, including hospitalizations, comorbid conditions, and medications, but does not include subjective patient-reported outcomes such as symptoms, functional status, or fatigue.

Roundtable Objectives:
The Supplement Roundtable will address two unanswered questions:

1. What are the best practices for capturing PRH data in pragmatic studies?
2. Once captured, what are the optimal analytic approaches for integrating this information with other data collected as part of a study, including data from the EHR?

Workgroups: The roundtable objectives will be addressed in breakout workgroups with 6-8 participants each. Workgroups will focus on the components of the white paper deliverable, with one workgroup member assigned to lead the discussion of each component.

Deliverable: The roundtable discussion will produce at least one jointly authored white paper publication on available resources for best practices, key challenges, information gaps, and future research needs for promoting best practices in the use of PRH data in pragmatic studies.

Agenda:

Time	Topic	Speaker/Discussant
10:00–11:00 a.m.	Welcome and orientation Supplement status update & discussion • Use of PRH data in ADAPTABLE • Tool development update • Strategies to connect with potential end-users	Wendy Weber Lesley Curtis Emily O'Brien
11:00 a.m.–3:00 p.m.	Breakout Workgroups	All
**Workgroup #1: Eliciting PRH Data in Pragmatic Studies** *(Participants: medical survey methodologists, health services researchers)*	
11:00–11:45 a.m.	Leveraging survey methodology for PRH data capture in pragmatic trials	Antonia Bennett
11:45 a.m.–12:30 p.m.	PRH data collection via mobile technologies: opportunities and best practices	Mattias Jonsson
12:30–1:30 p.m.	Working lunch • White paper overview and strategy	All
1:30–3:00 p.m.	Draft white paper outline *Possible sections* • Statement of the problem: Existing variability in PRH data capture methods & variability in PRH data types • Brief review of available best practices documentation • Recall periods • Lay terminology/phrasing • Inclusion of low literacy and underserved populations • Future research needs	Workgroup #1
**Workgroup #2: Analysis of PRH Data in Research Studies** *(Participants: clinical trialists, biostatisticians, health services researchers)*	
11:00–11:45 a.m.	Analytic approaches for integrating PRH data with other data streams (claims, EHR, etc.)	Keith Marsolo
11:45 a.m.–12:30 p.m.	Approaches to missing data using PRH data: medical history, medication use, and clinical events	Frank Rockhold
12:30–1:30 p.m.	Working lunch	All

	• White paper overview and strategy	
1:30–3:00 p.m.	Draft white paper outline *Possible sections* • Statement of the problem: Existing variability in PRH analytic methods • Brief review of available best practices documentation • In what settings is validation needed? • Recommendations for analytic approaches using PRH data to augment EHR data (including discussion of tradeoffs with each approach) • Future research needs	Workgroup #2
3:00–3:30 p.m.	Presentation of white paper components	Workgroups
3:30–4:00 p.m.	Discussion/wrap-up	All

Roundtable Working Group Participants

WG #1: Eliciting Patient-Reported Health Data in Pragmatic Studies	
Name	**Affiliation**
Antonia Bennett, PhD	Research Associate Professor, Health Policy and Management & Faculty Director, UNC Patient-Reported Outcome Survey System
Mattias Jonsson	Director of Systems Development for the UNC Patient Reported Outcomes Core Facility
Ronald Chen, MD, MPH	Associate Professor in the Department of Radiation Oncology at UNC-Chapel Hill.
Sana Al-Khatib, MD, MHS	Professor of Medicine at Duke University Medical Center
Kevin Weinfurt, PhD	Professor in the Department of Psychology and Neuroscience, Duke University

WG #2: Analysis of Patient-Reported Health Data in Research Studies	
Name	**Affiliation**
Frank Rockhold, PhD	Professor of Biostatistics, Duke University Biostatistics and Bioinformatics
Jen Nelson, PhD	Director of Biostatistics, Kaiser Permanente Washington Health Research Institute
Jessie Tenenbaum, PhD	Assistant Professor of Biostatistics and Bioinformatics, Duke University
Rachel Richesson, MS, PhD, FACMI	Associate Professor, Duke University School of Nursing
Keith Marsolo, PhD	Associate Professor, UC Department of Pediatrics

