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**CASE STUDY**

# The Michigan Clinical Research Collaboratory: Following the NIH Roadmap to the Community

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**ABSTRACT**

**PURPOSE** This case study describes a successful National Institutes of Health (NIH) Roadmap application that has created a new and innovative translational science partnership at the University of Michigan.

**METHODS** We describe the institution within which the grant application was developed, the role played by the Department of Family Medicine, the role of prior successes in translational and community-based research, the associated infrastructure development, the application development process, and some features of the final project.

**RESULTS** A partnership among 2 clinical and research centers of excellence at the University of Michigan, 3 practice-based research networks, and a clinical research center was created as the platform to support an NIH Roadmap. The result was a funded \$3.3 million, 3-year project supporting the creation of the Michigan Clinical Research Collaboratory (MCRC), a research infrastructure that will support the design, conduct, and dissemination of community-based clinical translation research. The MCRC depends to a considerable degree on the experience, expertise, and infrastructure in community-based translational research of the Department of Family Medicine.

**CONCLUSIONS** The successful funding of the MCRC grant will support influential translational research programs of high impact and visibility that would not otherwise have occurred. The MCRC grant is an acknowledgment of the important research to be done in the community, the critical nature of infrastructure investment and prior work in competing successfully for such funding, and the personnel and information technology investments required for success. Collaboration between practice-based family medicine investigators and traditional clinical investigators at the University of Michigan has led to successful competition for an NIH Roadmap grant, which has led in turn to greater institutional recognition for the importance and legitimacy of community-based translational research.

*Ann Fam Med* 2006;4(Suppl 1):S49-S54. DOI: 10.1370/afm.538.

*Conflicts of interest: none reported*

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**INTRODUCTION**

Many therapies that are determined to be efficacious in studies conducted in narrowly defined referral populations in academic centers are not necessarily effective in routine clinical practice.<sup>1</sup> As noted by Green, "if we want more evidence-based practice, we need more practice-based evidence."<sup>2</sup> Conversely, important observations and innovations made in primary care settings often go untested in rigorous clinical research investigations; moreover, when practicing physicians are geographically and organizationally distant from research performed in academia, they are less

likely to incorporate either practical findings or dramatic breakthroughs into routine clinical practice.

The National Institutes of Health (NIH) (Research Roadmap<sup>3,4</sup>) reflects the critical need to remedy these problems by reengineering and integrating clinical translational research within academia and bidirectionally among academic venues and community networks. Only then will interdisciplinary investigations address real medical care needs of patients in their home and community settings, account for the complexities of caring for patients with multiple chronic comorbid conditions (which is the norm in community-based primary care but often the basis for exclusion of patients in clinical trials), assess treatment effectiveness in real-life settings, and implement prevention and management strategies that have a positive impact on broader populations of patients.

The request for proposals to which the application described in this paper responded, BAA-RM-04-23, *Re-Engineering the Clinical Research Enterprise: Feasibility of Integrating and Expanding Clinical Research Networks*, is designed to specifically support the development of the collaborative network described in the original Roadmap white paper. The request for proposals is specifically aimed at what NIH calls clinical translation or phase II translation. The term translational research is traditionally defined at NIH to mean translation from the molecular level to usable technology. The often used phrase, "from bench to bedside," defines bedside as being ready for testing in humans. Clinical or phase II translation is the term used for translating to routine clinical practice something that has been tested in humans and found to be safe and effective in a controlled environment.

This article describes the formation of the Michigan Clinical Research Collaboratory (MCRC or Collaboratory). The MCRC is an infrastructure that will enable the conduct of clinical research designed for community-based adoption, implementation, and maintenance from the outset. A critical feature of this approach is to involve community-based implementation settings in research design and data collections throughout the process.

## METHODS

This case study derives from the materials used to develop the successful grant application to the NIH Roadmap initiative already described. The project is early in its second year; first-year deliverables have been met on schedule.

