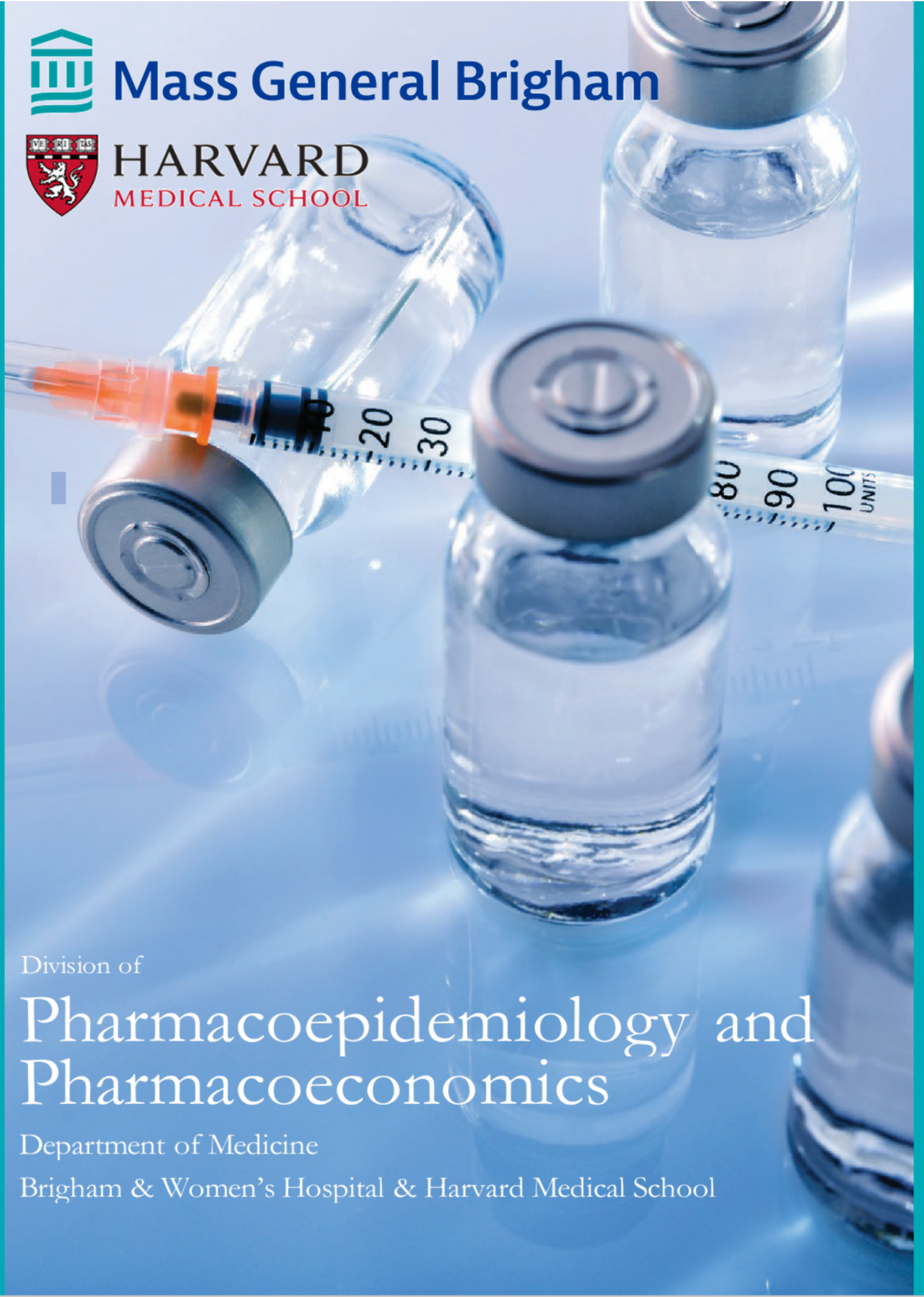
Mass General Brigham
HARVARD
MEDICAL SCHOOL
Division of
Pharmacoepidemiology and Pharmacoeconomics
Department of Medicine
Brigham & Women's Hospital & Harvard Medical School

Division of Pharmacoepidemiology and Pharmacoeconomics

The appropriate use of medications is a central aspect of health care

- Each year, basic and clinical research produce new treatments that hold the promise of major clinical benefit.
- Products carry risks, which must be rigorously evaluated against the treatment's efficacy.
- Drugs are 18% of health care expenditures, we need to better understand the costs of medications in relation to their benefits.