Moderators, Readings, and Discussion Questions

Working Group	Topic	Moderator	Relevant Readings	Discussion Questions
WG #1: Eliciting PRH Data in Pragmatic Studies	Leveraging survey methodology for PRH data capture in pragmatic trials	Antonia Bennett	Vigen C, et al. Validation of self-reported comorbidity status of breast cancer patients with medical records: the California Breast Cancer Survivorship Consortium (CBCSC). https://www.ncbi.nlm.nih.gov/pubmed/26797455 Skurtveit S, et al. The validity of self-reported prescription medication use among adolescents varied by therapeutic class. https://www.ncbi.nlm.nih.gov/pubmed/18538265 Leggett LS. Measuring Resource Utilization: A Systematic Review of Validated Self-Reported Questionnaires https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4998854/	• What opportunities exist for the use of patient-reported health data in pragmatic research studies? • What future research is needed to inform best practices for capturing patient-reported health data?
WG #1: Eliciting PRH Data in Pragmatic Studies	PRH data collection via mobile apps: case studies and best practices	Mattias Jonsson	Coons SJ, et al. Capturing Patient-Reported Outcome (PRO) Data Electronically: The Past, Present, and Promise of ePRO Measurement in Clinical Trials. https://www.ncbi.nlm.nih.gov/pubmed/25300613	• What are the advantages and challenges to the use of mobile technologies for patient-reported health data capture?

			Banerjee AK, et al. Web-based patient-reported outcomes in drug safety and risk management: challenges and opportunities?https://www.ncbi.nlm.nih.gov/pubmed/22551007	• What best practices exist for optimal use of mobile technologies in PRH data capture? • What are the considerations for use of mobile technologies in special or underserved populations?
WG #2: Analysis of PRH data in Research Studies	Analytic approaches for integrating PRH data with other data streams (claims, EHR, etc.)	Keith Marsolo	Eichler GS, et al. Exploring Concordance of Patient-Reported Information on PatientsLikeMe and Medical Claims Data at the Patient Level. J Med Internet Res 2016;18(5):e110 DOI: 10.2196/jmir.5130 http://www.jmir.org/2016/5/e110/ De-Loyde KJ, et al. Which information source is best? Concordance between patient report, clinician report and medical records of patient co-morbidity and adjuvant therapy health information. J Eval Clin Pract, 21: http://onlinelibrary.wiley.com/doi/10.1111/jep.12327/abstract;jsessionid=81AD88892CE57467A406C0CE0FBDFD9A.f04t01	• What are the major advantages to integration of patient-reported health data with other data streams in pragmatic studies? • What are the major challenges of integrating multiple data streams in pragmatic research? • What best practices exist for integration and use of health data from multiple streams?

| WG #2: Analysis of PRH data in Research Studies | Approaches to missing data using PRH data: medical history, medication use and clinical events | Frank Rockhold | Basch E, et al. Use of patient-reported outcomes to improve the predictive accuracy of clinician-reported adverse events. https://www.ncbi.nlm.nih.gov/pubmed/22157639

Yasaitis LC, et al. Comparison of self-reported and Medicare claims-identified acute myocardial infarction. https://www.ncbi.nlm.nih.gov/pubmed/25747935

Roderick JL. The Prevention and Treatment of Missing Data in Clinical Trials. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3771340/ | • For what purposes should patient-reported health data be used in pragmatic trial analysis (endpoint definition, only in the case of missing EHR/claims data, etc.)?
• What are the recommended analytic approaches for using PRH data to augment EHR data?
• What are the benefits/tradeoffs of these approaches? |

