Bridging the Translational Research Divide: What Happens when Clinical Trials Meet the Real World?

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Abstract

Efficacious clinical trials for chronic disease management, such as asthma, have typically been translated into healthcare practice with limited to no evaluation. This limited evaluation has made it difficult to assess if efficacious clinical trials demonstrate effectiveness when translated into the real world setting.

The Community Healthcare for Asthma Management and the Prevention of Symptoms (CHAMPS) study, funded by the Merck Childhood Asthma Network (MCAN), is designed to translate and evaluate interventions from successful NIH asthma clinical trials into the primary care practices at federally-qualified community health centers serving diverse and underserved populations. The CHAMPS interventions were based on evidence and lessons learned from: 1) National Cooperative Inner City Asthma Study (NCICAS), 2) Inner City Asthma Study (ICAS), and 3) Head-off Environmental Asthma in Louisiana (HEAL), all of which were conducted in minority, low income, urban populations.

Investigators from Rho, the Statistical and Clinical Coordinating Center for NCICAS/ICAS/HEAL, worked along with experts in health policy at George Washington University (GW) in partnership with MCAN, RCHN Community Health Foundation (RCHN CHF), and clinicians at 3 federally-qualified health centers to identify agreed-upon components of the prior trials to implement and evaluate for CHAMPS. In addition, traditional clinical trial protocols, including centralized training, quality control monitoring, manual of operations, case report forms, clinical data management, and participant recruitment and retention strategies were identified by Rho and considered by CHAMPS investigators, but not all were adopted and adapted. Through careful collaboration with our research partners, we were able to translate many of the elements from our clinical trials into the CHAMPS program while still being flexible enough to adapt to the unique needs of the clinic healthcare setting.

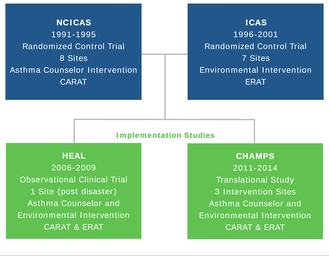
Our experiences will be useful to trialists looking to disseminate and evaluate clinical trial results in primary care settings that provide care to diverse and underserved populations.

Introduction

Clinical trials hold immense promise for improving healthcare, but only if the knowledge generated from the research makes its way into practice. Unfortunately, the translation from research to practice is often slow and challenging. To bridge the gap between the two, implementation and translational research is needed to determine if and how effective clinical trials can be implemented in a real world setting.

The CHAMPS study is designed to be one such implementation research program. CHAMPS is investigating how the successful asthma interventions of the NCICAS and ICAS clinical trials, and HEAL observational study, can be effectively translated into 3 federally-qualified health centers (FQHC) in Arizona, Michigan, and Puerto Rico. Figure 1 shows how the NCICAS and ICAS randomized control trials (RCT) have been translated into implementation studies – first HEAL, and now CHAMPS.

Figure 1: RCT to Implementation Studies



Statement from NIH's OBSSR

Health scientists have successfully developed and tested a plethora of clinical and community interventions demonstrated to treat and prevent medical and behavioral illnesses. However, as leaders in research and clinical practice have noted, there is still an enormous gap between what we know can maximize the quality of health care and what is currently being delivered in practice and community settings.

More present than ever within the research community is the belief that to optimize public health we must not only understand how to create the best interventions, but how to best ensure that they are effectively delivered within clinical and community practice. This is the focus of dissemination and implementation research, and building this knowledge base is imperative to get the best return on decades of investment in biomedical and behavioral research.

Methods

MCAN, RCHN CHF, GW, and Rho worked together to identify 3 FQHC CHAMPS intervention sites. Clinics were invited to respond to a request for proposals to participate in CHAMPS. Site visits were conducted to identify 3 clinics who were committed to participating in CHAMPS and who represented 3 different tiers of capacity for treating asthma.

