



Published in final edited form as:

WMJ. 2009 December ; 108(9): 453–458.

The Wisconsin Network for Health Research (WinHR): A Statewide, Collaborative, Multi-disciplinary, Research Group

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Abstract

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Financial Disclosures: None declared.

In response to the goals of the Wisconsin Partnership Program and the National Institutes of Health (NIH) Initiatives to Improve Healthcare, the Wisconsin Network for Health Research (WiNHR) was formed. As a collaborative, multi-disciplinary statewide research network, WiNHR encourages and fosters the discovery and application of scientific knowledge for researchers and practitioners throughout Wisconsin. The 4 founding institutions—Aurora Health Care/Center for Urban Population Health (CUPH), Gunderson Lutheran Medical Foundation, Marshfield Clinic Research Foundation, and the University of Wisconsin-Madison—representing geographically diverse areas of the state, are optimistic and committed to WiNHR's success. This optimism is based on the relevance of its goals to public health, the quality of statewide health care research, and, most importantly, the residents of Wisconsin who recognize the value of health research.

BACKGROUND AND OVERVIEW

Wisconsin has a long history of innovative health care research leading to changes in clinical practice. A few examples include the Wisconsin Longitudinal Study, which collected extensive health and social information from a random sample of 10,317 people;¹ the Wisconsin Epidemiological Study of Diabetic Retinopathy, which described the frequency, incidence, and risk factors for complications associated with diabetes;²⁻³ the Wisconsin Cystic Fibrosis Neonatal Screening Project, which screened more than 1 million Wisconsin infants;⁴ and, more recently, the Marshfield Clinic Research Foundation's Personalized Medicine Research Project, which resulted in one of the largest (approximately 20,000 participants) health care genetics databases in the world.⁵⁻⁶

The value of clinical research to foster medical discovery and to confirm best medical practice is self-evident. The National Institutes of Health (NIH) Roadmap Initiatives propose “re-engineering the clinical research enterprise” to increase the efficiency and effectiveness of clinical research and the pace of discovery.⁷⁻⁸ The societal imperative behind the desire to improve the efficiency of clinical research comes from 3 main premises about the future: (1) a rapid increase in the scope and rate of biomedical discovery, (2) growing public demand for clinical applications of biomedical discoveries, and (3) increasing calls to ensure equity in the availability of improvements in health care. The ability of clinical research to promote equity in health care availability is frequently underappreciated. Most evidence-based improvements in health care are implemented slowly and inconsistently;⁹ however, clinicians who participate in health care-related studies are most likely to incorporate evidence-based improvements more rapidly into their clinical practice.⁸

Improving the efficiency of clinical research is an important goal. One proposed way to increase efficiency is through more effective “regionalization” of research (more cooperative efforts among multiple regional medical facilities). For more than 4 decades, clinical practice has become increasingly reliant on evidence-based medicine. This evidence comes from a variety of sources, including observational studies, but the most definitive evidence comes from clinical trials, especially multi-center, randomized clinical trials. To facilitate clinical trials, many interested clinicians formed regional or national groups (cooperative groups within a disease/discipline or groups of clinical research centers organized for a specific trial). However, these research groups were often subspecialty-specific or transient. As a result, centers interested in research had either a varied portfolio of research options from different sponsors with different policies, standards, and data management requirements, or no portfolio at all. Increasing regulatory requirements, system redundancies, and the lack of wider availability/participation contribute to the inefficiencies of this ad hoc approach. Thus, there is a compelling need for more effective regionalization of research.

Wisconsin is an ideal arena for evaluating health care strategies. This is exemplified by the Cancer Intervention and Surveillance Network's examination of modeling data collected from

various states, which found that Wisconsin data closely represented composite data from across the country. Wisconsin citizens are traditionally interested in health, health care, and disease prevention, as shown by high research participation rates.¹⁻⁶ Moreover, the Wisconsin population is very stable, with small out-migration, which allows more accurate monitoring and follow-up of study participants.

