Yale Center for Clinical Investigation

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Photo Harold Shapiro

Leveraging the Learning Health System to Improve Care and Promote Research

Inside This Issue

Yale has built a strong integrated informatics infrastructure to support safe, effective patient care and innovative research. Epic, Yale's enterprise-wide electronic health record (EHR) and the cornerstone of this work, contains more than four million unique patient records that enable clinical scientists to harness the power of ever-increasing amounts of digital health data.

In September, Yale-New Haven Hospital (YNHH) was awarded the Healthcare Information and Management Systems Society (HIMSS) Stage 7 award, the highest stage in the HIMSS Analytics EMR Adoption Model, which evaluates the progress and impact of electronic health record systems in hospitals. Less than four percent of U.S. hospitals have achieved this prestigious designation. HIMSS noted that YNHH is leveraging its EHR technology in innovative ways that include saving time and improving the patient experience; implementing such functionality as the tele-ICU module, which allows intensivists to monitor ICU patients 24/7; integrating the recruitment of research subjects into the MyChart patient portal; and proving the value of clinical decision support.

"We're thrilled that we received recognition for our efforts to collaborate with our colleagues at the School of Medicine to leverage technology to improve patient care and promote research," said **Lisa Stump, MS,** senior vice president and chief information officer (interim) at Yale School of Medicine and Yale New Haven Health System.

YCCI has worked closely with the Yale Epic team to ensure that the EHR strategy integrates research with Yale's **Help Us Discover** clinical research recruitment and awareness campaign. This integration has led to novel research recruitment tools, including implementation of a Help Us Discover tab in **MyChart.** The tab includes a categorized listing of all clinical trials at Yale that are open to new accruals, as well as enabling patients to build and submit their personalized clinical trial profiles, including the kinds of trials they're interested in and how they wish to be contacted. The portal operates in conjunction with **yalestudies.org,** Yale's clinical trial website for patients, where they can learn about clinical research and search for available clinical trials.

MyChart is a powerful tool for connecting potential subjects to clinical trials that incurs no additional cost, as it leverages technologies and licenses already purchased for clinical use. So far, almost 700 patients have built profiles through MyChart, even though this feature has not yet been promoted; approximately 100 of these patients have been referred to a clinical trial for possible enrollment. The Yale MyChart team, led by Timothy Cooney, is also creating **MyHealth,** a patient education section that will contain information and links to relevant clinical trials specifically targeted to the patient's health issues.

Photo Robert Lisak

The Yale JDAT/OnCore team, l to r: Richard Hintz; Seth Luty; Allen Hsiao, MD; Kelly Anastasio; Mike Legg; Erica Sizemore; Mohan Subramanian; and Liat Modiano.

Yale also provides enterprise-wide access to patient data that enables cutting-edge research across the T1 through T4 spectrum. Yale's Joint

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Written by Jill Max

In this issue of our newsletter, you'll read about the tremendous strides we've made in our informatics capabilities to integrate and enhance Yale's learning health system in order to improve care and facilitate research.

The Yale New Haven Health System's dedicated Epic team continues to refine and optimize the EHR as they work with us to leverage its research potential. We're particularly excited about the Help Us Discover tab in the MyChart patient portal, which links patients directly to Yale's clinical trials. This innovation is already drawing the attention of patients to our research program. Equally exciting is the implementation of Yale's opt-out policy. Thanks to support from across the institution and health system, researchers with an IRB-approved protocol now have access to medical records from patients treated at our facilities unless the patient opts out.

We are continuing to integrate our EHR and CTMS in ways that ease the burden on research teams and increase the efficiency of conducting clinical trials. Our OnCore team, along with the Joint Data Analytics Team (JDAT), facilitates research analytics and reporting, utilizing Yale's customized data warehouse and other tools to move research forward.

Yale has a decades-long history of training the next generation of investigators in bioinformatics, a tradition that continues today. Several graduates of the Yale Center for Medical Informatics fellowship training program are now our informatics leaders, while training opportunities for clinician-scientists are being expanded in this burgeoning field.

I hope this newsletter conveys the many informatics resources and experts available to investigators across the health system. There are tremendous opportunities to harness the huge amount of data available and open up new avenues of research. I hope you'll take advantage of them.

Robert Sherwin, MD
YCCI Director

INFORMATICS SPECIAL ISSUE

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Photo Robert Lisak

Allen Hsiao, MD, chief medical information officer for the School of Medicine and Yale New Haven Health System, and associate professor of pediatrics (emergency medicine) and of emergency medicine

Data Analytics (JDAT) and OnCore teams help assess study feasibility and identify cohorts, while the recently adopted opt-out policy allows EHR data from the entire health system to be used for research unless the patient opts out. This policy gives researchers unprecedented access to the wealth of data available within the system. In addition, best practice alerts (BPAs) can be generated in the EHR to inform physicians of clinical research opportunities for patients at the point of care. These messages, which are triggered when predefined criteria are met, alert the health care provider that an individual patient may be eligible for a clinical study. The provider then has the option of sending an alert to the study team, providing contact information directly to the patient, or both. BPAs can also be set to fire behind the scene so they don't interrupt physician-patient interactions.

"Our ability to provide the highest-quality clinical care is intertwined with our ability to conduct research," said **Paul Taheri, MD, MBA,** CEO of Yale Medical Group and Deputy Dean for Clinical Affairs. "Our EHR plays an important role in both, and we are continually seeking ways to harness what it has to offer."

Led by **Allen Hsiao, MD,** chief medical information officer for the School of Medicine and Yale New Haven Health System, and associate professor of pediatrics (emergency medicine) and of emergency medicine, the Yale IT team has worked closely with Epic to refine its tele-ICU module; it was the first to deploy it nationally. The module is used to provide overnight intensivist coverage of several ICUs across Yale's hospital campuses. One innovation includes an early warning system that continually monitors and scores ICU patients, and is refined over time as patient data are acquired. At Yale's urging, Epic is working with the FDA on developing the ability to stream live cardiopulmonary data to increase the module's effectiveness – an improvement that will benefit the many patients cared for in hospitals using Epic.

Yale has also used the EHR to improve blood product ordering across the health system. A multidisciplinary group of hospitalists, hematologists, and informaticians studied the use of blood products and identified opportunities to improve ordering. The recommendations were incorporated into the provider workflow, with indications and guidelines built into the design.