### Setting

The University of Michigan Medical School is consistently ranked among the top 10 to 12 medical schools

for NIH funding, among the top 2 or 3 public medical schools for such funding,<sup>5</sup> and in overall ranking among the top 10 research-intensive medical schools.<sup>6</sup> The medical school is part of an equally research-intensive university (total research funding of \$750 million in 2004).

The Department of Family Medicine is 1 of 20 autonomous clinical departments of the Medical School and Health System. It was formed in 1978 and has grown over the past 27 years to become one of the top-ranked academic departments of family medicine in the country.<sup>6</sup> It has 65 full-time faculty members, an annual budget of approximately \$14 million, a clinical network serving 135,000 outpatient visits annually, 3 major inpatient services including 2 at the University of Michigan Hospitals, a required third-year medical student clerkship, and research programs funded by roughly \$1.5 to \$2 million annually in external grants.

### Organizational Context

The MCRC arose from a collaboration among 2 comprehensive, interdisciplinary clinical and research centers of excellence, the Depression Center and the Cardiovascular Center; 2 related community-based research networks devoted to disease-specific research; a medical school-based clinical research infrastructure, the Center for the Advancement of Clinical Research (CACR); and a large, well-developed primary care practice-based research network, the Great Lakes Research Into Practice (GRIN) network. GRIN consists entirely of primary care practices, mostly privately owned and widely distributed across Michigan. GRIN<sup>7</sup> is the major statewide primary care practice-based research network (PBRN) in Michigan, with more than 150 family physicians, general internists, pediatricians, obstetricians, and independent-practice nurse-practitioners. GRIN practices are approximately equally distributed among urban, suburban, small-town, and rural locations, and patients are demographically representative of Michigan's population.

GRIN resulted from the merger of 3 existing PBRNs in Michigan. The merger and initial development of GRIN were supported by a grant from the American Academy of Family Physicians to the joint Michigan State University–University of Michigan Michigan Consortium for Family Practice Research (MCFPR), and by a PBRN infrastructure grant from the (now) Agency for Healthcare Research and Quality. The collaboration required for the success of the MCFPR was critical for the subsequent success in organizing and operating GRIN.

GRIN is staffed by part-time faculty and staff members supported in kind by the 2 Michigan universities involved in the MCFPR. The 2 collaborating institutions contribute operational funds, such as funds for mailing and computer support. GRIN is overseen by a board that includes the chairs of the family medicine

departments at Michigan's 3 allopathic medical schools, 2 community physicians, and a patient representative.

GRIN's primary mission is clinical translational research, both the translation of evidence into practice and the generation of practice-based evidence. Proposed GRIN research projects are evaluated by a scientific review panel composed of 3 members with study section experience and a community physician with PBRN experience. GRIN projects are carried out in (and often planned by) member practices and typically emphasize the testing of effectiveness and external validity over efficacy and internal validity.<sup>8</sup>

Like many community physicians, GRIN members are understandably reluctant to let the conduct of research adversely affect clinical quality and routine work flow. They seek not only to mitigate such impact but also to gain actual added value for their practices. They therefore generally insist that the systems the network develops, "human" or informatics, should enhance the quality and stature of their clinical practice. These principles have informed the design of the MCRC accordingly.

### Historical Context

The Department of Family Medicine has labored, somewhat in obscurity relative to the larger institutional research enterprise, to develop a strong and viable research infrastructure in community-based research. Several department research themes are invested in community-based and practice-based methodologies, including screening for colorectal and cervical cancer; the improvement of the care of patients with depression in primary care settings<sup>9,10</sup>; the improvement of the care of patients with asthma, chest pain,<sup>11</sup> and hypertension<sup>12</sup>; and community-based epidemiologic studies of human papillomavirus infection. The department has supported considerable infrastructure development and unfunded research, conservatively estimated to exceed \$2 million over the past 10 to 15 years. Five community-based externally funded projects are currently active.