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Dr. Al-Khatib is a tenured Professor of Medicine at Duke University Medical Center, a board-certified clinical electrophysiologist and an experienced clinical researcher in cardiac arrhythmias. As a graduate of the NIH-funded Clinical Research Training Program, she is one of a few electrophysiologists nationwide with expertise in quantitative research methods. Her clinical expertise is in sudden cardiac death prevention, atrial fibrillation and ventricular arrhythmias, and implantable cardiac devices. Her research expertise lies in the design and conduct of clinical trials, outcomes research, and cost-effectiveness analyses. She is a recipient of a National Heart, Lung and Blood Institute's R-01 grant titled "Implantable Cardioverter Defibrillator Therapy in Patients with Heart Failure" (2009-2013) and of an American Heart Association Career Development Award (2002-2006). She is a Co-Principal Investigator on an NHLBI-funded T-32 Postdoctoral Training in Cardiovascular Clinical Research and on several Agency of Healthcare Research and Quality sponsored R-01 grants including the "Duke Cardiovascular Center for Education and Research on Therapeutics." She has more than 200 publications in peer-reviewed journals. She has established several collaborative research efforts both within and outside her institution. The goals of these collaborations are to synergize efforts aimed at improving the survival and quality of life of patients at risk for sudden cardiac death and those with atrial and ventricular arrhythmias through clinical trials and outcomes-based research and to evaluate study design and data analysis in order to improve the quality of research done in these arenas. Dr. Al-Khatib is an Associate Editor for Circulation and is on the Editorial Board for Circulation Arrhythmia and Electrophysiology, Heart Rhythm, the American Heart Journal, and the Journal of Cardiovascular Electrophysiology. Dr. Al-Khatib serves on multiple national committees including the Heart Rhythm Society Health Policy committee, the American College of Cardiology and American Heart Association Guideline Development Task Force, the American Heart Association Data Standards Task Force, and the National Quality Forum Cardiovascular Steering committee.

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Dr. Antonia Bennett is a health services researcher and patient-reported outcomes methodologist. She is a member of the Cancer Outcomes Research Program (Population Sciences) of the Lineberger Comprehensive Cancer Center and faculty member in the Department of Health Policy and Management, Gillings School of Global Public Health. Her research employs both qualitative and quantitative methods to investigate valid and reliable approaches for assessing patient-reported outcomes in longitudinal research in adult and pediatric populations. She is currently investigating the value of pedometry/activity trackers and other wearable device data in validation studies, oncology clinical trials, and clinical care.

Dr. Bennett recently led the evaluation of mode-equivalence across tablet, IVRS, and paper-based administration of the NCI Patient Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE).

Dr. Bennett is Director of the Measurement Core of the NINR-supported Palliative Care Research Cooperative Group (PCRC), a member of the Carolina Health Informatics Program (CHIP), and is Faculty Director of the UNC Patient-Reported Outcomes Survey System (PRO-Core).

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Kevin Chaney is a Health Scientist Administrator for the Office of the Chief Scientist at the Office of the National Coordinator for Health IT (ONC). While supporting the Chief Scientist and Deputy National Coordinator for Health IT. He oversees a multitude of projects across many domains ranging from precision medicine to artificial intelligence to clinical decision support. Prior to joining ONC, Mr. Chaney directed the Medicare Rural Hospital Flexibility Grant (Flex) Program at the Federal Office of Rural Health Policy, providing support to 1300 critical access hospitals. Mr. Chaney also spent time at the Agency for Healthcare Research and Quality as a Program Manager in the Health IT Portfolio, overseeing the development, implementation, and evaluation of large-scale health IT demonstration projects. Mr. Chaney earned a Masters in Gerontology from Miami University, Oxford, Ohio. He credits interning at AARP and analyzing the HITECH Act for prompting his interest in the field of health IT.