Photo Robert Lisak

MyChart team members Kathy Longley and Tim Cooney

"Our EHR has had a positive impact on how we practice medicine, and has opened up new avenues for research," said Hsiao. "As we continue to leverage this technology, patients will reap the benefits in unforeseen ways."

USING BPAs TO CONDUCT RESEARCH AND IMPROVE OUTCOMES

Steven L. Bernstein, MD, professor of emergency medicine and a leading expert on tobacco cessation, is exploring the use of BPAs in a tobacco intervention study. The two-arm randomized trial utilizes decision support in the EHR to promote tobacco treatment. Working with Epic orders coordinator **Michelle DeWitt,** Bernstein created an alert that fires when patients of physicians in the intervention group are admitted to internal medicine at YNHH and identified as smokers. The alert prompts the physician to consider prescribing smoking cessation medication; contains a link to the suggested order set for dosages; automatically sends a note to the primary care physician on record in the Yale system; sends an alert to Connecticut's Tobacco Quitline; and adds tobacco use to the patient's problem list. In the control group, the alert fires but is invisible so that Bernstein can track when these physicians see patients who are smokers.

So far, about 30 percent of the intervention physicians have made a referral to the Tobacco Quitline; 34 percent have ordered medications (versus 29 percent of controls); 41 percent have added tobacco use to the problem list (versus 3 percent of controls); and 99 percent have sent a message to the primary care provider. In addition to evaluating how physicians respond to the alert, Bernstein is looking at patient-centered outcomes by following patients for one year.

With support from YCCI, Bernstein is designing a multicenter trial to test the intervention in a big data way by using clinical information embedded in Epic to find out how physicians respond to the intervention. "The power of Epic to do clinical research is really astounding, and I think we've barely begun to scratch the surface," he said.

Photo Robert Lisak

Lisa Stump, MS

Lisa Stump, MS, recently assumed the role of chief information officer (interim) at the School of Medicine and Yale New Haven Health System. A pharmacist by training, Stump has been with the health system for 19 years in various leadership roles in pharmacy practice, informatics, and Information Technology Services. She brings considerable experience to this position, having led the implementation of Yale's Epic EHR and Revenue Cycle platform and in her role as associate chief information officer for two years.

Stump is eager to oversee the transition in health care IT from capturing data over the last decade to making use of it to improve health and health care delivery. She views the ability to use data from the EHR and other tools to potentially cure disease, enhance the patient experience, align with physicians more effectively, and predict and manage population health as both a challenge and an opportunity. Yale's JDAT team reports to her, and she is enthusiastic about its potential to use our data and analytics tools to enhance research. "The ability to gather clinical, financial, and consumer data and combine it in ways that allow us to do both predictive analytics and research to understand the basis of disease and target cures for a variety illnesses is incredibly powerful," she said. "What we've built in terms of a data analytics platform is fairly unique and positions us very well for advancing care and health outcomes."

EHR/CTMS INTEGRATION CONTINUES TO EVOLVE

By itself, OnCore, Yale's comprehensive clinical trials management system (CTMS), has a high level of functionality that eases the burden of conducting clinical research. As a leader in the integration of an EHR with a CTMS, Yale stands on the cutting edge of defining new industry standards to create a bi-directional interface. This integration has benefited clinical research at Yale and other institutions around the country.

Yale has worked with Epic and Forte Research Systems, the makers of OnCore, to define national standards for integrating research functions. These standards support an interface that moves information from the EHR to the CTMS, including:

- Demographic and laboratory data.
- Clinical research data.
- Patient enrollment and consent status.
- Serious adverse events.
- Clinical research billing and revenue management.

Data documented in the EHR by the clinician are automatically pushed to the CTMS and autopopulate case report forms for data collection and reporting. Integrating data can improve patient safety; allow for complete transparency; help with the management of timely reporting to regulatory authorities; and ensure appropriate clinical care for research subjects, especially if they have an adverse event related to a study intervention.

The Yale OnCore team is also working to build patient-facing questionnaires in MyChart for patient data collected throughout the life cycle of a clinical trial. These can be done prior to or during the study visit; it's convenient for patients and translates to more efficient workflow for study staff. This information can also be moved into the EHR where clinicians can view it, as well as into the CTMS, where it can be used for data collection.

Collaborating with Other CTSA Sites

Fellow CTSA institutions have leveraged Yale's standards-based approach to integrate clinical research management systems with EHRs, and Yale has been eager to share lessons learned. Through regular phone calls and a face-to-face meeting, Yale's OnCore team members shared with their UCLA counterparts how they planned the interface and workflow, as well as how they developed and implemented fee schedules, calendar builds, and other sets of functions. Such collaborations highlight how Yale's pioneering work with emerging data standards is helping

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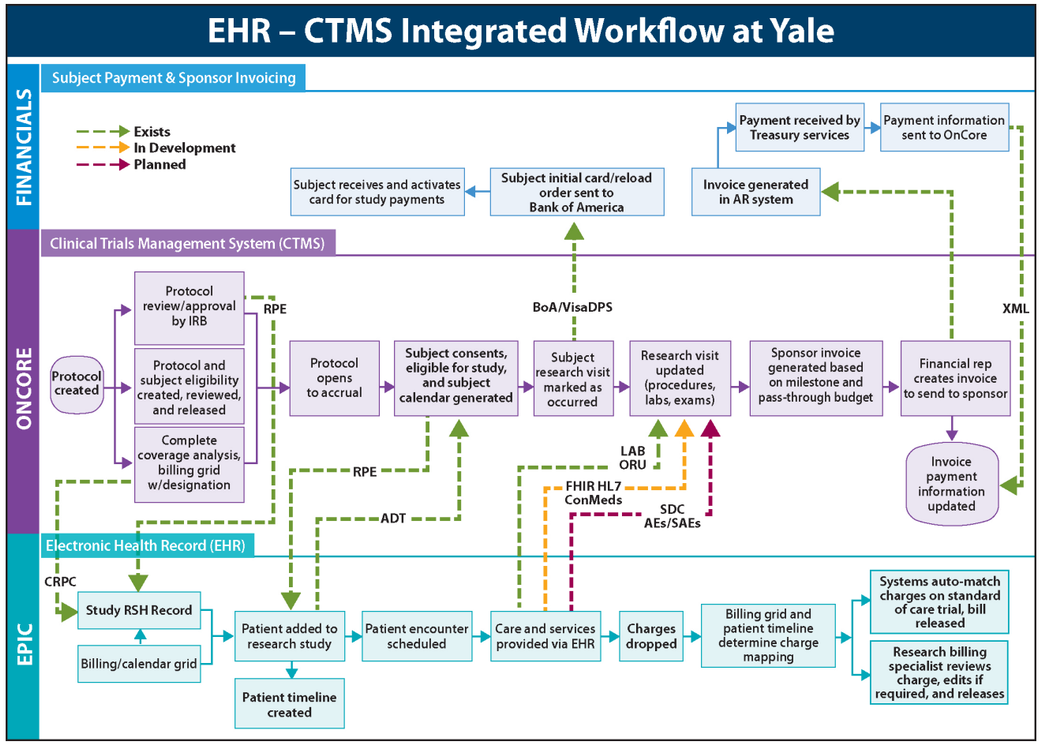