The success of this wide range of community-based and practice-based studies is enhanced by ClinfoTracker,<sup>13</sup> a sophisticated computer-based structured problem list and clinical reminder system designed to support both real-time clinical quality improvement and research studies in primary care practices. The initial development of ClinfoTracker in 1993 and subsequent enhancements have required department support exceeding \$1 million. In addition, considerable support has been provided to support faculty members collaborating with the American Academy of Family Physicians, The Robert Graham Center, and the World Organization of Family Doctors (Wonca) in the development of the International Classification of Primary

Care,<sup>14</sup> a basic science platform of disease classification critical to the success of clinical translation.

ClinfoTracker is designed to exchange data easily with other information systems. It uses demographic information and chronic problem lists to determine appropriate chronic care and preventive health care services recommended by published guidelines, and compares those benchmarks against actual care delivered as reflected in electronic health records, billing data, and locally maintained data. It produces hard copy or Web-based reminders at patient visits, generates reminder lists for nurses or other staff to use in proactively contacting patients, and prints reminder letters for patients. ClinfoTracker can print almost any document, such as a depression screening questionnaire, patient education materials, or research study enrollment criteria, at the time of visits or for mailing to patients.

ClinfoTracker's relatively straightforward implementation in practices both with and without electronic medical records, its sound information technology (IT) architecture, and its flexible set of products made it a very suitable choice for the practice-based infrastructure of the Collaboratory.

## RESULTS

### Grant Development Process

The University of Michigan CACR (described below) led the initial development of a University of Michigan-based application designed to connect several research centers, but it soon became apparent that a stronger connection with community practices was required. Through a variety of informal working relationships, particularly through the Depression Center with which the Department of Family Medicine is substantially involved, CACR investigators learned of the department's clinical translational research focus and partnership in GRIN, at which point a senior department investigator (LAG) was invited to join the grant team. Contributions by the department thus derived less from its department research programs and more from its leadership of GRIN. The RE-AIM model<sup>8</sup> (Reach, Efficacy/Effectiveness, Adoption, Implementation, and Maintenance) influenced the grant development team to shift its approach from viewing practices as laboratories to viewing them as collaborators and sources of insight that would improve research.

GRIN became the keystone to the project's design and eventual success. Additionally, ClinfoTracker's ease of dissemination and use, and its clean 3-tier architecture, which makes powerful connections to other information systems relatively easy, made it the immediate choice for the practice-based IT component of the MCRC.

## Organizational Structure

The MCRC is a 3-year, \$3.3 million demonstration project designed to show that a university-community partnership and infrastructure can successfully link university-based, disease-specific research centers and networks of community physicians in a clinical translation enterprise.

The overall objective and aims of the MCRC project are as follows:

1. Reengineer clinical research processes at the university by integrating established and functional primary care research networks (ie, GRIN), academic research centers of excellence (Depression Center and Cardiovascular Center), and a clinical research infrastructure (CACR)
2. Develop an integrated informatics network to address the needs of both academic and primary care community networks, with the capability to incorporate additional research networks in the future
3. Conduct a feasibility project demonstrating that the reengineered network can successfully design and carry out clinical investigations in a bidirectional translation between academic and community-based primary care domains
4. Assess the strengths and weaknesses of the processes and IT systems using the results of the feasibility project
5. Disseminate findings, tools, and strategies from this project to other reengineered networks and research centers, and ultimately interface with National Electronics Clinical Trials and Research (NECTAR)

The clinical research infrastructure, CACR, is a unit funded by the medical school to support the development of clinical research. One of the functions of CACR is to identify external funding opportunities to which the medical school or university should respond, identify faculty members who could lead such efforts, and assist in the preparation of grants. This organizational entity and its associated development process worked particularly well in the case of this grant, as both the grant application and actual performance of the funded study represent a partnership between CACR and faculty members from family medicine, psychiatry, and cardiovascular medicine, with the CACR as a catalyst.