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Lesley H. Curtis, PhD, is Professor and Interim Chair of the Department of Population Health Sciences in the Duke University School of Medicine, and directs the Center for Pragmatic Health Systems Research in the Duke Clinical Research Institute. A health services researcher by training, Dr. Curtis oversees a portfolio of projects that use observational data to address questions related to clinical and comparative effectiveness, pharmacoepidemiology, health care delivery, and epidemiological trends across a broad array of clinical conditions and clinical care settings. Dr. Curtis serves as Co-Lead of the Data Core for the FDA's Sentinel Initiative, Co-PI of the NIH Health Care Systems Collaboratory, and Lead of the Distributed Research Network Operations Center for PCORI's National Clinical Research Network (PCORnet), working with

health systems and patient networks to develop a harmonized data infrastructure for robust observational and interventional research.

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Laura Lee Johnson, Ph.D. is the Acting Director of the U.S. Food and Drug Administration (FDA) Center for Drug Evaluation and Research's (CDER) Division of Biometrics III and the Clinical Outcome Assessment liaison for CDER's Office of Biostatistics. She provides guidance on design, logistics, implementation, and analysis of research studies ranging from person reported outcome (PRO) measure qualification to safety and randomized studies of all sizes. She works across CDER and other parts of FDA on patient focused drug development initiatives. Prior to working at the FDA she spent over a decade at the U.S. National Institutes of Health (NIH) working on and overseeing clinical research and research support programs. At NIH she contributed to programs such as the CTSAs, PROMIS, and the NIH Collaboratory. She has been involved with numerous projects developing, validating, and using clinical outcome assessments in both patient care and research and received several NIH Director's Awards and an FDA award for her work involving clinical trials in various populations, health related quality of life, and teaching. She has co-authored several articles and book chapters across a variety of disciplines and served on NIH and PCORI review and methods panels. Among her many activities Dr. Johnson serves on the FDA-NIH Interagency Clinical Outcome Assessments Working Group, the IMI PREFER Scientific Advisory Board, co-directs the NIH Principles and Practice of Clinical Research course, and volunteers with the Montgomery County Maryland Science Fair. Dr. Johnson received her Ph.D. in Biostatistics from the University of Washington.

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Mr. Jonsson is the Director of Systems Development for the UNC's Patient Reported Outcomes Core Facility (PRO-Core). He the architect and main developer of the PRO-Core system platform and has more than 10 years of experience in database design, systems development, and health care survey research.

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Dr. Marsolo's research interests include methods to characterize the quality and suitability of electronic health record (EHR) data; approaches to collect and extract research data from the EHR at scale; the design and instantiation of common data models to facilitate distributed research queries; and the development of informatics architectures and standards that can support multi-center learning health systems.

Dr. Marsolo serves as faculty advisor for BMI Data Services, which provides services in these areas. He is currently building on several grants from the Agency for Healthcare Research and Quality to design and implement an EHR-linked registry architecture for ImproveCareNow, a 94-center quality improvement and research network that focuses on improving the care and outcomes of children with inflammatory bowel disease (IBD). He and his team are extending the platform to support a pragmatic clinical trial that is being funded by the Patient-Centered Outcomes Research Institute (PCORI). This pragmatic trial will serve as an initial use case for a recently funded grant from the Office of National Coordinator for Health Information Technology (ONC) to pilot the use of interoperability standards and embed case report forms in the EHR, decreasing the amount of time spend on double data entry during research study visits.

Other recent highlights include work on Phase I and II of PCORI's National Patient-Centered Clinical Research Network (PCORnet), including a pediatric-focused Clinical Data Research Network (CDRN), and a Patient-Powered Research Network (PPRN) with ImproveCareNow. In addition, Dr. Marsolo is a co-investigator within the Distributed Research Network Operations Center of the PCORnet Coordinating Center, served as one of the co-chairs of the PCORnet's Data Standards, Security and Network Infrastructure (DSSNI) Task Force during Phase I of the project, and is a member of the Data Committee as part of Phase II.

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Patty McAdams is a Communications Specialist with the Duke Clinical Research Institute. She provides communications support to the ADAPTABLE Study and the National Patient-Centered Clinical Research Network (PCORnet). Ms. McAdams received her BS from Bowling Green State University and her MS from Case Western Reserve University. She is a Certified Clinical Research Associate by The Association of Clinical Research Professionals.