The above social and demographic factors, coupled with the excellent health care facilities and outstanding research institutions in Wisconsin, led us to pursue building a statewide health care research network. Four large, multi-specialty health care groups united to form WiNHR in 2005 as an initial step toward establishing a statewide research network. These 4 institutions provided significant coverage of the state both in terms of population (>3 million residents) and geographically (>50 counties). Additional financial support was provided by the Wisconsin Partnership Program and the University of Wisconsin (UW) Institute for Clinical and Translational Research. WiNHR has the following goals:

- Improve health in Wisconsin.
- Improve consumer and physician access to state-of-the-art therapeutics/preventive care and up-to-date knowledge through clinical trials and web-based resources.
- Improve health care professional and researcher access to larger academic center resources.
- Enhance ability for evaluating new health care interventions.
- Establish new or improved collaborative relationships among medical centers throughout the state.
- Increase cross-discipline exploration and discovery.
- Facilitate trainee education in health-related sciences at sites across the state.
- Form a multi-disciplinary, statewide research infrastructure that researchers could use as needed.

NETWORK IMPLEMENTATION: OPPORTUNITIES AND CHALLENGES

The development of a statewide health research network like WiNHR is consistent with the NIH Roadmap for Medical Research⁷⁻⁸ and holds great potential to enhance integrated and collaborative opportunities. Some of the main recommendations of the NIH Roadmap include greater interdisciplinary research, increased regionalization of research, and better integration of existing single discipline research networks. The potential success of a multi-disciplinary statewide research network in Wisconsin is reinforced by this alignment of WiNHR with the NIH Roadmap. The long history of successful single-discipline research networks in the state (eg, Wisconsin Research and Education Network [WREN], Wisconsin Oncology Network) also suggests the potential for WiNHR success. However, there are both unique and common challenges to overcome as we build an effective and durable statewide health research network including building and fostering communication and relationships, human subject protection, intellectual property, governance, informatics, funding, and expansion. Table 1 lists some of the hurdles encountered to date and solutions that were implemented. Foremost among problems that were resolved were (1) establishing memorandums of understanding that covered transfer of funds to support WiNHR and detailed responsibilities of the founding members, (2) coordinating IRB approval across 4 institutions, and (3) completing material and data-transfer agreements.

Establishing Partnership

One of the first and most important steps in uniting a group of institutions toward a common goal is building trust in the mutual benefit for participants and the common purpose of conducting research to improve the health of Wisconsin. Part of the trust developed in the WiNHR mission and governance results from the decision to undertake initial planning and implementation as a group operation, rather than having 1 institution assume all planning and implementation before asking others to participate. In addition, all participants have an opportunity to comment on proposed research prior to implementation, choose which research projects they participate in, and receive credit/acknowledgment for their participation through authorship on research reports. Mutual benefit is pursued via related paths including performing health research that is pertinent to all Wisconsin residents, broadening opportunities for participation in research through conduct of the research at multiple institutions, and performing research of interest to the majority of the participating health care professionals.

Table 2 shows a list of completed or ongoing WiNHR studies. The study *Genetics of Warfarin Dosing* was proposed by researchers at Marshfield Clinic Research Foundation. These investigators spent years developing models in white subjects that predict stable warfarin dose based on genetic markers as well as personal factors like age and body surface area.¹⁰ To extend these studies and potentially improve the health of blacks, blacks were recruited from the Milwaukee area by investigators at Aurora Health Care/Center for Urban Population Growth (CUPH). Results from this study have been provided to PharmGKB (www.pharmgkb.org) and will be published as part of a national collaboration.

The study *Infectious Disease and Pre-term Labor* was proposed by investigators at Gundersen Lutheran Medical Foundation, who had investigated genital mycoplasmas among sexually active young adults in the La Crosse, Wisconsin area.¹¹ These investigators realized the importance of extending their studies on mycoplasma and pre-term labor to the other sites in WiNHR in order to gather data on distinct regions of the state as well as minority populations that are not prevalent in La Crosse. This study is being performed by UW physicians at Meriter Hospital, where a significant portion of the patients are under-served minorities; at Aurora/CUPH, where a significant portion of the patients are black; and at Marshfield Clinic Research Foundation to cover the northern part of the state.

These 2 projects highlight the potential translational value of WiNHR projects for Wisconsin's residents. The *Pre-term Labor* study is directly applicable to a pertinent Wisconsin health issue—infant mortality. The *Genetics of Warfarin Dosing* study is similar to prior studies on the impact of genetics on warfarin dosing that resulted in a change in warfarin labeling by the Food and Drug Administration.

Human Subjects Protection

The protection of human research subjects from unacceptable risk is critical both to performing high-quality clinical research and to maintaining the trust of the community being studied. A hallmark of human subjects' protection is the tension between applying universal protection rules versus local community standards. The application of human subjects protection at a single institution can be complex; the application across multiple, linked groups raises even more issues. Is the community standard from institution to institution similar enough that differences in acceptable risk are rare and easily resolved when they do occur? How much does redundancy in the review process across multiple sites negatively affect research efficiency?

