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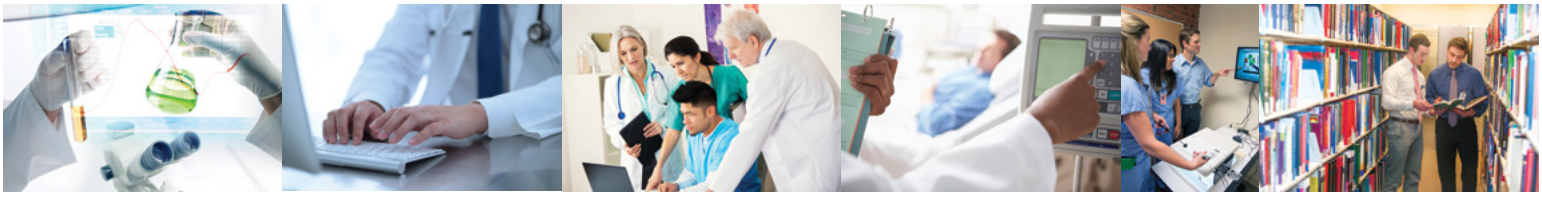
The Innovator

Baystate Health | ADVANCING CARE. ENHANCING LIVES.



AAHRPP Awards Full Reaccreditation to Baystate Health Research

The Association for the Accreditation of Human Research Protection Programs (AAHRPP) has reaccredited Baystate Health's Human Research Protection Program (HRPP) for five years. This important achievement reflects our organization's commitment to protecting the rights and welfare of research participants.

A nonprofit organization, AAHRPP, provides accreditation for organizations that conduct or review human research and can demonstrate that their protections exceed the safeguards required by the international guidelines and laws governing research involving humans in the U.S. and other countries.

AAHRPP has accredited more than 600 research entities across the U.S. and in Australia, Belgium, Brazil, Canada, China, India, Japan, Jordan, Mexico, Republic of Korea, Saudi Arabia, Singapore, Taiwan and Thailand. All major U.S. independent institutional review boards have earned AAHRPP accreditation. In addition, over 85% of the top U.S. National Institutes of Health-funded academic medical centers and 70% of U.S. medical colleges are AAHRPP accredited or have begun the accreditation process.

Association for the Accreditation of Human Research Protection Programs, Inc. — Full AAHRPP Accreditation

For more information on Baystate's HRPP, visit https://bit.ly/3QFIJwW

OnCore Clinical Trials Management System Updates

Advarra will be moving to a cloud platform in the coming months. Hosting in a modern cloud infrastructure offers considerable benefits. These benefits include security, reliability, scalability, integration, flexibility, and ease of maintenance. The transition to Advarra Cloud is seamless with no impact to the end user, and requires little to no reconfiguration of the OnCore application.

In addition, the Research Systems team is working with the Clinically-Driven Revenue Cycle (CDRC) project and other areas around Baystate to examine different flows associated with scheduling, orders, and billing in order to determine the best way to identify a research encounter/charge. The goal is to make research billing more automated and accurate than it is now when CDRC goes live. Alert process improvements will start in the Fall/Winter, and the research PowerPlans will be aligned to go live with CDRC. If you have any questions or ideas about these topics, please contact Deb Leclerc at Deb.Leclerc@baystatehealth.org.

For more information, the latest updates, and training guides, please visit the CTMS Page on The Hub or contact Research_Office@baystatehealth.org.

Research & Education Celebration 2023

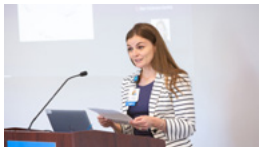
Thank you to all who joined us June 12-16th as we showcased the research activities and educational innovations of our Baystate community. This year's Research & Education Celebration (REC) was a hybrid event with more than 14 presentations and 81 posters on the vFairs virtual conference platform. This event was particularly noteworthy as it was the first REC since the covid-19 pandemic.