DIGGING DEEP INTO DATA

Until recently, clinical and other types of data were siloed in data warehouses throughout the institution. Now, the implementation of a single unified EHR database offers new and varied opportunities to delve into data for research and analytics.

To help manage the vast amounts of data contained in the EHR and other databases, Yale utilizes Epic's data warehouse, renamed Helix and customized with the capacity to contain all the clinical, research, financial, quality, and operational data across the **Yale New Haven Health System (YNHHS)** and the School of Medicine. Helix draws from such varied sources as the EHR; the Help Us Discover database with approximately 7,000 potential research subjects; patient satisfaction surveys; the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS); private databases; and the Social Security Death Index to provide clinicians and researchers with unprecedented access to information. "Having a unified database allows us to ask questions that are multidisciplinary, whereas before that was much harder to do," said Medical Information Officer **Prem Thomas, MD,** who leads the YNHHS data warehouse development team.

In one initiative, a multidisciplinary group of hospitalists, hematologists, and informaticists studied the use of blood products across the health system. Variances in blood utilization were analyzed using data from Helix. When variances in certain cardiothoracic surgeries were noted to be high compared to benchmarks, analyses were conducted that led to changes in equipment. Ultimately this process translated to dramatic decreases in intraoperative blood loss and a corresponding decrease in the need for transfusions.

For large data sets such as genomics and medical device data, Helix uses Hadoop, an open-source software framework that allows for the compression, storage, and fast processing of extremely large data sets at a low cost. In an effort to reduce noise from monitoring devices in the hospital's neonatal intensive care units, alarm data—some 40,000 messages per second—were streamed into Hadoop. After examining the alarm thresholds, the Information Technology Services (ITS) team was able to reduce noise by almost 50 percent. "Now we can open this up to all nursing units at Yale-New Haven and eventually Greenwich and Bridgeport Hospitals, because Hadoop can handle the volume of data streaming in," said Charles Torre, Jr., ITS System Executive Director for Yale New Haven Health System. "It's a patient and staff satisfier." Torre and his team are starting to incorporate genomic data as well so that clinical researchers will be able to look at outcomes in the EHR and link them to genomic variants.

Recognizing the need to provide investigators with data warehousing support, Yale has developed a toolkit that includes such resources as i2b2 (Informatics for Integrating Biology and the Bedside), an open source database structure originally developed at Harvard and used by Clinical and Translational Science Award (CTSA) institutions. This resource allows investigators to query for de-identified clinical cohorts for research. Other resources include the Shared Health Research Information Network (SHRINE), also used by CTSA sites, which expands this concept to other institutions and incorporates security measures; and Slicer Dicer, Epic's data warehouse tool that works with Helix. Epic is also developing a platform that will allow institutions to opt in and share data on various disease registries and performance metrics, ultimately contributing to national and international benchmarking. With Epic's patient base—the system is used with more than half of the U.S. population—this database will be very useful for investigators interested in extremely large cohorts and/or multicenter subject populations.

The EHR contains a wealth of data captured in clinical notes accessible only by reading them. Yale is working on implementing a natural language processing (NLM) engine to utilize this untapped source of potentially useful information. Data from written or dictated physician notes will be exported to Helix in real time. The data will be useful for qualifying diagnoses and accessing data for research, and could eventually be expanded to include pharmacy, diagnostic radiology, and lab notes.

It's not just the quantity of data contained in these platforms that is relevant to clinical care and research. Data quality is also a concern. Thomas and his colleagues are responsible for ensuring that the underlying database structures, technologies, and data models provide the answers clinicians and researchers are seeking. For example, there are about 15,000 terms within the EHR for categorizing the various types of diabetes and their complications, so discerning which patients meet certain criteria is critical. Thomas thinks of his role collaborating with ITS and the Joint Data Analytics Team, which coordinates all clinical and research analytics, as being an "information gardener" responsible for pruning and checking the quality of data, often working at the interface between how data are stored and what they mean.

"All of the informatics tools we put in place are helping investigators leverage, manage, and access the vast amount of data that's available, but that was previously scattered in different places," said Allen Hsiao, MD, chief medical information officer for the School of Medicine and Yale New Haven Health System. "We're excited to see the research that will take place as a result."

l to r: Ziaul Mannan, Yauheni Solad, Charlie Torre, Jr., Wade Schulz

Photo Robert Lisak

JDAT: DATA ANALYTICS IN ONE PLACE

The increasingly complex and intertwined landscapes of health care and research require collaboration. That's the underlying philosophy of the **Joint Data Analytics Team (JDAT),** formed in October 2014 to handle clinical and research analytics and reporting across the health system and the School of Medicine.

Comprising more than 60 informaticists and analysts working in a single location at 300 George Street, JDAT centralizes and coordinates all data analytics, and supports Helix, Yale's customized data warehouse system. Instead of users having to gather reports from different sources, the JDAT team navigates the complicated back end of finding the data; does all of the reporting, analytics, and dashboards; and works with Epic to refine and develop Helix.

