



Stanford Center for
Biomedical Informatics Research

Connection

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Winter 2022

We Connect Data to Health

Collaborating with the NIH

Despite our best hopes for an end to the pandemic, as 2022 begins, we continue to concentrate on COVID-19. No institution is more focused on that than the National Institutes of Health (NIH).

As you will read below, BMIR is aiding that effort through the Rapid Acceleration of Diagnostics (RADx) initiative, which the NIH launched to speed the development, validation, and commercialization of innovative point-of-care and home-based tests, as

well as improve clinical laboratory tests, that can directly detect the virus.

In collaboration with the Broad Institute and the Renaissance Computer Institute at the University of North Carolina, BMIR will extend the RADx Data Hub to incorporate updated, standardized metadata descriptions, which will ensure that the information can be used reliably to perform new scientific research to support COVID-19 testing.

Our commitment to building truly useable software presents us with opportunities to engage in collaborative research that enables BMIR to partner with a host of organizations to develop practical solutions to real-world problems.

Mark Musen, MD, PhD
Director, Stanford Center for Biomedical Informatics Research

RESEARCH

BMIR to Help Improve COVID-19 Testing Under RADx Initiative Through NIH

BMIR will be contributing to development of metadata and semantic solutions to help the [National Institutes of Health \(NIH\)](#) improve COVID-19 testing. The work is being performed under a four-year, \$6 million contract as part of the NIH [Rapid Acceleration of Diagnostics \(RADxSM\)](#) initiative.

BMIR is pursuing a strategy to consolidate all research data and metadata for the RADx program into a single repository so that all its medical information will become much more findable, accessible, interoperable, and reusable, or [FAIR](#). The work on this RADx Data Hub supports ongoing research efforts to advance the ability to combat future outbreaks of COVID-19 and other infectious diseases.

“For many years BMIR has been advocating for strategies, tools, and approaches for dealing with metadata and semantics. Our involvement in this project gives us a chance to apply all of those standards, and the project’s success will validate them,” said BMIR Director Mark Musen, MD, PhD.



“In addition to what RADx participants expect to learn, harmonized and precise metadata will allow much more re-use of these results,” added John Graybeal, BMIR project manager. “And many of the approaches that researchers will consider for COVID-19 testing could potentially be used for many other kinds of diseases.”

By reusing its [CEDAR](#) and [BioPortal](#) systems, BMIR expects to complete a first version of the metadata and semantics components of the RADx Data Hub during the first half of 2022. The next three and a half years will be spent refining that system and improving the metadata submissions that it contains.

If the work proves scalable, then it should generate increased interest from the NIH and other organizations in the techniques, technologies, and approaches that BMIR is using for metadata and semantics.

Because Congress allocated considerable money into quick turnaround COVID investigations, the RADx initiative has greater national visibility than many NIH projects.

“If we can achieve the goal of making the data readily findable, available and reusable, then that will generate a positive response within and beyond the entire RADx community. That includes all the RADx principal investigators, all the existing RADx data coordination centers, the NIH, and even Congress,” Graybeal said.

The NIH requested that BMIR work on the project with two other entities. The Broad Institute is handling all the infrastructure aspects, and the Renaissance Computer Institute (RENCI) at the University of North Carolina is focused on the project management. In addition, the GO FAIR Foundation is supporting BMIR by providing training for this community.

Building on the success of existing partnerships with the departments of Medicine, Neurosurgery, Neurology, Pediatrics, and Pathology, the [Quantitative Sciences Unit \(QSU\)](#) is currently recruiting a faculty member who practices data science for Emergency Medicine.

“The entry into Emergency Medicine demonstrates the increasing appreciation of the QSU’s value,” said BMIR Director Mark Musen, MD, PhD.

The goal of the partnerships is to build out the research infrastructure where needed in the School of Medicine by leveraging the entire QSU to help meet the needs of the particular department. At the same time, the department’s new faculty member will be developing their own lab and growing their career.

Maya Mathur, PhD, is a good example. Simultaneous with her 2019 appointment as an assistant professor in the QSU, she joined the Department of Pediatrics as an assistant professor, focused on causal

inference and evidence synthesis methods. “As a recent recipient of a Research Project (R01) Grant from the National Institutes of Health on her first submission, Maya is furthering maternal child health related research through novel study design and optimal application of methods,” said Manisha Desai, PhD, Director of the QSU.

“Addressing complex biomedical questions requires quality data science at the faculty level. When I established the QSU in 2009, I saw a need for high quality scientific engagement with quantitative experts who were faculty, and I shared that thinking with other entities in the School of Medicine.

“Departments that establish a partnership with the QSU allow us to mentor one of their faculty so they can grow professionally, build research infrastructure, and develop their own lab into a thriving unit. The joint appointment within the QSU also gives the faculty member a cohort – an intellectual community – of other practicing data scientists that can act as a sounding board, because it’s lonely as a single quantitative



scientist in a clinical department and the departmental faculty resources may not be tailored toward growth as a data scientist.