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Dr. Sandra A. Mitchell is a Research Scientist and Program Director in the Outcomes Research Branch in the Healthcare Delivery Research Program. Her primary research interests focus on the measurement of symptoms and impairments in physical functioning, and the testing of interventions to improve these outcomes, especially in vulnerable populations (senior adult, mulitmorbid, frail, and medically underserved). She has extensive experience in the collection, analysis, and interpretation of patient-generated health outcomes data in clinical trials and advanced multivariate statistical analysis. She has methodologic interests in latent variable mixture modelling, as well as the use of performance-based measures of physical functioning. Her program of research has an emphasis in cancer care delivery science, including dissemination and implementation of evidence-based interventions, quality measurement, and the use of health information technologies and decision support to improve care quality and strengthen patient self-management.

Dr. Mitchell serves as the NCI Scientific Director for the development and testing of the National Cancer Institute's Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE), a new electronic patient-reported outcomes measurement system to integrate patient-reporting of symptomatic adverse events into cancer clinical trials. PRO-CTCAE integrates the patient perspective into adverse event reporting, and may ultimately prove useful as an outcome measure in comparative effectiveness research and to profile the severity and impact of therapy-related symptom burden in patients undergoing treatment for cancer.

A board-certified acute care nurse practitioner, Dr. Mitchell received her undergraduate and master's degrees from the University of Toronto and the University of Rochester, and received a PhD from the University of Utah with a focus in quantitative methods. She is the author of numerous peer-reviewed publications in the areas of symptom management, cancer

survivorship, measurement of physical function, and the application of patient-reported outcomes to evaluate treatment effects, including toxicity and therapeutic response. A Fellow of the American Academy of Nursing, Dr. Mitchell's work has also been recognized with two NIH Clinical Center Director's Awards, the Oncology Nursing Society's Award for Excellence in Nursing-Sensitive Patient Outcomes, and the Relentless for a Cure Award from the Leukemia and Lymphoma Society.

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Jennifer Nelson is Director of Biostatistics and a Senior Investigator at Kaiser Permanente Washington Health Research Institute and an Affiliate Professor of Biostatistics at the University of Washington (UW). She received her PhD in Biostatistics at the UW in 1999. Dr. Nelson's research focuses on methods to assess post-market drug and vaccine safety and effectiveness. She is particularly interested in addressing the statistical challenges of multi-site safety studies that use electronic health record data from large health care systems and has authored over 75 publications, primarily in this area. Since 2009, Dr. Nelson has provided national leadership a Methods Core Lead and Senior Statistician for the Food and Drug Administration's (FDA) Sentinel Initiative, a program designed to facilitate active and rapid safety surveillance for FDA-regulated medical products. She has also led the Methodology Committee for the Centers for Disease Control and Prevention sponsored Vaccine Safety Datalink (VSD) project, a national collaboration that has involved 10 health care systems and monitored vaccine safety in the U.S. since 1990. Dr. Nelson's honors include the 2009 VSD Margarette Kolczak Award for outstanding contributions in biostatistics and epidemiology in the field of vaccine safety and a 2013 American Journal of Epidemiology Article of the Year award.

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Emily O'Brien, PhD is an Assistant Professor in the Department of Population Health Sciences at the Duke University School of Medicine and an outcomes researcher at the Duke Clinical Research Institute. After completing undergraduate training at Duke University, she received a PhD in Epidemiology at the University of North Carolina in Chapel Hill in 2012. Dr. O'Brien's research focuses on comparative effectiveness, patient-centered outcomes, pharmacoepidemiology, and pragmatic health services research in cardiovascular and pulmonary disease. She has expertise in the use of administrative claims data for longitudinal outcomes assessment in Medicare populations and national registries. Dr. O'Brien's projects include a PCORI-funded study examining commonly-used stroke therapies, an NHLBI-funded study assessing cardiovascular risk factors in the Jackson Heart Study, in addition to multiple projects evaluating patient-reported outcomes in idiopathic pulmonary fibrosis, atrial fibrillation, and familial hypercholesterolemia. She is the Director of the DCRI Research Conference serves on the editorial boards of the *American Heart Journal* and *Stroke*.