On the clinical side, the JDAT team, led by **Michael Legg,** Executive Director, Reporting and Analytics for the Yale New Haven Health System, is focused on improving patient care and safety by identifying variations in care and understanding how they occurred. On the research side, there is a dedicated group that handles research requests. About 15 percent of the 300 or so requests that JDAT receives each month are related to research, looking for patients who may be eligible for a particular protocol, for example. Although JDAT has been operating for only just over a year, Yale is already recognized as a national leader in creating a centralized analytics team for both clinical and research data.

JDAT staff members work collaboratively, drawing upon one another's expertise as necessary. They are trained and certified by Epic in analytics, database administration, and maintenance. Those dedicated to research receive additional training in order to understand research protocols, patient safety and protection guidelines/processes, and how to navigate Yale's CTMS.

"We've been spending the last year cross-training people and trying to make sure we're a more agile group," said Legg.

Gathering data electronically is faster and easier today compared to the era of paper charts, but it also requires vigilance in order to protect patients. JDAT uses both technology and processes—including policies, auditing, and data governance—to ensure data security. Researchers are required to have IRB approval or a waiver before gaining access to identified clinical data. Since JDAT handles all requests for data and has a single pipeline and set of protocols that are followed before data are released, the process is transparent.

The School of Medicine provided the additional resources needed to hire JDAT's dedicated research team—an investment that is already paying off. "I'm delighted that faculty members are already making use of this service," said YSM Dean **Robert J. Alpern, MD.** "It's gratifying to see what they've accomplished in a short time, and I look forward to building on the momentum we've begun."

HOW TO SUBMIT A REQUEST TO JDAT

The JDAT request form is available in several places:

http://medicine.yale.edu/ycci/oncore/
Select "Please click here for procedures" in the lower right corner of the page

http://medicine.yale.edu/jdat/
Select Helix.

https://helix.ynhh.org/

Photo Robert Lisak

The Joint Data Analytics Team (JDAT), led by Mike Legg and Allen Hsiao, MD (pictured far right), is a centralized department that supports financial, quality, and Epic reporting and analytics. JDAT works closely with YCCI and the OnCore team.

Help Us Discover | *Be Part of* Clinical Research at Yale.

Yale has hundreds of clinical studies under way for a wide variety of conditions. None of them would be possible without volunteers who were willing to take part in clinical studies. Volunteers like you are the only way for medical breakthroughs to reach the public. Please consider participating in a clinical study and helping Yale continue its tradition of advancing medical knowledge.

Treating And Preventing Diabetes

"Clinical research is really important and it's the only way things are going to change."

- Amy Rosenfield

When Hannah Rosenfield was diagnosed with type 1 diabetes at age 10, her mother Amy immediately looked beyond the standard treatment for something that might benefit her daughter long term. Amy's search led her to a clinical trial at Yale for those newly diagnosed with type 1 diabetes, sometimes called juvenile-onset diabetes. Within weeks of her diagnosis, Hannah was enrolled in the two-year study.

Hannah responded well to the experimental treatment. Almost four years after her diagnosis, she was still producing small amounts of insulin. Hannah also participated in a follow-up study to find out the longer-term effects of the new drug she had taken.

Hannah's three siblings have participated in a clinical trial for relatives of type 1 diabetes patients – part of a series to prevent and treat the disease in its early stages. Knowing whether their other children are at risk for developing diabetes has given Hannah's parents peace of mind. For the Rosenfields, participating in clinical trials has offered both hope and encouragement. They know they've done everything possible not just for Hannah and her siblings but also for countless others who suffer from diabetes.

Please watch and like our new video on Yale School of Medicine and Yale University YouTube Channels.

Moving Science Forward – Yale Center for Clinical Investigation

Alcohol Drinkers Study

Do you drink alcohol?

If you are **21 to 55 years old, a heavy alcohol drinker, do not smoke cigarettes,** and **are medically healthy,** you may be eligible to participate in this brain imaging research study.

Compensation up to $750

For more information or to see if you qualify for the study, please call (203) 737-4833.

Supported by the National Institute on Drug Abuse

HIC #1305011987

Biorepository Study

Someday they will thank you for the few minutes you gave today.

Your clinical samples are important components of medical research. A new program will bring thousands of samples together so researchers can more easily develop life-saving treatments. Volunteering is as quick and easy as giving blood or other clinical samples. Your donation will be held completely secure and your information in the strictest of confidence.

Compensation will be provided.

To learn more, visit www.yalestudies.org or call 1-877-y-studies

Supported by the National Institute of Allergy and Infectious Disease

HIC #0807004033

Clinical Cancer Trials

Yale Cancer Center, one of only 41 comprehensive Cancer Centers in the country designated by the National Cancer Institute, harnesses the resources of the Yale School of Medicine and Yale-New Haven Hospital in order to advance cancer research and develop effective therapies for cancer treatment. None of these advances would be possible if people like you weren't willing to take part in clinical trials. Our portfolio includes over 100 active trials, providing options beyond the standard care for patients with most cancers.

By participating in a study, you can help Yale continue its tradition of advancing medical knowledge. For more information about cancer trials, visit www.yalecancercenter.org or call (203) 785-5702.

Yale CANCER CENTER

SMILOW CANCER HOSPITAL AT YALE-NEW HAVEN

The Cancer Center is partially funded by the National Cancer Institute

Restless Legs Syndrome Study

Do you suffer from restless legs syndrome (RLS)?

Neurologists at Yale-New Haven Hospital are conducting research concerning restless legs syndrome (RLS). There is evidence to suggest that RLS may be associated with a particular skin-related hormone and genetic mutations in the receptor which binds this hormone. The research involves determining if you have these genetic mutations and/or increased levels of this hormone. The research requires one visit to the New Haven area.

If interested, please contact: Brian Koo, M.D at (203) 932-5711 x 5416 or email: Brian.koo@yale.edu

Supported by the Restless Legs Syndrome (RLS) Foundation

HIC #1507016119

Congenital Ichthyosis Study

Does your baby have congenital ichthyosis?

If you have a **child who was diagnosed with congenital ichthyosis within their first 6 months**, they may be eligible to participate in a study to help understand variations in genetic mutations in order to tailor standards of care to the genetic diagnoses.