The work in our Division improves medication treatment in clinical practice through evidence generation, evidence translation, and dissemination.

The Division comprises 30 Harvard Medical School faculty members from the disciplines of medicine, epidemiology, biostatistics, decision science, biomedical informatics, regulatory science, medication policy, and ethics, as well as 12 research fellows, 62 research support staff, and 15 graduate students and visiting trainees.

Research Enterprise

The rigorous study of the benefits, risks, cost-effectiveness, and affordability of medications in typical patient populations is increasingly becoming a major resource for understanding medication effects in clinical practice. It helps inform healthcare delivery and policymaking in the public and private sectors. So-called "real-world evidence" developed from analyzing large healthcare databases is an important means of assessing outcomes in the regulation, deployment, and reimbursement of medications. In addition, the relationship between medication costs and their clinical benefits is once again at the center of national debate. These are all areas in which the Division has built considerable interdisciplinary expertise since its establishment.
To manage the Division's rapidly increasing research portfolio three senior investigators oversee its growth: Dr. Krista Huybrechts (Director for Research Operations), Dr. Elisabetta Patorno (Director for Research Training), and Dr. Shirley Wang (Director for Research Compliance).

Research Groups

The Division houses 12 research groups that are led by faculty members with national and international reputations and a central data and analytics core. The programs are highly interconnected and together solve interdisciplinary questions:

Active Surveillance Analytics in Pharmacoepidemiology (ASAP)

ASAP seeks to advance the development and application of rigorous epidemiological and statistical methods for rapidly generating effectiveness and safety information about medical products. The program houses the U.S. Food and Drug Administration (FDA) Sentinel Innovation Center and develops analytic tools that can expedite analyses across the Sentinel System's data partners. Together with other federal and non-federal partners, including the Patient-Centered Outcomes Research Institute (PCORI) and the Biologics and Biosimilars Collective Intelligence Consortium (BBCIC), ASAP performs a range of methodological and substantive inquiries related to signal detection, drug-drug interaction screening, and prospective monitoring. ASAP is led by Drs. Rishi Desai and Kate Bykov.

Center for Healthcare Delivery Sciences (C4HDS)

The Center for Healthcare Delivery Sciences (C4HDS.org) is dedicated to improving healthcare by identifying, designing, rigorously evaluating, and reporting transformational solutions to engage

patients and providers in care delivery. Its studies rely on the principles of implementation research and incorporate influences from a broad range of fields including cognitive psychology, behavioral economics, biostatistics, epidemiology, and clinical medicine. The Center hosts a fellowship program for implementation researchers and is led by Dr. Niteesh Choudhry with Drs. Julie Lauffenburger, Nancy Haff, and others.

MGB Center for Integrated Healthcare Data Research (C4IHDR)

This Mass General Brigham-wide Center is specialized in linking claims with electronic health record data and developing tools to access unstructured and semi-structured EHR information for improving causal inference on the effects of medications and medical devices and describe continuity of care in an academic medical center. Embedded in the Center are workflows for computational phenotyping and endpoint validation for a broad spectrum of diagnoses, medical tests, and other markers of health.
The center is co-chaired by Drs. Shawn Murphy and Sebastian Schneeweiss, Dr. Joshua Lin is the Executive Director.

Dermato-Pharmacoepidemiology (Derm-PE)

With the slew of new immunomodulating agents to treat chronic inflammatory skin diseases the need for well-conducted pharmacoepidemiologic studies to inform clinical practice is larger than ever. The Dermato-Pharmacoepidemiology work group studies the use and safety of systemic dermatologic medications with large population-based healthcare databases. The program is funded by the NIH, collaborates with clinical dermatologists at BWH and beyond and is led by Drs. Mia Schneeweiss and Robert Glynn.