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Rachel Richesson, MS, PhD, MPH, FACMI, a noted informaticist, joined the DUSON faculty in December 2011. Dr. Richesson earned her BS (Biology) at the University of Massachusetts in 1991, and holds graduate degrees in Community Health (MPH, 1995) and Health Informatics (MS, 2000 and PhD, 2003) from the University of Texas Health Sciences Center in Houston. Her dissertation involved the integration of heterogeneous data from multiple emergency departments. Dr. Richesson spent 7 years as at the University of South Florida College of Medicine directing strategy for the identification and implementation of data standards for a variety of multi-national multi-site clinical research and epidemiological studies housed within the USF Department of Pediatrics, including the NIH Rare Diseases Clinical Research Network (RDCRN) and The Environmental Determinants of Diabetes in the Young (TEDDY) study. Dr. Richesson has conducted original research on the quality and usability of various terminological data standards, particularly in the context of clinical research, and has presented

dozens of posters and invited talks on the topic of data standards in clinical research. She has fostered numerous interdisciplinary research collaborations and is nationally and internationally recognized for her extensive clinical informatics experiences. In 2012, she edited Clinical Research Informatics, the first textbook dedicated to this topic, and co-authored several chapters.

Dr. Richesson is particularly interested in new applications and technologies and standards specifications that will increase the efficiency of clinical research data collection and analysis, and that will enable interoperability between clinical research and health care systems. She co-leads the Phenotyping, Data Standards, and Data Quality Core for the NIH Health Care Systems Research Collaboratory, a demonstration program for the transformation of clinical trials based upon use of electronic health records (EHRs) and healthcare systems partnerships. In this role, she is developing standard approaches and guidance for the extraction of clinical data to support research and learning healthcare systems. She is also the co-lead of the Rare Diseases Task Force for the national distributed Patient Centered Outcomes Research Network (PCORnet), specifically promoting standardized EHR-based condition definitions ("computable phenotypes") for rare diseases, and helping to develop a national research infrastructure that can support observational and interventional research for various types of conditions.

At DUSON, Dr. Richesson teaches Health Information Exchange Standards, Methods and Models (N410) and Health Information Systems (N409), supports informatics practica (N498), and co-teaches Data-Driven Health Care Improvements (N653). She also engages in informatics-focused initiatives across the Duke campus, particularly within the Duke Center for Health Informatics and Duke Clinical Research Institute programs. Dr. Richesson was elected as a fellow of the College of Medical Informatics 2014.

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Prior to joining the Duke faculty in 2014, **Frank Rockhold's** career included senior research positions at Lilly Research Laboratories, Merck Research Laboratories and GlaxoSmithKline, where he recently retired as Senior Vice President of Global Clinical Safety and Pharmacovigilance.   He has been a leader in the scientific community in promoting data disclosure and transparency in clinical research. Frank served for 9 years on the board of directors of the non-profit CDISC, most recently as Chairman and is past president of the Society for Clinical Trials. He is a member of the PCORI Advisory Panel on Clinical Trials and on the board of the Frontier Science and Technology Research Foundation. Frank has many publications in major scientific journals across a wide variety of topics and has held faculty appointments at five other universities, including a current post as Affiliate Professor of

Biostatistics at Virginia Commonwealth University Medical Center. He is also currently Managing Partner of HunterRockhold, Inc., which provides strategic consulting to Industry, Government, and Academia in the areas of clinical trials, safety and pharmacovigilance, data disclosure and transparency.   He holds a BA in Statistics from The University of Connecticut, an ScM in Biostatistics from The Johns Hopkins University, and a PhD in Biostatistics from the Medical College of Virginia.   Frank is a Fellow of both the American Statistical Association and the Society for Clinical Trials and an Accredited Professional Statistician, PStat®.