To learn more or see if your child is eligible to participate, please contact Kristin DeFrancesco at (203) 785-3852 or email kristin.defrancesco@yale.edu

Supported by the Foundation for Ichthyosis and Related Skin Types (FIRST)

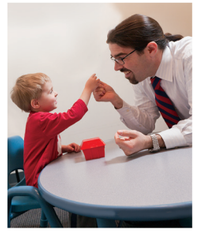
HIC #1504015620

Autism Study

Is your child on the autism spectrum?

ABC-CT Autism Biomarkers Consortium for Clinical Trials

If you have a child who has been **diagnosed with Autism Spectrum Disorder (ASD)**, Yale has clinical studies available that examine your child's social, communication, and emotional skills. This research will lead to new methods to develop, track, and assess treatments in ASD. You will receive a psychoeducational evaluation describing your child's development over six months.



James McPartland, PhD, *Principal Investigator.* To find out more about the ABC-CT, call 1-877-978-8343 or visit www.asdbiomarkers.org

Supported by the National Institute of Mental Health

HIC #1509016477

Pregnancy & New Mothers Study

Are you about to give birth or have an infant under 9 months old?

You may eligible to participate in a paid research study at the Yale Child Study Center.

We are looking for pregnant women (7 or more months) and women who have given birth within the last 9 months to participate in a study that looks at how people respond to seeing photographs of infant faces and to hearing infant cries. This study monitors brain activity while you perform simple tasks. Non-invasive, safe, and no medications involved.

Compensation up to $230

To learn more, please call (203) 785-3502 or email yucare@yale.edu

Supported by the John and Geraldine Weil Foundation; National Institute on Drug Abuse

HIC #0903004833, 12378

Children's Air Pollution Study (CAPS)

Does your child have asthma?

Millions of children suffer with asthma. Please join us in studying how cleaner indoor air can help.

If you have a **5 to 11 year old child with asthma**, you may be eligible to participate in an 18-week clinical trial of indoor air cleaners. The study involves a brief phone screening, sampling of your home's indoor air, and home visits every 6 weeks to install a new air cleaner and collect information on your child's asthma symptoms and medication use.

Compensation of $200 for full 18-week study

To learn more or to see if you are eligible, contact (203) 737-6469 or email CAPS@yale.edu. Visit our website for more information: www.yale.edu/cppee/CAPS.html

Supported by the National Institute of Environmental Health Sciences

HIC #1308012531 | ClinicalTrials.gov NCT02258893

Homeownership, Reverse Mortgages & Well-Being Study

If you are **age 62 or older and own your home or have a reverse mortgage** (or have applied or are applying for a reverse mortgage), you may be eligible to participate in a study for older homeowners to share their experiences, aspirations, and expectations related to reverse mortgage loans.

Compensation up to $50

To learn more or see if you are eligible to participate, please call (203) 479-0528 or email reversemortgagestudy@gmail.com

Supported by the Russell Sage Foundation

HIC #1410014791

Weight Loss Trial Study

Are you overweight or obese and interested in losing weight?

The John B. Pierce Laboratory and Yale University are looking for individuals who are **18 to 45 years old, non-smoking,** and **right-handed** to participate in a study that focuses on taste, smell, and food to help us understand how the brain works. The study may involve consuming beverages and food, filling out questionnaires, taking a nutritional supplement, undergoing an fMRI scan, and giving blood samples.

Compensation up to $1,120

To learn more or see if you qualify, please contact (203) 562-9901, ext. 210, email foodandflavor@jbpierce.org, or visit www.jbpierce.org/foodandflavor

Supported by the National Cancer Institute

HIC #1308012537

To find out more about trials at Yale, visit our website, www.yalestudies.org. Or call 1-877-y-studies for more information.

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Yale

MANAGING AND ANALYZING MASSIVE DATA SETS

SUPPORTING DATA MANAGEMENT AND STATISTICS

The **Yale Data Coordinating Core (YDCC)** provides data management and statistical expertise to support multicenter studies. The core is a partnership among YCCI; the Yale Center for Analytical Sciences (YCAS); Emergency Medicine; the Yale Program on Aging (POA); and the Yale Center for Medical Informatics (YCMI). It comprises faculty from the School of Medicine and School of Public Health with decades of expertise in biostatistics, epidemiology, clinical trials, and informatics, along with a highly trained technical staff skilled in systems programming, data management, data analysis, and statistical programming. Headed by YCAS director **Peter Peduzzi, PhD,** its faculty members include YCAS deputy director **James Dziura, MPH, PhD; Peter Charpentier,** associate director for data management; **Heather Allore, PhD,** director of the Yale Program on Aging biostatistics core; **Cynthia Brandt, MD, MPH;** and **Charles Lu,** associate director for technology and system development/bioinformatics.

The center works with the Program on Aging, the Alzheimer's Disease Research Center, Yale Cancer Center, and other programs to support such projects as:

- The Autism Biomarkers Consortium for Clinical Trials (ABC-CT), a multicenter study to develop objective measurements of social functioning and communication in children with autism, for which it is the Data Coordinating Core.
- Guanfacine for the Treatment of Hyperactivity in Pervasive Development Disorder, a multicenter trial that involves managing regulatory matters, data management, and biostatistical services.
- Integrated Stepped Care for Unhealthy Alcohol Use in HIV, a multicenter trial that involves data management services, preparation of Data and Safety Monitoring Board (DSMB) reports, and statistical analysis.
- Strategies to Reduce Injuries and Develop Confidence in Elders (STRIDE), a multicenter trial that involves data management services, DSMB reports, and statistical analysis.

"We recognized that supporting large multicenter trials requires high-quality analytics and data cores," said YCCI Director Robert Sherwin, MD. "We're excited to be able to bring these resources together to support this work, which can benefit so many patients."

Photo Robert Lisak

YCAS faculty and staff

We recognized that supporting large multicenter trials requires high-quality analytics and data cores. We're excited to be able to bring these resources together to support this work, which can benefit so many patients. Robert Sherwin, MD

EHR/CTMS Integration Continues to Evolve *continued from page 3*

to improve patient safety, reduce errors, and improve the research environment for institutions around the country, regardless of the systems or vendors they use.