“Different departments have very specific types of biomedical questions they want to address, all concerning how to improve human health, how to improve delivery of care, and other multifaceted areas. So, we need statisticians, epidemiologists, computational biologists, and informatics experts at the forefront, partnering with the clinicians, to be able to answer those complex questions. It is very much aligned with the mission of the School of Medicine,” Desai said.

EDUCATION AND TRAINING Fostering Informatics in the Community



A course in implementing clinical informatics solutions is preparing future bioinformatics leaders to make substantive changes in health care communities.

The course was the brainchild of Albert Chan, MD, Chief Digital Health Officer for [Sutter Health](#), a health care system serving three million patients in Northern California. Dr. Chan devised “[Biomedicine 226: Digital Health Practicum in a Health Care Delivery System](#)” as thanks for the excellent education he received some 20 years ago as

an informatics trainee under BMIR Director Mark Musen, MD, PhD, and his thesis advisor, Mary K. Goldstein, MD, MS.

Biomedicine 226 enables students to learn practical aspects of informatics projects that support the use of electronic health records, engagement of patients and providers via a personal health record, the use of patient service centers, and improvement of patient access to clinical data.

As an adjunct professor in BMIR, Dr. Chan teaches the course with Veena Jones, MD, Sutter Health’s medical director of Digital Health and a Stanford affiliated faculty member. They select one student per quarter to augment their formal informatics education with a hands-on, in-the-trenches look at digital health in an integrated health care delivery system.

Students in the course may also pursue an individualized informatics project. As an example, Nicolai Ostberg, a bioinformatics master’s candidate, worked with Stanford Children’s Clinical Informatics fellow

Keith Morse, MD to evaluate an artificial intelligence-powered symptom assessment tool Sutter Health recently deployed for its patients. The project ultimately resulted in a peer-reviewed academic [publication](#) in the *Journal of Medical Internet Research*.

While BMIR benefits from the partnership with Sutter Health, the program is symbiotic.

“Solving big problems like improving access to care depends on getting new ideas, which we get from our BMIR students. They ask questions that make us reconsider how we do things, and they offer suggestions that can lead to innovations for the good of our patients,” Dr. Chan says.

Another student had a front row seat for Sutter Health’s 2020 telemedicine deployment, which was accelerated due to COVID-19. The student observed the practical skills that future informatics leaders need to thrive in their careers, such as leadership, change management, communication, meeting facilitation, and negotiation.

Gevaert Lab Uses Tool Developed for Cancer Prognosis to Predict Severity of COVID-19 and Other Diseases

Machine learning techniques developed in the lab of Olivier Gevaert, PhD, for the prognosis of cancer patients are now being used to triage COVID-19 patients.

Previously, Dr. Gevaert led a team of researchers in biomedical informatics, radiology, data science, electrical engineering, and radiation oncology to create a machine learning tool called [LungNet](#). Using LungNet with CT images of lung cancer patients, the team developed a model to predict the prognosis of those patients.

A [paper](#) in *npj Digital Medicine* describes how Qinmei Xu, Xianghao Zhan, and other members of the Gevaert lab used the same machine learning techniques to look at images of COVID patients.

“We applied our ideas in biomedical data fusion and quantitative imaging to integrate features extracted from CT images with clinical and lab data in hopes of predicting the severity of COVID-19 patients,” Dr. Gevaert said.

After applying their machine learning techniques, they found that features extracted from COVID-19 lesions in CT images improved significantly the prediction of ICU admission, machine ventilator use, and death of COVID-19 patients compared to radiologists’ standard interpretation of these images.



The lab is pursuing ongoing work to keep validating these models with data from other medical centers and also on current variants and others that may emerge.

Additionally, anticipating another pandemic sometime in the future, Dr. Gevaert has

been working with electronic health records to transfer what we know from machine learning models of existing diseases to predict outcomes of unknown diseases that will surely arise.

“Although the initial flood of COVID-19 modeling efforts have been reported, it’s expected that validation efforts and implementation will need to be carried out to have any chance of having an impact on this devastating disease. Even if the impact of this work does not directly affect the ongoing pandemic, any lessons learned are still going to be important to the study of other complex diseases. Particularly in the context of biomedical decision support, innovations in data fusion, deep learning, quantitative imaging, machine learning, and distributed learning will prove invaluable across biomedicine,” Dr. Gevaert said.

The Gevaert Lab’s COVID-19 research is being supported by The Weintz Family COVID-19 Research Fund.

POWERING THE LEARNING HEALTH SYSTEM

BMIR Research Lays Foundation for Use of Aggregate Patient Data to Deliver Better Care

Using data from electronic health records (EHR) to improve patient care has been a focus of BMIR for the past decade. Two companies spun out from Stanford University illustrate the practical results of BMIR’s work in that area.