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Scott R. Smith, Ph.D. is Director of the Division of Health Care Quality and Outcomes in the Office of the Assistant Secretary for Planning and Evaluation (ASPE) at HHS. His division conducts research on how health policies influence health care quality and outcomes in State and Federal programs. In addition, he is responsible for managing the Office of the Secretary's Patient-Centered Outcomes Research (PCOR) data infrastructure portfolio across HHS, coordinating with the National Quality Forum (NQF), and supporting the Physician-Focused Payment Model Technical Advisory Committee, which was recently established by the Medicare Access and CHIP Reauthorization Act (MACRA).   His interests are studying alternative payment models in Medicare and Medicaid, building national data capacity for conducting patient centered outcomes research, strengthening delivery system reform initiatives, and facilitating support for a learning health care system. Before joining ASPE, Smith directed research programs on comparative effectiveness and pharmaceutical outcomes at the Agency for Healthcare Research and Quality (AHRQ).

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Jessica Tenenbaum, PhD is a faculty member in Duke's Department of Biostatistics and Bioinformatics, Division of Translational Informatics. Her primary research interests are 1. Infrastructure and standards to enable research collaboration and integrative data analysis; 2. Informatics to enable precision medicine; 3. Mental health informatics, and 4. Ethical, legal, and

social issues that arise in translational research, direct to consumer genetic testing, and data sharing. At Duke, Dr. Tenenbaum has overseen the development of the MURDOCK Integrated Data Repository (MIDR) for the management of clinical, omics, biobanking, and consent data as well as experimental and protocol metadata in the context of the MURDOCK Study. ([www.murdock-study.com(link is external)](http://www.murdock-study.com)) She is also the informatics faculty lead for the Alzheimer's Disease Metabolomics Consortium. Nationally, Dr. Tenenbaum plays a leadership role in the American Medical Informatics Association, serving as Chair of the Genomics and Translational Bioinformatics Working Group and as an elected member of the Board of Directors. She is an Associate Editor for the Journal of Biomedical Informatics and serves on the advisory panel for Nature Publishing Group's Scientific Data initiative. After earning her bachelor's degree in biology from Harvard, Dr. Tenenbaum worked as a program manager at Microsoft Corporation in Redmond, WA for six years before pursuing a PhD in biomedical informatics at Stanford University.

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Wendy J. Weber, ND, PhD, MPH, joined NCCIH as a program director in 2009. She oversees NCCIH's portfolio of health services research, studies of complementary medicine to promote of healthy behavior, and complex complementary/integrative medicine intervention research to include traditional Chinese medicine, naturopathy, integrative medicine, and Ayurveda. Dr. Weber's interests include the use of complementary medicine interventions for common pediatric conditions, mental health conditions, promoting healthy behaviors, and health services research.

Dr. Weber is the coordinator for NCCIH's Preliminary Clinical Studies in Preparation for Large Interventional Trials of Complementary and Alternative Medicine Therapies (R34) program. She is also the NCCIH representative to the NIH Common Fund Science of Behavior Change program and the NIH Prevention Research Coordinating Committee.

Dr. Weber earned a Doctorate of Philosophy in epidemiology and a Master of Public Health from the University of Washington. She earned a Doctorate of Naturopathic Medicine (N.D.) from Bastyr University. Prior to joining NCCIH, she was a research associate professor at Bastyr University, where her research included the study of herbal treatments for pediatric conditions. Her clinical practice focused on the treatment of children and adolescents with mental health conditions, abdominal pain, headaches, and allergies.

She has published on echinacea's effect on colds in children, naturopathic treatment of children, and complementary medicine treatments for attention deficit hyperactivity disorder.

Her articles have appeared in *JAMA: The Journal of the American Medical Association*, *The Journal of Alternative and Complementary Medicine*, and *Pediatrics*

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