The basic structure of the MCRC is a new infrastructure that networks together the CACR, the University of Michigan Depression Center, the University of Michigan Cardiovascular Center, and GRIN. The disease-specific research networks in depression and cardiovascular disease will supplement research in those areas, although not in a direct connection with GRIN. The 3 central infrastructure elements that provide the operational connections are ClinfoTracker, an electronic clinical trial support system, and a new

"Honest Broker" information system hub that can pass information securely between them in a manner compliant with the Health Insurance Portability and Accountability Act (HIPAA).

## Role of the Department of Family Medicine

The Department of Family Medicine played a key role in developing and now implementing the MCRC grant. Without GRIN, the University of Michigan would have been substantially less competitive in an NIH grant initiative that is now famous for its intense competition. GRIN's eventual critical contribution to the success of the BAA proposal could not have been foreseen in the early years of its development, but those early efforts have paid enormous dividends with these new linkages.

Several faculty members of the Department of Family Medicine were key players in developing the proposal, including one who held a leadership role in the Depression Center's depression-specific PBRN that supports a major Robert Wood Johnson Foundation project. For a variety of institutional and political reasons, leaders from the Depression Center and CACR originally served as principal investigators for the NIH grant application, but that leadership has now been appropriately turned over to one of the coauthors (LAG) as co-principal investigator with primary responsibility for grant implementation. The department thus provided infrastructure resources, methodologic and conceptual creativity, grant-writing and grant preparation expertise, and grant leadership expertise in bringing this critical institutional venture to successful fruition.

The MCRC's contributions to University of Michigan missions are profound. The Collaboratory provides an infrastructure for clinical research projects of a size and nature that will compete far better for funding than was previously the case, including an application currently in development to the Clinical Translational Science Award (CTSA) program.<sup>1</sup> Less obvious, but perhaps more profound, is its influence on changing a fundamental research paradigm (one not unique to the University of Michigan). The Roadmap white paper itself<sup>3,4</sup> addresses the need to make this paradigmatic shift, which concerns the traditional 1-way communication from academic investigator to community physician. The questions addressed, the methods chosen, and the implementation of results have traditionally flowed in this 1-way manner, with little or no 2-way conversation. The Roadmap, in general, and the MCRC, in particular, emphasize the critical importance of enfranchising community-based clinicians to inform and influence the research agenda. This bidirectional flow of communication and influence is a little-appreciated feature of such partnerships with PBRNs and of the MCRC proposal.

## DISCUSSION

### Lessons Learned

The University of Michigan offers considerable added value to any initiative to reengineer a clinical research enterprise. It is a world-class research-intensive university with strengths in many areas of clinical and basic science research. GRIN and the associated disease-specific PBRNs have already demonstrated success in developing effective and mutually beneficial relationships with academic colleagues. Together, the constellation of more traditional academic and less traditional community-based resources and expertise provides a firm foundation on which to build the MCRC. It is strongly expected that clinical translation research portfolios will grow and provide a strong foundation for even larger translational ventures. When coupled with the existing "human process" bridges, the IT progress to date, and the enthusiastic endorsement of institutional leaders, there is strong likelihood that the Collaboratory will make critical contributions to reengineering the entire biomedical research enterprise, locally and perhaps nationally.

The lessons learned to date include the following:

1. Successful application to the NIH Roadmap initiative required the full partnership of the Department of Family Medicine and its expertise and experience in PBRNs and information systems appropriate to primary care.

2. Institutions that are research intensive in traditional basic and clinical science arenas may have an advantage in moving to major phase II translational research initiatives, such as the current CTSA initiative,<sup>1</sup> if they can partner with, recruit, or otherwise engage experienced community-based and practice-based investigators in 2-way partnerships.

3. Practice-based research requires the same level of investment and infrastructure as is required by basic science research, although the investment is made more in human and IT resources than in bench ("wet") laboratory facilities.

4. Leadership is critical to the success of developing and funding systemwide research ventures like this and must often come from the institutional level, such as a medical school dean or health system executive, rather than from a department as is often true for traditional basic and clinical science ventures.

5. The emphasis on community-based translation is coming at an extraordinarily opportune moment for academic family medicine, but the reason this type of research has been poorly developed in the past is due, to a considerable extent, to its difficulty and expense.<sup>15</sup> The amount of unfunded work required to develop the necessary infrastructure to be competitive for such grant initiatives may be prohibitive in most institutions (Table 1).