Not unexpectedly, our multisite research group has found the review process for protection of human subjects cumbersome. This has led to expedited discussions between institutions to

make the review process across our sites more efficient and less redundant. Some of the measures being discussed include more standardization of clinical research protocols and consent forms across participating sites, and having an Institutional Review Board (IRB) at 1 WiNHR site (usually the Principal Investigator's site) serve as the lead IRB for all sites. Local review of protocols continues, but the lead IRB takes the responsibility for regulatory oversight, rather than individual participating sites. National examples of other procedures to improve the review process across multiple sites already exist. These include use of a single, private IRB by multiple sites or deferral to a federal, disease-specific IRB for specific studies (eg, National Cancer Institute's IRB). These ongoing national examples offer multiple options for our statewide research network to consider.

Intellectual Property

When research ideas are generated from multiple institutions, any individual site's intellectual property related to an idea or health care device should not be jeopardized by inclusion in the group. WiNHR researchers have agreed that ideas initially proposed by 1 site will not be pursued by the other sites independent of WiNHR. WiNHR's charter includes specific language relative to intellectual property to emphasize the importance placed on avoiding conflicts related to intellectual property.

Governance

Longstanding, successful single-discipline research groups invariably have an agreed-upon governance plan built on the core values of mutual benefit and trust. Effective governance also requires establishing central authority/responsibility to assure adherence to joint policies, completion of regulatory requirements, and performance of high-quality health research. Central responsibility allows a research group or network to accommodate varying degrees of experience from site to site and from researcher to researcher. WiNHR governance is accomplished by an executive committee in the form of agreed-upon standard operating policies and procedures. The executive committee is composed of equal representation from the institutions and is the central authority in WiNHR, providing review and final decisions on bylaws, standard operating procedures, funding, and specific health care research performed within the group.

Medical Informatics

An increasingly important component of modern health care delivery and research is the secure and efficient transmission of either critical health information or research data. This is especially true for a network of health research sites jointly collecting and reporting research observations. Critical issues are the ability of lead investigators to access ongoing data collection at any site from any location, the ability to monitor data quality, and the ability to efficiently compile data within and across studies. This is currently being pursued by WiNHR via proprietary research database software designed to provide a web-based system to securely provide and maintain all relevant study and subject characteristics plus all data normally collected on a case report form (CRF).

Electronic medical records (EMR) are 1 example of the informatics opportunities provided by networked health research. Marshfield Clinic has been at the forefront of incorporating EMRs and exploring ways to integrate electronic records into health research (eg, Personalized Medicine Research Project). There is a huge potential research value in being able to electronically survey health outcomes/events for up to 3 million Wisconsin residents across health care groups' EMR systems without requiring hundreds of hours to manually extract or de-identify data.

Funding

Currently, WiNHR is funded by the UW School of Medicine and Public Health from the Wisconsin Partnership Program, with supplemental funds provided by the UW Institute for Clinical and Translational Research and “in-kind” funds from Marshfield Clinic Research Foundation, Aurora Health Care/CUPH, and Gundersen Lutheran Medical Foundation. Other potential sources of support include federal and non-federal reimbursement for research performance. Whether WiNHR can or should try to become entirely funded from research performance is debatable. The advantages of self-sufficiency, like greater administrative autonomy, are apparent. However, self-sufficiency may come at the cost of performing research that is not a priority for the state’s residents or researchers. An effective funding mixture might include both stable infrastructure funds supplemented by research performance reimbursement. Given the potential benefits of research for improving cost-effective health care delivery in Wisconsin, current health care payers (eg, the health insurance industry or state) might be willing to underwrite core services. At a minimum, infrastructure support should include administrative and regulatory research personnel at numerous sites across the state. Ideal infrastructure costs might include “buying out time” of key researchers around the state as long-term local advocates of health care research. Unfortunately, in the current fiscal climate, such costs may exceed available funding.

Expansion

While the current composition of WiNHR provides greatly enhanced access for the state’s residents to health research participation and benefits, further improvements are slowed by the participation of only 4 health care systems. As a first step in expansion, WiNHR partnered with WREN. This partnership benefits both organizations since WiNHR research projects can now be carried out in participating primary care physician offices statewide, and WREN studies can reach additional patients at WiNHR sites. To ensure continued success in this collaboration, the executive director of WREN holds a voting seat on the WiNHR executive committee. Additional expansion of WiNHR will occur to allow quality health care and health care research to reach beyond the current members of WiNHR. A continued goal of WiNHR is greater access and inclusivity throughout the state. Recruitment of other groups will be balanced against current funding and regulatory constraints.