Table 1 shows some of the differences between the selected sites that were considered when determining their capacity. The objective was to measure how the efficacious clinical trial interventions could be implemented in sites with varying degrees of preparedness and infrastructure.

Table 1: Site Differences at Time of Site Selection

	Site 1	Site 2	Site 3
Population type	Rural	Urban, in flux	Mix
Estimated pediatric asthma population	700	4850	1800
Electronic Medical Records in use	No	Yes	Transitioning
Existing Asthma Infrastructure			
Site Asthma Champion	Pharmacist	Physician	Asthma Counselor
Asthma Counselors (AC) on staff	No	Yes	Yes
AC completed certification	No	No	2 of 3
Existing asthma care program	No	Clinic program	Clinic program Community program
Allergen testing resources	Blood testing off site	Skin testing in clinic	Blood testing in clinic
Spirometry testing resources	Pulmonologist off site	AC in clinic	AC in clinic
Home visitation resources	Physician visits	AC in past	Community program
Perceived capacity for implementing CHAMPS	Low	High	Medium

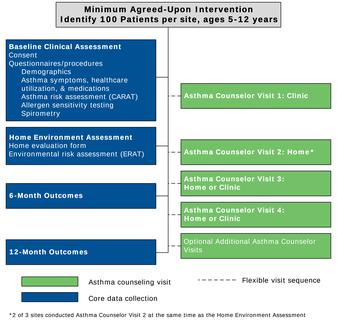
Once sites were selected, investigators:

- Conducted weekly planning calls with the sites to identify which intervention elements could be implemented in the clinic setting, including paring down data collection instruments from the clinical trials to a set of bare minimum variables essential for CHAMPS analyses.
- Hosted an in-person meeting to establish final consensus between the research partners on a core set of intervention and data collection components to be implemented at each site (Minimum Agreed-Upon Intervention).
  - Sites were also given the freedom to adopt additional procedures from the clinical trials that went beyond the core components if they had the interest and capacity.
- Developed a Manual of Operations to provide instructions for every program activity.
- Conducted teleconference and webinar-based "e-trainings" on the intervention and data collection procedures.
  - E-trainings diverged from the more intensive, face-to-face, "hands-on" trainings used in the clinical trials.
  - E-trainings were conducted as a series of 6 weekly trainings (with supplemental follow-up trainings provided as needed).
- Developed a web-based electronic data capture (EDC) system to allow the sites to remotely enter questionnaire data directly into our database.
  - Two of the 3 sites opted to use the EDC system directly. One site had an electronic medical record system and opted to set up the CHAMPS data collection forms in their system and export data into the CHAMPS EDC on a weekly basis.
- Collected extensive qualitative data on the implementation process by documenting decisions made by the researchers, and by surveying clinic staff (including those not directly involved in the project), participants, and fellow researchers.

Results

Figure 2 shows the minimum set of agreed-upon intervention elements for CHAMPS.

Figure 2: Agreed-Upon Intervention Visits



Each site agreed to:

- Enroll 100 children ages 5-12 with moderate-to-severe asthma
- Assess each child's:
  - Demographics via questionnaire
  - Asthma symptoms, healthcare utilization, and medications via questionnaire
  - Clinical risk assessment via CARAT (Child Asthma Risk Assessment Tool)
  - Environmental exposures risk via home assessment visit and ERAT (Environmental Risk Assessment Tool)
  - Allergen sensitivity via skin prick test or IgE test
  - Lung function by spirometry
- Provide a minimum of 4 patient-tailored asthma counseling sessions
- Collect outcome data on asthma symptoms, healthcare utilization, and medications via questionnaire at baseline, 6 months, and 12 months

Specific differences between the Clinical and Translational Research Studies

The CHAMPS intervention criteria were not a perfect match to the in-depth procedures of the tightly-controlled clinical trial environments, but they reflected the researchers' best efforts to honor the fundamental components of the trial intervention while adapting to the needs and constraints inherent in the "real world" settings of the clinics (Table 2).