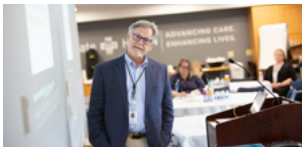
The event started with a presentation from Chief Research Officer Dr. Peter Friedmann, who provided an overview of clinical research at Baystate and discussed ongoing and future initiatives. Other highlights include keynote speaker Dr. Arvin Garg from UMass Chan Medical School presenting "Equity is Quality: Achieving Health Equity in Safety New Healthcare Systems" and the two-day focus on nursing research led by nurse scientist Cidalia Vital PhD, RN, CNL, CRRN.

Our virtual poster hall remains available to the public for viewing at https://baystatehealth.vfairs.com/.

As the first event of its kind, Research & Education Celebration 2023 proved to be a success. The event demonstrated Baystate's ongoing commitment to research and its bright future.

Nursing research symposium day 2





(left) Michelle Whitney, MSN, RN and Jenn Gold, RN (center) Cidalia Vital, PhD, RN, CNL, CRRN (right) Paul Visintainer, PhD

Research Question? *Call the Office of Research at: 413-794-3391*

Epidemiology and Biostatistics Research Core (EBRC) Classroom Missing Data in Clinical Research: One Approach NOT to Use

Paul Visintainer, PhD, Professor of Medicine, UMass Chan-Baystate, Director, EBRC

Missing data is the bane of research. Despite our best efforts to ensure completeness of a database, some observations will have missing data on one or more variables. The effect of missing data and how to handle missingness in analyses has and continues to generate much research and opinion. Missing data mechanisms and their acronyms do a great job of confusing researchers: (missing completely at random (MCAR), missing at random (MAR), and missing not at random (MNAR) (Heymans & Twisk 2022). In addition, modern causal inference methods are often thought of as a missing data problem (Hernan & Robbins 2020). However, the basics of handling missing data are often overlooked, and some solutions can create more problems than the missingness itself.

Some typical approaches include: "complete-case" analysis – restrict analysis to those cases with complete data; "mean-imputation" analysis – replace the missing data with sample mean; "condition-mean" analysis – replace the missing data with a single estimate from a regression model; and "multiple imputation" – impute multiple values for each missing value and create several complete datasets where missing values have been replaced with plausible values. Austin and colleagues (2021) discuss the advantages and disadvantages of various approaches to handling missingness in clinical research.

However, one approach that should be avoided is called the "missing indicator method" (MIM). Although bias introduced by MIM has been noted earlier (Knol et al 2010), the method is still frequently seen in the clinical research literature. In the MIM, an extra category is created that captures those observations where the value for the variable of interest is missing. For example, consider the hypothetical data in the table above. Suppose these are the results for the influence of BMI on patient length of stay (LOS) after surgery. LOS is dichotomized as either discharge within the standard for the DRG or they remained in the hospital for longer than the expectation for the DRG.

There are four categories of BMI in which patients with a known BMI may be classified. However, an extra category, "unknown," was created to capture the 50 patients with missing BMI values. This is the approach of MIM. We see that underweight patients (BMI < 20) and those who are in the obese range have longer lengths of stay (60% and 56%, respectively). How should we interpret those patients in the unknown category?

BMI	Discharge within DRG LOS	Discharge after DRG LOS	Total
< 20	20 (40%)	30 (60%)	50
20 – 24.9	43 (83%)	7 (17%)	50
25 – 29.9	38 (76%)	22 (24%)	50
30+	22 (44%)	38 (56%)	50
Unknown	30 (60%)	20 (40%)	50

First, it is obvious that patients in the unknown category have a BMI and could be classified in one of the other categories if their BMI was known.

Second, patients in each of the four known BMI categories are homogenous regarding their assigned BMI category. While there is variability in their BMIs within a category, patient classification to a BMI category is mutually exclusive with regard to BMI classification. Thus, the risk estimate for the surgical DRG outcome may be assigned to each BMI category and compared relative to any other BMI category (except for "unknown"). In other words, one may state that patients with a BMI > 30 have a higher risk of staying longer after than patients with a BMI between 20 and 24.9 (56% vs 17%, respectively). If we designed the study using a causal framework, we might also consider a potential intervention – if we were able

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A Look Inside the Baystate Research Facility