Completed Study Presentations

Research study outcomes will be disseminated across the state through publication of manuscripts and presentations at state meetings. Examples of relevant forums include WREN convocations, UW Institute for Clinical and Translational Research (ICTR) Research Learning Series, and Grand Rounds at Aurora Health Care, Marshfield Clinic, and Gundersen Lutheran Clinic. Publications may be presented in peer-reviewed journals, including the *Wisconsin Medical Journal*, *Clinical Medicine and Research* (Marshfield Clinic Research Foundation), and *Gundersen Lutheran Medical Journal* (Gundersen Lutheran Medical Foundation).

SUMMARY

The preceding issues are a subset of those this group has encountered and addressed moving toward its stated goals. WiNHR was founded on and will continue to seek the full support of the leadership of current (and future) participating health care groups. One major determinant of success will be the perceived value each clinician and each potential research subject has in health research. Other measures of success will be credit attributed to WiNHR as new drugs, protocols, or technologies enter clinical practice and advancements in health care are made across the state. Thus one of the most important tasks of WiNHR researchers is articulating to busy clinical colleagues the advantages of clinical research participation to their clinical practice and individual patients. Another important task is the ability of WiNHR researchers

to translate research knowledge into improved health of our communities at local sites and across the state.

Acknowledgments

The authors wish to acknowledge the following individuals and institutions for their valuable assistance in establishing this collaborative research network: Deborah L. Brostrom, Gundersen Lutheran Medical Foundation, La Crosse, Wis; Laila Borokhim, Ann Schensky, and Valerie Schend, University of Wisconsin, UW Hospitals and Clinics, Madison, Wis; Patrick Falvey, PhD, Senior Vice President and Chief Integration Officer, Aurora Health Care, Inc.; George Hinton, MBA, Vice President of Operations, Aurora Sinai Medical Center, Aurora Health Care, Inc.; Bruce VanCleave, MD, Senior Vice President of Academic Affairs, Aurora Health Care, Inc.; Melissa Lemke, BS, Associate Research Specialist, CUPH; Trina Salm Ward, MSW, CICC, Research Program Manager, CUPH, UW School of Medicine and Public Health; and Jane Carl, CCRC Clinical Research Manager Marshfield Clinic Research Foundation. The authors thank Marshfield Clinic Research Foundation for its support through the assistance of Marie Fleisner in the preparation of this manuscript.

Funding/Support: The Wisconsin Network for Health Research (WiNHR) is funded by University of Wisconsin School of Medicine and Public Health and the Medical Education and Research Committee (MERC) Fund of the Wisconsin Partnership Program for a Healthy Future. Howard Bailey, MD, also indicated that he has a financial interest and/or other affiliation or arrangement with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject or content of this article.

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Table 1

Challenges and Solutions to Building a Statewide Research Network

Challenge	Solution
Establishment of the network	Memorandum of understanding
Funding	Wisconsin Partnership funds
Intellectual property protection	Memorandum of understanding
Human subjects protection	Institutional Review Board (IRB) administrators conference calls
	Universal Material Transfer Agreements
	Centralized study coordination
	Statewide IRB with deferral process
Credit for multiple investigators	Authorship policy
Biological sample ownership	Tissue policy
Network growth and expansion	Expansion of Central Administration
Human subjects protection with additional community members	To be determined
Subject enrollment and data management	Oncore data management system, a secure web-based electronic database

Table 2

Completed and Ongoing WiNHR Studies

Study	Participating Sites
Chronic Kidney Disease Focus Groups	WREN, UW, GL, CUPH, MCRF
Infectious Disease and Pre-term Labor	UW, GL, CUPH, MCRF
Genetics of Diabetes	UW, CUPH, MCRF
Genetics of Scoliosis	UW, GL, MCRF
Vertebral Malformations	UW, GL, MCRF
Azithromycin Asthma Trial	WREN, UW, CUPH, MCRF
Genetics of Warfarin Dosing	CUPH, MCRF
COPD and Heliox	UW, MCRF

Abbreviations: CUPH, Aurora Health Care/Center for Urban Population Health; GL, Gundersen Lutheran Medical Foundation; MCRF, Marshfield Clinic Research Foundation; UW, University of Wisconsin-Madison; WREN, Wisconsin Research and Education Network.