The prevailing themes when comparing the clinical trial intervention components to the intervention components of CHAMPS are:

- A reduction in frequency and intensity of visits in CHAMPS
- Utilizing staff with less protocol-specific training and experience in CHAMPS

Table 2: Research Implementation Differences between Clinical Trials and CHAMPS

Component	Clinical Trials	CHAMPS
Protocol Development & Implementation	Prescribed	Collaborative with sites
Training	Central, in-person meetings	Series of teleconference & web-based sessions
Evaluation & Quality Control Monitoring of Staff	At outset & throughout trial	One interim site visit
Allergen Sensitivity Testing	Skin prick tests	Skin prick test (1 site) IgE blood test (2 sites)
Home Assessments	Visual assessment & dust collection by home evaluator	Visual assessment by AC
Asthma Counselor Visits	6 AC visits 6 telephone calls (NCICAS)	4 AC visits (at least 1 in the home)
Home Remediation Visits	Remediation performed over 5-7 visits followed by telephone calls (ICAS) In-home demonstration over 2 visits followed by telephone calls (HEAL)	Verbal instruction during asthma counselor visit
Outcomes	Collected every 2 months	Collected at 6 & 12 months
Data Collection	EDC	Varied
Data Collectors	Independent staff	Interventionists
Home Visitation Resources	Physician visits	ACs in past
Perceived capacity for implementing CHAMPS	Low	High

We also noted general differences between how research is conducted between the clinical trial environment and the FQHC environment (Table 3). We also observed between site differences in terms of: Population, Healthcare infrastructure, Environmental exposures, Asthma treatment, and Housing.

Table 3: Research Differences between Clinical Trial Sites and FQHC Sites

Clinical Trial Site	FQHC
Established institutional IRB	May or may not have an institutional IRB Not used to working in a regulated research environment
Familiar with clinical research practices	Lack of familiarity with clinical research practices
Familiar with research data collection	Lack of familiarity with research data collection Implementing EMR systems, not EDC systems
Time dedicated to participant-based research	Time dedicated to patient-oriented care
Led by Principal Investigator	Led by Physician or Clinic Director
Staff establish & maintain frequent, persistent contact with participants to collect data	Staff establish initial contact with patients, but rely on patients to maintain contact with the site

Enrollment and Visit Completion

Two sites enrolled more than 100 participants, while the third site enrolled 90 of the target 100 participants. While all 3 sites adopted the Minimum Agreed-Upon Intervention, we noted that sites with greater capacity – due to existing asthma treatment infrastructure (Site 2 and 3) – seemed to be more resistant to following the precise CHAMPS procedures compared to the site that had almost no existing asthma infrastructure (Site 1). This can be seen by comparing visit completion progress across sites (Figure 3).

Figure 3: Visit Completion to Date by Site

Conclusions and Recommendations

- Translational trials are needed to determine if the evidence from efficacious clinical trials can reasonably be replicated in the "real world" setting.
- Collaboration with clinics is essential for balancing fidelity to clinical trials with the constraints of the clinic setting. Clinical trialists must be flexible when it comes to maintaining strict adherence to the clinical trial interventions, but clinics must also be willing to adopt procedures that are faithful to the underlying evidence.
- In addition to collecting clinical outcomes for analyses, implementation and process data should also be collected to understand how the intervention is adopted at a clinic level.
- Clinics frequently lack the infrastructure and personnel to duplicate the tightly-controlled environment of clinical trials. However, clinics may be motivated to implement successful clinical trial interventions if they are given the freedom to carefully adapt the interventions to their unique clinic setting.
- Clinics with existing treatment programs may struggle to implement new intervention programs that differ from their established procedures. Additional collaboration may be needed to determine how the intervention can be integrated into the existing program frameworks.
- Clinics may need to look for ways to expand existing programs and partnerships to implement successful clinical trial interventions.

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