**Table 1. Timeline, Development Activities, and Investments for Positioning a Family Medicine Department to Participate in Large-Scale Institutional Research Initiatives**

Timeline	Faculty Development	PBRN Development
Years 1-4	<ul style="list-style-type: none"> <li>Recruitment of initial cadre of faculty members with research training</li> <li>Initial development of research skills and working experience</li> <li>Small unfunded research projects</li> <li>Small research projects funded by grants covering less than full direct costs (pilot funds, institutional seed money)</li> <li>Moderate grants from foundations and funding agencies with minimal to no indirect cost recovery</li> <li>Support for faculty travel and attendance at national research meetings, developing contacts, and understanding research culture</li> </ul>	<ul style="list-style-type: none"> <li>Launch of network by a small group of enthusiastic practices</li> <li>Basic information gathering, card studies</li> <li>Leadership and administrative support informally assigned and funded by university or state academy support</li> </ul>
Years 5-8	<ul style="list-style-type: none"> <li>Expansion of department research infrastructure, project management support, statistical and methodologic expertise</li> <li>Substantial external funding, larger foundation grants, smaller federal grants (eg, R03, R21 grants)</li> <li>NIH investigator grants (eg, K grants)</li> <li>Development of project management skills</li> <li>Service on institutional committees (eg, IRB, practice guidelines committees)</li> </ul>	<ul style="list-style-type: none"> <li>Substantial investment (\$60,000 to \$280,000/y) in dedicated personnel, space, travel for practice recruitment, and maintenance</li> <li>Recruitment of large numbers of practices with varying levels of participation</li> <li>Health services research studies and clinical trials</li> <li>Increasing size and sophistication of grants, with small amounts of network infrastructure support</li> </ul>
Years 9-12	<ul style="list-style-type: none"> <li>Large project and program grants (eg, R01 and P grants)</li> <li>Service on study sections, national leadership positions</li> <li>National network of contacts</li> </ul>	<ul style="list-style-type: none"> <li>Multiple, externally funded concurrent studies</li> <li>Increasing grant support for secretarial, financial, and administrative personnel</li> <li>Continued support needed for network expansion and maintenance</li> </ul>
Year 13 onward	<ul style="list-style-type: none"> <li>Participant and leadership roles in major cross-departmental and institution-wide projects (eg, center grants)</li> </ul>	

PBRN = practice-based research network; NIH = National Institutes of Health; IRB = institutional review board.

Perhaps the most important consequence of the successful competition for the BAA grant and the subsequent early development of the MCRC is the realization by both the traditional research community and the practice-based investigators at the University of Michigan that using a "mutual gains" strategy for competing for major grant support can lead to influential research programs of high impact and visibility that would not otherwise have occurred if these 2 research cultures were left to work in separate spheres.

## Conclusion

At the University of Michigan, collaboration between practice-based researchers in the Department of Family Medicine and traditional basic science and clinical investigators has led to successful competition for an NIH Roadmap grant supporting the development of the MCRC, a clinical translation infrastructure designed to connect in operational, informational, and philosophical ways a community-based and medical center-based research infrastructure that will support a new and exciting era of clinical translational research.

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**Key words:** Translational research; practice-based research; NIH Roadmap; academic medical centers; collaboration; family medicine; primary care; community health care

Submitted September 22, 2005; submitted, revised, February 2, 2006; accepted February 13, 2006.

This paper was presented in part at the annual meeting of the Association of Departments of Family Medicine, November 5, 2005, Washington, DC.

**Funding support:** This work was funded in part by National Institutes of Health grant N01-HC-45219.

**Acknowledgments:** The authors acknowledge the critical contributions of Daniel J. Clauw, MD, Professor of Internal Medicine and Director of

the Center for the Advancement of Clinical Research, who was the driving force and initial Principal Investigator for the grant described in this case report.

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