Harvard Program on Perinatal and Pediatric Pharmacoepidemiology (H4P)

H4P (harvardpreg.org) generates evidence regarding the safety of medications used during pregnancy and in childhood, using advanced epidemiological and statistical methods applied primarily to large databases derived from health data collected in the context of routine medical care. The group established the International Pregnancy Safety Study (InPreSS) consortium in collaboration with investigators from several Scandinavian countries. This collaborative network provides a unique opportunity to increase study power for rapid follow-on analyses to refute or confirm early signals. The program includes investigators from Brigham and Women's Hospital (BWH), Harvard Medical School (HMS), and the Harvard T.H. Chan School of Public Health (HSPH) and is co-led by Drs. Krista Huybrechts, and Sonia Hernandez-Diaz.

Integrated Healthcare Data Analytics Center (IDAC)

The IDAC with the Program on Data Science and Biostatistics houses a wealth of projects that develop methodologies, analytic tools, and infrastructure to analyze healthcare databases. Through the MGB Center for Integrated Healthcare Data Research (C4IHDR) and the FDA Sentinel Innovation Center (SIC) Analytics Center, it has developed EHR+claims linked data resources, covering 25 million patient-lives. The program has supported the growth of an expanding toolkit of open source, reusable software tools to carry out complex analytics. Numerous ongoing projects focus on machine learning and statistical simulation approaches to augment causal study design and analytics. The program is co-led by Drs. Shirley Wang and Robert Glynn,.

Meta-research in Pharmacoepidemiology

The meta-research program has multiple projects aimed at improving the transparency, reproducibility and robustness of evidence from claims and electronic health records databases. Recent projects have focused on empirical evaluation of the reproducibility of 150 database studies (repeatinitiative.org) and close collaboration with the FDA to understand when and how database studies can draw valid causal conclusions to inform regulatory decision-making (rctduplicate.org). The latter project involves large scale emulation of 40+ randomized controlled trials using real-world data and evaluation of agreement in results. The meta-research program has developed guidance, tools, and templates for the rigorous conduct of pharmacoepidemiology studies that have been cited by and endorsed by various stakeholders. The

program is co-led by Drs. Shirley Wang and Sebastian Schneeweiss.

Oncology-Pharmacoepidemiology (Onco-PE)

The newly founded Onco-PE program leverages large oncological EHR databases to enhance our understanding of the benefits and safety of cancer therapeutics for oncological decision-making. We develop and validate research methods to guide when and how real-world evidence studies lead to causal conclusions in oncology and can complement clinical trial findings. In the age of precision oncology, it is more important than ever to consider patient biomarkers to draw conclusions about the comparative effectiveness and safety of an ever-growing landscape of novel systemic treatments. The group conducts an FDA-funded large-scale cancer trial emulation project (ENCORE), and multiple methods development projects that combine multimodal information from electronic health records, imaging, genomics and digital pathology. Dr. Janick Weberpals leads the program with Dr. Schneeweiss.

Pharmacoepidemiology in Aging Populations

The program on Pharmacoepidemiology in Aging Populations is focused on generating high-quality safety and effectiveness real-world evidence to support optimal and individualized prescribing and deprescribing decisions in older adults. As this vulnerable population is substantially underrepresented in randomized controlled trials, the contribution of pharmacoepidemiology is critical. The program adapts advanced methods in pharmacoepidemiology using integrated databases containing rich clinical information to optimize validity when studying causal treatment effects in older patients. Drs. Joshua Lin, Jerry Avorn, and Robert Glynn co-lead this program.

Program on the Pharmacoepidemiology of Metabolic Diseases (PROMISE)

PROMISE is conducting studies on the comparative safety, effectiveness, utilization, and cost-effectiveness of medications in patients with cardio-metabolic-renal diseases to understand the effects on clinical and healthcare utilization endpoints in clinical practice. The program uses multiple very large databases of older adults (Medicare) and commercially insured patients, linked with electronic health records and registries, applying modern pharmacoepidemiologic methods. The group works intensely on methods and innovative linkages between data sources, e.g., between health insurance claims and randomized controlled trials, to reduce confounding and other biases when studying medications in clinical practice. Internist Dr. Elisabetta Patorno is Director of the program and nephrologist Dr. Julie Paik is Associate Director.