Yale is leading an initiative with Forte to develop the **Research Evaluation System (RES),** an enterprise-wide system to track metrics around the CTSA and more than 20 other NIH center grants. While some centers have their own tracking systems for specific center grants—UCLA has one for cancer that includes grants, publications, membership, and core use—RES is a comprehensive enterprise-wide tracking system that includes not only these metrics but also institutional support and investments; pilot grants; community projects; such data related to trainees as educational outcomes, awards and collaborations; patents; and survey data. RES also contains such innovative functions as the ability to pull publications directly from PubMed, and the ability to store and collect success stories that are critical to funding applications and reporting. Accessibility to these data in a single system greatly facilitates and eases the burden of institutional and grant reporting. Yale was the beta site for RES 1.0 and 1.5, which included the loading of 10 years of Yale evaluation data. RES 2.0 incorporates lessons learned from the beta implementation; lessons learned from UCLA's system; and input from several other cancer centers and CTSA sites.

"This will change the landscape for reporting to funding agencies and institutional reporting," said **YCCI Chief Operating Officer Tesheia Johnson, MBA, MHS.** "It's the kind of innovation that will have a big impact on the way our investigators and research staff work by allowing them to track their progress and understand what's successful."

Optimizing IT platforms that support research is an ongoing task that requires the collaboration of multiple institutions and vendors. Going forward, YCCI will continue to evaluate the functionality and integration of the CTMS and EHR, and to spearhead improvements that facilitate research across the national research community.

CORES: UTILIZING NEW APPROACHES

Several of YSM's core research facilities utilize state-of-the-art technologies to generate data that shed light on human diseases. YCCI helps support these facilities and the underlying informatics resources and expertise necessary to manage and analyze the data they generate.

At the **Yale Center for Genome Analysis (YCGA), James Knight, PhD,** research scientist in genetics, leads the development of new analytical tools and pipelines for exome sequencing, transcriptome analysis, and interfacing with clinical studies. Hadoop, the data management system, compresses and stores sequencing data, which are placed in Yale's Helix data warehouse for clinical use and comparison with other databases. Knight is working with colleagues at Yale Cancer Center, for example, to match variant data from tumor profiling with laboratory and pathology data.

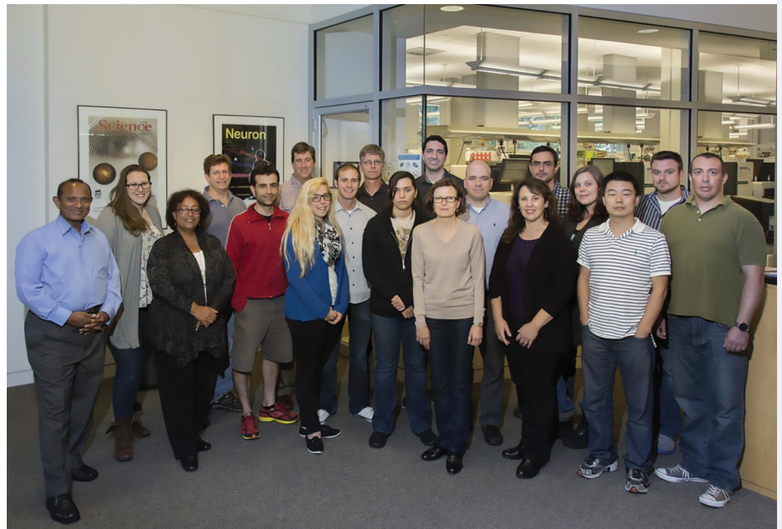
"From a research perspective, clinicians are interested in variant data," noted **Shrikant Mane, PhD,** director of the Yale Center for Genome Analysis. One early example that laid the groundwork for this concept involved three members of a family in which whole-exome sequencing revealed a genetic mutation causing an illness that had never been described before. As a result, YCCI, YSM, and Yale-New Haven Hospital established a program to sequence the exomes of children and adolescents with unexplained illnesses. More broadly, the availability of genomic information will allow clinicians to mine these data in order to identify proactively disease-causing variants in clinical situations.

The emerging CyTOF (cytometry by time-of-flight) Core is an exciting new technology for cell analysis that overcomes many of the limitations of flow cytometry; it is another illustration of the marriage of informatics and core technologies. CyTOF uses heavy metal ions as labels combined with mass spectrometry to analyze complex human cell samples, providing more than 40 crystal-clear markers in samples as small as 1,000 cells. Yale's highly ranked immunology department and cancer research community are utilizing CyTOF to explore numerous conditions in which modulating the immune system may offer better treatments.

CyTOF allows investigators to obtain an unprecedented level of detail about cells, generating complex data that have required a new field of computational analysis. "The data is now so high-throughput that it's beyond routine analysis," said CyTOF director **Ruth Montgomery, PhD,** associate professor of medicine (rheumatology) and associate dean for scientific affairs, who has used CyTOF to show the diversity of natural killer cell responses in West Nile virus infections.

The massive data sets generated by CyTOF, exome sequencing, and other core technologies have required new bioinformatics-based approaches and collaborations. "Several generations ago, you measured one thing and you could keep track of it yourself, but we can't do that anymore," said Montgomery. "The problems are so big, and the methods of study have become so complex, we have to bring in another element, but we can make more progress."

YCGA faculty and staff



YCCI Events Calendar

Research-in-Progress Meetings

These meetings feature presentations from YCCI Scholars and Investigative Medicine Program students as well as trainees from the Medical Research Scholars Program. We encourage all faculty and staff to attend.

January 25, February 8 and 22, March 14 and 28, April 11 and 25
Noon; lunch is provided

TACN203

Please visit the YCCI website to find the list of presenters and projects.

Coffee and Conversation

YCCI Coffee and Conversation: "Regulatory Binders: Preparation and Maintenance"
Susan Anderson

January 19, February 16, March 15, April 19, May 17
9 a.m. – 10:30 a.m.

Cohen Auditorium

These monthly presentations on topics related to clinical research operations are open to all Yale faculty and research staff.

Lunch and Learn

YCCI Lunch and Learn: "Biorepositories"
Stephanie Eisenbarth, MD, PhD
David Rimm, MD, PhD

January 27, February 24, March 24, April 14, May 12
Noon – 1:30 p.m.

Cohen Auditorium

These monthly sessions address broader research issues and are open to all Yale faculty and research staff. Lunch is provided.