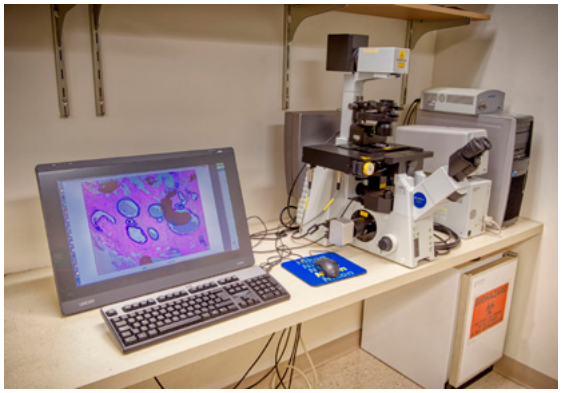
Did you know that Baystate has a large, multi-function research facility that offers various cutting-edge laboratories and research equipment available to Baystate and the local research community? The Baystate Research Facility (BRF) is a research complex where clinicians and students from across the region work together to solve problems, innovate, and make discoveries that can translate into better patient care.

One Building, Various Facilities and Resources

The 25,000-square-foot facility comprises bench space for basic science research, private labs, and a dedicated histology lab - all available to Baystate clinicians for their research needs. The BRF includes the Pioneer Valley Life Sciences Institute (PVLSI) and its state-of-the-art HistoSpring research histology core. "There is a lot of great work happening here that people may not know about, and I think that many Baystate clinicians, students, and staff don't realize this resource is available," says Carol Lovewell, Director of the Baystate Research Facility. "Within these areas, there is opportunity for research to be conducted."

Precision Tissue Research & Analysis

The on-site research histology lab, HistoSpring, provides access to state-of-the-art technologies for fixed tissue processing, sectioning, histochemical specialty stains, immunostaining, and analysis. Interested in sectioning or tissue staining as part of your research but need help knowing where to start? Sallie Schneider, PhD, Director of Histology at HistoSpring, and her team are experts in histology and are available to help solve your complex research problems. "We are here to help. If there is research that you have, that requires wet lab technical expertise. We are happy to support you from grant proposals to experiments," says Schneider.



Microscope with LCM Technology

All the equipment in the lab used for staining and processing tissue is fully automated. "It is the same high-tech equipment and the same process they use in the hospital, but these are used specifically for research tissues," says Schneider. This cutting-edge, automatic equipment isn't generally

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to reduce the BMI of patients in 30+ category to a lower BMI level prior to surgery, we might be able to reduce their LOS. Alternatively, we may also explore barriers to discharge in the group of patients with BMI >30 or BMI <20 to provide enhanced care. Can the same interpretation be applied to the "unknown" category? Consider this ludicrous question, "Would we reduce a patients' risk of an extended LOS simply by not entering their BMI into the database?" (If you answered "yes" to this question, please see me ASAP!)

Third, because the "unknown" BMI category is not a measure of BMI (but of missing BMI), the category comprises an unknown mix of patients who may be classified into the other BMI levels if their BMI was known. That is, patients in the unknown category are heterogenous in regard to their actual BMI. This means that the risk estimate (i.e., 40% with LOS outside the DRG) is a "weighted average" of those patients within the category. If the mixture had a greater proportion of those with a BMI > 30, then the risk estimate for this category would be similar to the BMI > 30 category. If the mixture was largely composed of those in the 20 – 24.9 category, then the risk estimate would be lower. In fact, it is difficult, if not impossible, to generalize a risk estimate with an "unknown" category because the "weighted average" of the mixture is also unknown.

In summary, if you have missing data, please do not create a missing category and proceed with the analysis. In addition, be very critical of published literature that utilizes this method. There are much better solutions to this statistical problem ranging from a simple description of the missing data followed by complete-case analysis to multiple imputations. What you choose is dependent on the missing data mechanism and the extent of the missingness. If you encounter an issue like this in your research, feel free to reach out to the Epi/Bio Core. We would be happy to discuss it with you! If you have any questions, or other ideas for the EBRC Classroom, email us at: biostatistics@baystatehealth.org.