Program On Regulation, Therapeutics, And Law (PORTAL)

PORTAL (portalresearch.org, @PORTAL_research) studies how laws and regulations intersect with therapeutic innovation, product approval and use, and optimal delivery of care. This vibrant group uses a combination of quantitative and qualitative empirical tools to assess issues such as the efficiency of drug pipelines, outcomes from various FDA regulatory pathways, the cost of brand-name and generic drugs, and the competitiveness of the generic drug market. From 2021-2022, PORTAL investigators helped lead over 150 publications in the medical, health policy, and law literatures, and directly contributed to the development of legislation enacted by Congress, such as the Inflation Reduction Act, and innovative proposals being pursued by the FDA including how the accelerated approval pathway is implemented. It is led by Drs. Kesselheim, with Dr. Ameet Sarpatwari as assistant director and Dr. Ben Rome as assistant director for health services research.

Program in Rheumatologic, Immunologic, and Musculoskeletal Pharmacoepidemiology (PRIME)

PRIME studies a range of systemic biologic and non-biologic disease-modifying antirheumatic drugs in patients with chronic systemic inflammatory diseases. As randomized clinical trials are rarely available for the various medication combinations in a field with rapidly evolving

therapeutic choices, pharmacoepidemiology critically contributes to the evaluation of the safety and effectiveness of treatments of chronic systemic inflammatory, autoimmune, and musculoskeletal conditions. The group uses a number of different large longitudinal electronic healthcare databases with and without linkage to clinical data from disease registries, as well as modern causal study designs and analytics. Dr. Rishi Desai leads the program.

Clinical Enterprise

While the Division does not maintain a clinical program of its own, several faculty members are active clinicians participating on the inpatient medical services (Drs. Niteesh Choudhry, Joshua Lin), as well as in primary care (Drs. Aaron Kesselheim, Nancy Huff, Ben Rome), rheumatology (Drs. Candace Feldman, Seoyoung Kim, and Daniel Solomon,), nephrology (Dr. Julie Paik), pediatrics (Dr. Tim Savage), clinical pharmacy (Dr. Julie Lauffenburger), psychiatry (Dr. Lauren Moran), and pulmonary and critical care (Dr. Will Feldman).

Educational Activities

Clinical Training

Division clinical faculty are active educators throughout HMS and its affiliated institutions. Several teach BWH trainees as well as HMS students as part of their patient-care activities while attending on the general medicine service (Drs. Choudhry and Lin) or nephrology (Dr. Paik). Faculty members also see ambulatory patients and precept house officers in primary care clinics (Drs. Haff, Kesselheim, and Rome), the Brigham Arthritis Center (Drs. Feldman and Solomon), and the Department of Pulmonary and Critical Care (Dr. Feldman).

Selected Faculty Teaching Activities

All faculty of the Division of Pharmacoepi-demiology and Pharmacoeconomics are intensely engaged in teaching graduate students and mentoring postdoctoral fellows and junior faculty. Several have received teaching and mentoring awards.

- At Harvard Medical School Division faculty lead the Advanced Integrated Science Curriculum course “Medications and Evidence” (AISC604) for 3rd and 4th year MD students and teach in the postgraduate course “Translational Pharmacology.”
- At Harvard Catalyst our faculty direct Implementation Research and Education and teach “Introduction to Clinical Investigation,” “Fundamentals of Clinical and Translational Research,” and “Comparative Effectiveness Research.”
- At the Harvard T.H. Chan School of Public Health our faculty leads several core courses of the pharmacoepidemiology curriculum, including “Pharmacoepidemiology” (EPI 221), “Database Analytics in Pharmacoepidemiology” (EPI286), “Analysis of Healthcare Databases for Effectiveness Research” (EPI 253), “Epidemiologic Methods in Health Services Research” (EPI 235) “Introduction to Clinical Epidemiology” (EPI208). Other faculty lead the JD/MPH program and teach “Public Health Law” (HPM213) as well as “Implementation Research in Health and Healthcare” (HPM284).
- At the Harvard Center for Bioethics, our faculty teaches “Health Law, Policy, and Bioethics” (BETH706).
- At HarvardX, faculty lead the course “Prescription Drug Regulation, Cost, and Access”
- At the Boston University School of Public Health, our faculty leads the course “Drug Epidemiology”(EP748).
- At Yale Law School, our faculty lead the course “FDA Law and Policy” (20616).