Faculty Dinner Series

This quarterly dinner series focuses on topics relevant to Yale clinical research faculty.

"Intellectual Property Protection and Commercialization" (panel discussion)

January 25, 2016, 5:30 – 7:30 pm

"Good Clinical Practice"

April 18, 2016, 5:30 – 7:30 pm

For schedules and registration information for training events, visit http://ycci.yale.edu/education/stafftrain/.

ENGAGING PATIENTS THROUGH A PERSONAL HEALTH RECORD

HUGO PHR is a personal health platform that will empower people with their own data and put them in a position to leverage the data for their clinical care as well as participate actively with researchers.

Research is evolving from considering patients as subjects to be studied to partners who are actively engaged in many aspects of the research. That engagement can be increased when people are in a position to choose to participate actively in research and donate their data. The NIH Precision Medicine Initiative is setting the pace for this new era of relationships between scientists and study participants. The challenge is that people have not been in a position to donate their data because they have had limited access to the data. Moreover, when data have been available, they have been in formats that often require manual entry.

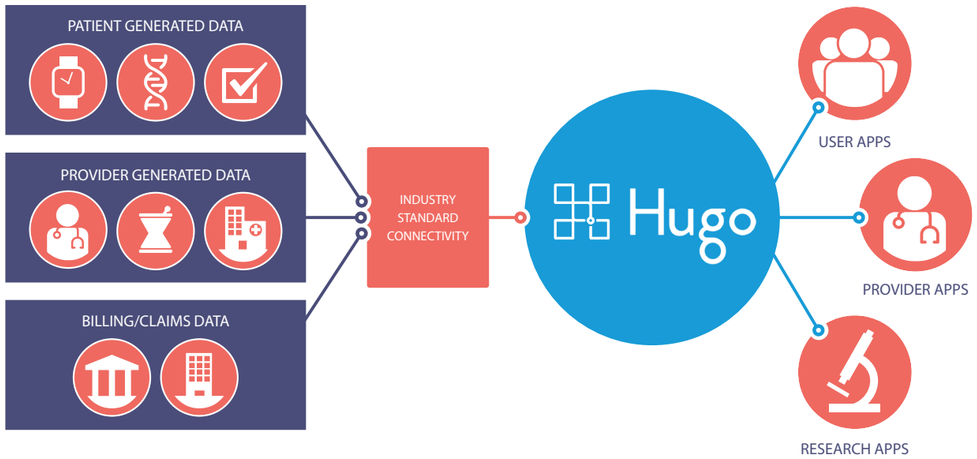
A new initiative led by **Harlan Krumholz, MD, SM,** the Harold H. Hines, Jr. Professor of Medicine and director of the **Yale Center for Outcomes Research and Evaluation (CORE),** is developing HUGO PHR, a personal health platform that will empower people with their own data and put them in a position to leverage the data for their clinical care as well as participate actively with researchers. Developed in partnership with Yale New Haven Health System, HUGO is a cloud-based highly secure personal health platform that can be autopopulated and updated with data and images from the EHR, as well as receive data from wearable devices and other sources. When available to Yale patients in 2016, HUGO will be free of charge, and easily accessible via the Internet and on mobile devices. It conforms to new standards and can be easily applied regardless of the electronic health record vendor.

HUGO offers an efficient way to:

- Match individuals to clinical studies.
- Move data to researchers with participants' authorization.
- Ensure that patients are vital components of the research process.
- Enable researchers to communicate easily with participants and share study data and results.
- Provide a conduit for patient-generated data from patient-reported outcome measures and wearable devices.

YCCI is helping Krumholz and his team assess the suitability of integrating HUGO in clinical research studies as well as evaluate the system with feedback from the IRB, the Yale New Haven Health System, the informatics team, community organizations, and patient representatives. If successful, HUGO has the potential to be adopted readily by other CTSA sites and academic medical centers.

HUGO could mark the end of an era in which patients are simply research subjects who never learn about study results or how their data were used, said Krumholz. "They will be the ones who make the decision to partner with us; to share their data; and to help us work together to generate the knowledge that will help them and the people that will follow them."



INFORMATICS OVERSIGHT REDUCES BARRIERS TO CONDUCTING RESEARCH

Informatics support requires oversight to ensure that institutional policies and practices don't become barriers to research. **The Clinical Research Leadership Committee,** led by **Brian Smith, MD,** professor and chair of laboratory medicine, is responsible for this guidance. Formed by the School of Medicine, Yale Medical Group (YMG), and Yale New Haven Health System (YNHHS), the committee is responsible for coordinating Yale's health care delivery system with the translational research enterprise.

The committee is charged with shaping policy and resolving research issues identified in the context of health care delivery. The group was instrumental in the approval of Yale's opt-out policy, which required changes in YMG and YNHHS privacy policies in order to allow for the use of blood, tissue, and health record data for research unless the patient opts out.

"The idea is to have a governance structure in place so that our informatics policies facilitate research, instead of standing in the way," said Smith.

The committee's membership includes senior faculty and leaders from the Human Research Protection Program, YNHHS, YMG, YCCI, and the Schools of Medicine, Nursing, and Public Health. **Amy Justice, MD, MSc, PhD,** professor of medicine (general medicine) and public health (health policy) and section chief of general medicine in the VA Connecticut Healthcare System, provides additional oversight, serving as lead advisor and representing faculty users of informatics resources. She has extensive experience in analyzing large and complex observational datasets, including comparing results across databases and conducting observational studies. She works to ensure that informatics services are research- and user-friendly. "I was delighted to be asked to serve in this role to help YCCI ensure that its informatics resources and investments meet the needs of faculty carrying out research," she said.

The Research Prioritization Subcommittee comprises senior faculty and staff members from the health system and the university. The committee works on behalf of the School of Medicine and the entire health system to guide the Joint Data Analytics Team (JDAT) in prioritizing requests and allocating resources. This guidance ensures that the needs of investigators as well as institutional goals are met.

Brian Smith MD

Amy Justice, MD, MSc, PhD

The idea is to have a governance structure in place so that our informatics policies facilitate research, instead of standing in the way.