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Knol MJ, Janssen KJM, Donders ART, et al. Unpredictable bias when using the missing indicator method or complete case analysis for missing confounder values: an empirical example. Journal of Clinical Epidemiology. 2010;63(7):728-736. doi:10.1016/j.jclinepi.2009.08.028

Call for Project Submissions: Baystate Health President's Excellence Award

Baystate Health continues to do outstanding work and we have so much to be proud of, so let's highlight and celebrate your work! Please consider submitting a project for the President's Excellence Award. The President's Excellence Award acknowledges the ongoing pursuit of excellence across Baystate Health.

Submissions should showcase the ongoing improvement work that emphasizes the importance of safety, quality, experience, health equity, and value across Baystate Health. To submit a project, please complete and email the submission form along with 3-4 original project graphics (excel charts, jpegs, pictures, etc.) to Lori.Cohen@baystatehealth.org.

The President's Excellence Award Ceremony will be held virtually on November 10, 2023, 2:00-3:30pm.

The deadline for project submission is October 27, 2023.

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available in research facilities. In fact, Mount Holyoke College, Western New England University, and UMass Amherst all utilize the equipment at HistoSpring, "but we would love to have more Baystate individuals interested in utilizing the lab," adds Schneider.

Bench Space at the Baystate Research Facility

HistoSpring also provides extensive microscopy equipment and services supporting both beginner and experienced investigators. "We have an inverted fluorescent microscope as well as a confocal microscope with an environmental chamber for live cell time lapse imaging.," says Schneider. "We also have a microscope with state-of-the-art laser capture microdissection (LCM) technology." The LCM technology allows for precise, contact-free, and uncontaminated specimen collection and dissections with the ability to isolate specific groups of cells or single cells."

An Abundance of Bench Space

At the BRF, investigators interested in bench research have access to ample lab space and equipment as well as an area for communication and collaboration among the research community. "This is beneficial for researchers because they have the opportunity to use our shared equipment for their study rather than purchasing their own. We also have staff here to help train them," says Rebecca Greene, Manager of the Baystate Research Facility. Faculty and students mainly use the lab, but other universities, organizations, and industry partners also use it. "Local startup companies are able to utilize bench space and lab services, and researchers from Western New England University frequently utilize the facility for specialized studies," adds Greene.

The BRF provides an environment for the advancement of knowledge and understanding of living systems. There, clinicians can investigate new ideas and translate them into successful products or techniques. "The research outcomes from work at the BRF can have an important translational impact.," adds Lovewell.

For more information about the BRF, contact BaystateResearch@baystatehealth.org

Meet the Baystate Research Facility Team on Page 4!

Tissue processing equipment at HistoSpring

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We are interested in ensuring that Baystate employees and patients (and their families) are aware of the important research that goes on at Baystate and how it contributes to better patient care. *The Innovator* welcomes feedback and story ideas. Contact Matthew Hamel at *matthew.hamel@baystatehealth.org* to submit yours.

Meet the Researcher: Mustafa Babhuiya, PhD, FACSc

Mustafa Babhuiya, PhD, FACSc

Title: Medical Director of Clinical Chemistry and POCT

Academic Rank: Assistant Professor of Pathology

Number of Years at Baystate: Two Years

What research training do you have: I completed the Clinical Chemistry Fellowship (2018-2020) at the Department of Pathology and Laboratory Medicine, Penn State University College of Medicine, Hershey. I earned a Doctorate in Biochemistry (2013) from Jiwaji University, Gwalior, India, and subsequently completed postdoctoral studies (2013-2018) from Johns Hopkins University School of Medicine, Baltimore, USA. I am broadly trained in clinical biochemistry, clinical laboratory management, medical laboratory sciences, cancer epidemiology, cancer biomarkers, next-generation sequencing, and mass spectrometry.

What got you interested in research overall: Research is all about counting on possibilities of an infinite number of data points and observations, deriving solutions to the problems based on those, or making a fundamental discovery. Growing up in the northeastern part of India, known for its biodiversity, vast rivers, and river valleys, the enormity of nature seeded an element of love for the unknown in me. I am an explorer of the majesty of the sun, the vastness of rivers, and oceans and I look for countless opportunities on sand fields. I thrive in search of the unknown or quest for solving a difficult problem -this seeds my passion for science and research.