Fellowship Activities

The Division is home to five fellowship programs.

The Division has a vibrant postdoctoral fellowship program in pharmacoepidemiology directed by Drs. Schneeweiss and Patorno) and collaborates closely with the Department of Epidemiology at the Harvard T.H. Chan School of Public Health training doctoral students (Ph.D., Dr.P.H.). Between 6 and 12 post-doctoral fellows work closely with world-leading faculty on NIH and FDA-funded projects. Students are supported by four T32 programs that the Division collaborates with. Graduates from these programs take leading positions in academia, regulatory agencies and industry across the world.

The Division is a training site for the Harvard-wide fellowship program in general internal medicine, under the direction of Dr. Kesselheim and Dr. Rome. Fellows from this program have gone on to faculty positions at top academic centers, work at the FDA, and continue to be involved in patient care.

The Division opened a new research fellowship pathway for select M.D. graduates who enter a 2-year fellowship in pharmacoepidemiology and population medicine instead of traditional residency programs. Graduates go on to faculty positions and fruitful research careers in academia. The Division has a 100% success rate with the NIH student loan repayment program.

The Division offers a postdoctoral fellowship in prescription drug law and policy through the PORTAL research center, with up to six fellows. Past and current fellows have studied FDA regulation, patents, drug access and costs, advances in pre-approval clinical trial design, and competition in the therapeutic marketplace.

The Center for Healthcare Delivery Science in the Division offers a one-to-two-year research fellowship that trains physicians in designing and implementing programs that improve care delivery with a focus on medications and other medical products. Graduates from this program have gone on to leading physician-scientist faculty positions and quality improvement roles in major healthcare systems.

Future Directions

The Division continues to expand in several directions. Two examples are:

• Interconnecting with medical subspecialties: Embedded in the Department of Medicine, the Division is closely connected with clinical care and medical innovation across many therapeutic areas. Our physician faculty includes several medical disciplines often with secondary affiliations in other Divisions. Together with non-physician faculty, we turn data into evidence utilizing a central analytics infrastructure with massive amounts of data. We will expand on this successful strategy and plan to deliberately build new collaborations with other Divisions and departments across the Harvard medical campus.

• Expanding access to deep data and new methodological capabilities: The newly started Integrated Healthcare Data Analytics Center (IDAC) brings together large data assets that link electronic health records with insurance claims data form many million patients. The use of unstructured data in conjunction with well-described coded data provides tremendous opportunities for robust etiologic studies on the effects of medications in clinical practice. The Division's Data Science and Biostatistics group is at the leading edge of developing statistical methods that overcome challenges of unstructured healthcare data.

Faculty Roster

Professors
Jerry Avorn, MD
Niteesh Choudhry, MD, PhD
Robert Glynn, PhD, ScD*
Aaron Kesselheim, MD, JD
Sebastian Schneeweiss, MD, ScD (Division Chief)
Daniel H. Solomon, MD*
Philip Wang, MD, DrPH

Associate Professors
Krista Huybrechts, PhD
Julie Paik, MD, ScD, *
Elisabetta Patorno, MD, DrPH
Shirley Wang, PhD

Assistant Professors
Katsiaryna Bykov, PharmD, ScD
Rishi Desai, PhD
Candace Feldman, MD, ScD*
Julie Lauffenburger, PharmD, PhD
Joshua Lin, MD, ScD
Lauren Moran, MD
Ameet Sarpatwari, PhD, JD
Richard Wyss, PhD
Jie Yang, PhD

Instructors
Rajendra Aldis, MD*
Will Feldman, MD, DPhil
Nancy Haff, MD
Ben Rome, MD
Maximiliano Russo, PhD
Timothy Savage, MD
Maria Schneeweiss, MD
Karine Suissa, PhD
Janick Weberpals, RPh,PhD
Yanmin Zhu, PhD

*Denotes secondary appointment in Division