Brian Smith MD, professor and chair of laboratory medicine

CLINICAL RESEARCH LEADERSHIP COMMITTEE

Brian Smith, MD
Chair; Professor and Chair of Laboratory Medicine

Susan Anderson RN, BSN, MFA
Director of Training, YCCI

Thomas Balcezak, MD, MPH
Chief Medical Officer, Yale-New Haven Hospital

Richard Carson, PhD
Professor of Radiology and Biomedical Imaging and of Biomedical Engineering;

Kevan Herold, MD
Professor of Immunobiology and of Medicine; Deputy Director, YCCI

Howard Hochster, MD
Professor of Medicine (Medical Oncology)

Allen Hsiao, MD
Chief Medical Information Officer, Yale School of Medicine and Yale New Haven Health System

Amy Justice, MD, MSc, PhD
Professor of Medicine (General Medicine) and of Public Health (Health Policy)

Alexandra Lansky, MD
Professor of Medicine (Cardiology)

Stephanie O'Malley, PhD
Professor of Psychiatry

Joseph Paolillo
Director, Data Network Operations, Yale University

Chirag Parikh, MD, PhD
Professor of Medicine (Nephrology)

Pat Seymour
Interim Director, Human Research Protection Program

Robert Sherwin, MD
C.N.H. Long Professor of Medicine (Endocrinology); Director, YCCI

Lisa Stump
Senior Vice President and Chief Information Officer (Interim), Yale New Haven Health System

Robin Whittemore, PhD, APRN
Professor of Nursing

Committee Staff:

Tesheia Johnson, MBA, MHS
Chief Operating Officer, YCCI

Sharlene Seidman
Executive Director, Corporate Business Services, Yale New Haven Health System

INFORMATICS TRAINING FOCUSES ON ADVANCED TOOLS AND APPROACHES

Photo Robert Lisak

Perry Miller, MD, PhD

Perry Miller, MD, PhD, is a physician and a computer scientist whose research includes clinical informatics, genomic informatics, and neuroinformatics, and who is particularly interested in the intersection of these broad areas. He also works at the West Haven VA Medical Center, where he is building up informatics research and training activities closely integrated with those at Yale.

"Biomedical Informatics has been growing extremely rapidly as a field," said Miller. "It impacts virtually all areas of clinical medicine and biomedical research, including their translational intersection. A major national priority is training people to meet the needs of new programs and rapidly expanding existing programs at virtually all academic medical centers."

For nearly three decades, the **Yale Center for Medical Informatics (YCMI)** has been widely known for its research training program supported by the National Library of Medicine (NLM), serving as a hub for biomedical informatics education, training, and research.

YCMI has trained roughly 100 postdoctoral fellows and graduate students over the past 30 years. Many have gone into academic careers nationwide. Many others are working for health systems, industry, consulting, and government agencies.

Led by **Perry Miller, MD, PhD,** professor of anesthesiology, with co-directors **Cynthia Brandt, MD, MPH,** professor of emergency medicine, and **Michael Krauthammer, MD, PhD,** associate professor of pathology, now heading the NLM-supported training program, YCMI has produced many leaders in the field of informatics, including those at Yale. Among them are Brandt and **Allen Hsiao, MD,** associate professor of pediatrics, who serves as chief medical information officer for the School of Medicine and Yale New Haven Health System (YNHHS). Other graduates of YCMI's biomedical informatics postdoctoral training program include **Prem Thomas, MD,** who leads the health system's data warehouse development team; **Nitu Kashyap, MD,** executive director of clinical informatics for YNHHS; **Ryan O'Connell, MD,** vice president for performance and risk management for Bridgeport Hospital; **Yauheni Solad, MD,** medical information officer for Greenwich Hospital; and **Hyung Paek, MD,** medical information officer, Fair Haven Health Center.

"When we were going through the fellowship, it wasn't clear how it would play out, but informatics needs and activities have exploded," said Thomas, who works closely with the Joint Data Analytics Team and the population health team in building Yale's underlying database structures, technologies, data models, and data quality. "There's a whole set of concepts and topics that have sprung up out of this new field and there's now a huge need for clinicians who understand this."

Together with **Mark Gerstein, PhD,** professor of molecular biophysics & biochemistry and computer science, Miller also co-founded Yale's PhD program in Computational Biology and Bioinformatics. He and **Richard Shiffman, MD,** professor of pediatrics, co-direct the Clinical Informatics Pathway of Yale's Master of Health Science program, which trains postdoctoral clinicians. YCMI faculty members also teach workshops and didactic courses on such topics as data management and analysis; database design for clinical research; and clinical and translational informatics.

For medical students, who will need to be proficient in utilizing EHRs in their clinical practice and research, Yale Information Technology Services has created a version of the Epic application. The virtual EHR contains the same order sets, documentation templates, and modules as the version used to care for patients. Medical school staff will also be able to create standardized patients for students to follow, populating their records with new results and other content. This initiative is part of the new medical school curriculum, allowing students early in their preclinical years to follow and virtually care for patients over time in a real and dynamically changing system.

YCMI and YCCI will continue to expand informatics training activities to help investigators develop key competencies that include managing big data; integrating population sciences; and the ability to use data across platforms.

I to r: Michael Krauthammer, MD, PhD; Cynthia Brandt, MD MPH; Perry Miller, MD, PhD.

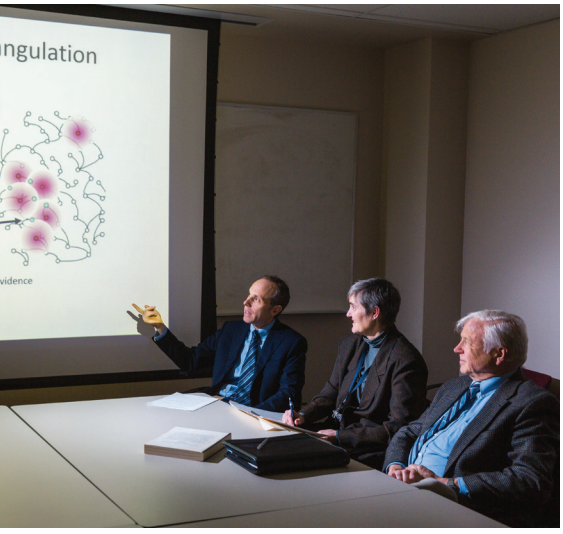


Photo Robert Lisak

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