What is your area of research: At Baystate Health Pathology, while practicing the science of medicine that is 'Laboratory Medicine,' I study diseases with my colleagues, 'Pathology- the study of diseases' in formal and informal settings. My basic and translational research interests include liver and biliary tract cancer biomarkers and molecular mechanisms. My secondary research interest at DHDPS is to research the role of essential diagnostics lists in health care delivery and population health. I also participate in service line-specific quality improvement projects within Baystate Health that directly impact patient safety and care and add value.

How do you see your research improving care for patients: Through my research, I envision bringing the best of 'Laboratory Medicine' to the forefront of public health and healthcare delivery. Every single clinical test result from my laboratory is one data point for beginning an investigation, knowing and learning of a disease state, and finally, a life-changing diagnosis for our patients. One of my first significant system-wide quality improvement research projects at Baystate was to implement a High Sensitivity Troponin T (hsTnT) assay for patient care to evaluate myocardial injury and rule out AMI.

What have been some of your favorite research projects to date that you have organized or participated in: My PhD research project introduced me to the amazing hepato-biliary tract of the human body. I extensively studied the molecular pathogenesis of gallbladder cancer, and my research led to several leads in the discovery of several potential biomarkers and therapeutic targets for the cancer. I used multi-omic approaches to study molecular mechanisms of metastasis in hepatocellular carcinoma in relation to epithelial mesenchymal plasticity employing in vivo mouse and in vitro cell line models. Most recently, within Baystate Health, I am developing a panel of biochemical tumor markers for early diagnosis of hepatocellular cancer. I set up a global non-profit organization called the Foundation for Advancement of Essential Diagnostics. The overall goal of this foundation is to promote and further augment the 'essential diagnostics list' published by the World Health Organization in the context to global public health. Locally, I envision developing a county and community-based Essential Diagnostics List for the population of Western Massachusetts. This interest is at the interface of laboratory medicine and health care delivery.

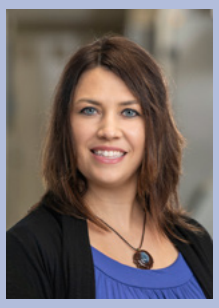
What do you like most about your job: I am a pathology and laboratory medicine geek. I get fascinated by over 6 million blood tubes a year I get to see going through my service line Clinical Laboratory instrumentations resulting in clinical tests that would finally be used for a patient's diagnosis, disease prognosis, or simply monitor a treatment. Some tubes representing some patients are difficult, so we may touch them three times (run in triplicate!) and say the third time is the charm. Beyond that, I love my core clinical lab team, teaching pathology residents, and collegiality in the Department of Pathology.

What do you do to unwind outside of work: Deep reading of old classics- fiction, non-fiction, scriptures/paperback (no screen, no Kindle), walking and trekking in solitude. I trekked Robert Frost Trail in Mount Holyoke Range this summer. I love to play a soccer game too. I could appear a loner, but I am a fantastic host and chef on request from friends and love to cook and feed a good friend.

Meet the Baystate Research Facility Team

Sallie Schneider obtained her PhD from UMASS Amherst and has been working at Baystate since 2002 as a breast cancer researcher. She has published over 70 manuscripts which range in topic from critical changes in breast tissue associated with the progression to cancer or risk of cancer or the impact of environmental exposures to testing the efficacy of polymer associated chemotherapy delivery systems or utilizing a Tibetan herb to prevent cancer metastasis. Grant funding for new projects will be taking her in the direction of biomarkers for ovarian cancer and determining the impact of the microbiome of breast milk production/ nutrition and infant health.

Carol Lovewell has 29 years' experience working in research. She began her research career at the UMass Medical school in Worcester as a Research Manager. She then joined Baystate in 2002 where she set up the Baystate Research Facility.



Rebecca Greene has been with the PVLSI and BRF since 2005. She utilizes her prior managerial experience as well as working knowledge gained over the past 18 years to facilitate research projects with all types of investigators to ensure regulations are met. She enjoys seeing the outcomes of the research conducted at the BRF and knowing that she has played a part in helping researchers achieve their goals.