The laboratory of Nigam Shah, MBBS, PhD, pioneered the use of EHR for generating evidence from similar patients to inform the care of new patients. The Shah lab built a temporal search engine that understands how drugs and diseases relate and perfected the analysis workflow to effectively generate evidence for any clinical situation.

The work, which has been documented in numerous papers, including a recent [article](#) in the *New England Journal of Medicine*, led to an IRB-approved study that successfully informed the care of over 150 patients and was recognized nationally by clinicians and the National Library of Medicine. Upon completion of the study, Dr. Shah and several colleagues founded [Atropos Health](#), which takes massive amounts of data from “real world” patients to answer pressing

questions about patients’ care within hours. In the past, it might have taken months for clinicians to understand the effects of certain treatment pathways in observational data. *The Wall Street Journal* recently noted the work.

A second company, [Prealize Health](#), is using machine learning to transform care from reactive to proactive. That company uses data on prior patients to figure out who will get into a medical problem and what that medical problem might be, and suggest what a doctor could possibly do to prevent the problem from occurring in the first place.

“Prealize Health is about building risk prediction models for what someone will get into trouble for,” said Dr. Shah, who founded the company with several colleagues in 2016 after preliminary work in BMIR several years earlier.

An [article](#) in *BMJ Open* describes how Dr. Shah and his team sought to create predictive models for identifying which patients would be at risk for a major medical ex-



pense in the next year. They showed that it’s possible to know about those patients a year in advance, given the development of new learning algorithms and the explosion in the availability of large observational data sets from EHR and low-cost computation.

“Paired with large and diverse health data sets available at the population level, modern statistical learning methods may present new opportunities to advance methods underlying health care cost-prediction,” the authors wrote.

COLLABORATION

Q&A with Mike Pfeffer, Stanford Health Care and Stanford School of Medicine CIO

Michael Pfeffer, MD, wears several hats. He is the chief information officer for Stanford Health Care and Stanford University School of Medicine as well as associate dean for the School of Medicine and a BMIR clinical professor. He recently answered a few questions for *Connection*:

What attracted you to this job?

Given the incredible faculty and strong IT organization at Stanford Medicine, coupled with the innovation and technology surrounding us in Silicon Valley, I saw a great opportunity for leading digital transformation and innovating around the way we provide patient care. In addition, as a clinical faculty member, I believed I could help bring new insights to Technology and Digital Solutions (TDS), the IT organization for Stanford Health Care and the School of Medicine.

How do you envision BMIR helping the hospital?

Both informatics and electronic health records are fairly young fields, with great opportunity to transform those technologies to benefit clinical care. From that standpoint, BMIR seeks to enhance clinical care and biomedical research through information management. Since I oversee health information technology, I think there's really an opportunity for BMIR to be able to take great research ideas and implement them to scale so they can be successful in Stanford Health Care.



Since you hold an academic appointment, how will you be working with fellow faculty in BMIR?

As a faculty member in BMIR I understand how important it is to teach informatics to our residents and medical students. I also know that people choose to work for TDS because they believe deeply in the mission of Stanford Medicine. They realize that what they are doing is going to have a positive impact on patient care, help researchers

discover the next great therapeutic, and train future physicians. So, I will be looking for greater collaboration between BMIR and TDS – to have fellow BMIR faculty present more to TDS and teach what they're working on and thinking about.

Do you expect to work with BMIR's Clinical Informatics Consultation service?

The Clinical Informatics Consultation service allows a physician to call an informatics consult to determine, based on all the available information data we have, the best option or decision for the treatment on a particular patient. That's something pretty unique to Stanford. It comes down to taking all the data from electronic health records and putting it into a system that is searchable. That requires a division like BMIR, with the faculty to figure out how we're going to do that – because even if you have all this data, you have to figure out how to actually turn the data into usable information that you can trust. And all that comes before providing that as decision support in a way that clinicians can understand it and use it to make appropriate decisions. It's really a valuable opportunity that exists as a collaboration among Professor Nigam Shah and many other BMIR faculty who are working with the IT organization. It's a very successful program, which I want to see continue because of its great value to physicians and patients.



BMIR

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WE CONNECT DATA TO HEALTH

The Stanford Center for Biomedical Informatics Research (BMIR) uses advanced research techniques to discover, apply, translate, and organize data that make a difference for health and health care. With its expertise in clinical and translational informatics research and biostatistics, the division works to uncover new ways to ad-

vance personalized medicine and to enhance human health and wellness.

Collaboration is in our DNA. We are excited about the prospect of working with other experts who share our goal to connect data to health and medicine. We encourage you to contact Mark Musen, Director of BMIR (musen@stanford.edu), to learn more.

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