FROM THE DIRECTOR

The PhD program had a terrifically busy spring. This year concluded our 8th academic year. With the graduation of Drs. Engmann, Tai, Ray, and Aiemjoy, we now have 17 alumni. Alyssa Mooney and Sarah Ackley will finish in the coming weeks. This puts a lot of pressure on Josh Demb to graduate as scheduled in December and bring us to 20 graduates before 2019.

Lest you worry that our ranks will be too small, we are welcoming an incoming class of 10 new students in the fall. This exceptional group is our largest incoming class ever due to a substantial increase in applications and higher than usual take-up rates for accepted students. We anticipate the boomer class of 2018 will be a great and lively addition to Mission Hall, even if we are considering installing double-decker-cubicles so everyone has a place to sit.

This year’s Society for Epidemiologic Research annual conference was especially fun because so many of our students presented their research. First year students Crystal Langlais and Adrienne Epstein were both selected for oral presentations of the projects they completed as part of 1st year PhD seminar. Assistant Prof Jackie Torres, my co-instructor for the seminar, and I enjoyed watching the projects develop over the course of the year. Kudos are due to Drs. June Chan and Sheri Weiser, who have been generous and effective mentors for Crystal and Adrienne.

Efficacy and safety of primaquine and methylene blue for prevention of Plasmodium falciparum transmission in Mali: a phase 2, single-blind randomized controlled trial

Michelle Roh, who just completed her third-year as a PhD student, published a paper in The Lancet Infectious Diseases in February. Michelle, along with researchers at the UCSF Malaria Elimination Initiative, University of Bamako, Mali, Radboud University at Nijmegen, and London School of Hygiene and Tropical Medicine, showed that two compounds, primaquine and methylene blue, can be safely and effectively added to current antimalarial treatment regimens to block transmission of the most common and deadliest form of malaria in Africa, P. falciparum.

Remarkable progress has been made in reducing malaria morbidity and mortality, and currently malaria interventions have helped to reduce the malaria incidence by 50% and death rates by 60%. Yet, an estimated 216 million cases and 450,000 deaths have been documented in 2016 and despite progress, new tools will be needed to control and eliminate malaria.

Malaria has several different forms and transmission of the parasite is perpetuated through a cycle in which it is passed from mosquitoes to humans and back again. When a person is bitten by an infected mosquito, malaria parasites travel through the liver to the bloodstream, where they circulate for several weeks.
The majority of parasites replicate into asexual forms in red blood cells, which cause the symptoms of malaria when they burst. But a small percentage develop into male and female forms, called gametocytes, which play an important role in transmitting the disease back to mosquitoes. Since these gametocytes are not killed by the current, artemisinin-based combination therapies used to treat P. falciparum, people can continue to transmit the infection to mosquitoes for weeks after they’ve been treated, unless something is added to the treatment regimen to block their transmission.

The study, a phase 2 randomised controlled study conducted in Mali, randomised 80 asymptomatically infected P. falciparum participants with detectable levels of gametocytes to receive either: sulfadoxine-pyrimethamine and amodiaquine; sulfadoxine-pyrimethamine plus a single dose of primaquine; dihydroartemisinin-piperaquine; or dihydroartemisinin-piperaquine plus a three-day course of methylene blue. Among participants who were infectious at baseline, the study found that by day two, median withinperson mosquito infectivity was reduced by 100% among participants who received primaquine or methylene blue, which was significantly higher than the 10.2% reduction observed with sulfadoxine-pyrimethamine plus amodiaquine alone and a 6.0% reduction observed with dihydroartemisinin-piperaquine alone. After exclusion of blue urine, which was commonly found among participants who received methylene blue, adverse events were similar between groups.

This study highlights the potential role of primaquine and methylene blue as two potent transmission blocking drugs which can be safely added to current antimalarial regimens to prevent the spread of P. falciparum malaria, including its drug-resistant forms. Countries moving towards malaria elimination could consider adding primaquine or methylene to first-line treatments, as recommended by the World Health Organization, or to community-wide mass drug administration to rapidly reduce population-level malaria transmission and prevent the spread of drug resistance. However, more empirical evidence will be needed to confirm whether the addition of these drugs would have a community-level effect.

**Figure.** Percent (95% CI) of infectious individuals (A) and percent (median [line], IQR [box], and range [whisker]) of infected mosquitoes among those infectious at baseline (n=54) (B) by group and visit. Percent of infectious individuals defined by percent of individuals who infected at least one mosquito. Percent of infected mosquitoes defined by the number of mosquitoes with oocysts present over the total number of mosquitoes survived up to day of dissection. None of the participants in the SP-AQ +PQ arm were infectious on day 7 and none of the participants were infectious on days 2 and 7 in the DP +MB arm. P-values represent testing for between-group differences.
Our students and post-docs had so many presentations at SER that I couldn’t attend them all (check out the list on page 6) and it was gratifying when I realized the students had formed a UCSF support posse providing for impromptu last minute practices and showing up at one another’s sessions.

Last year, we had a few curriculum changes, including Dr. Justin White’s new class on econometric methods for epidemiologic research. This was a great success and provides a toolset that I see as increasingly essential for epidemiologists. Although few econometric methods were formally taught in epidemiology programs until recently, these tools are invaluable for more rigorous and policy relevant research in many domains. In the coming year, Dr. Chiung-Yu Huang will lead a new class to provide richer mathematical foundations for our ongoing biostatistics classes. Dr. Huang’s own research emphasis focuses on handling truncated or censored data for survival analyses or analyses of recurrent events. Her class will run concurrently with the core biostatistics courses to provide students more in depth understanding and extensions to the core applications discussed in the primary biostatistics courses. We are very excited about this new class and wonder if it is open to faculty.

There’s more news but fortunately some of it is now provided in our wonderful departmental newsletter (https://epibiostat.ucsf.edu/department-newsletter). Enjoy the summer and get ready for a great 2018/2019 academic year events (page 8), perhaps by reading The Book of Why for fall book club!

Maria Glymour, S.D.
Professor and Director, Doctoral Program in Epidemiology and Translational Sciences

Kristen Aiemjoy (2018 graduate) doing research in Ethiopia on a trial on interventions to reduce smellflies in latrines. Shown here with a colleague, measuring fly density near latrines with a scudder fly grill.
Sarcopenia research to understand disability risk in older adults

Sarcopenia, or the age-related loss of muscle mass and its accompanying decline in strength and physical performance, has been gaining attention in recent years. In fact, the condition of sarcopenia was recently assigned an ICD-10 code, which is a critical step in the ability to diagnose and bill for this condition, particularly in the US. Despite this recent attention, there are many important outstanding issues to resolve in sarcopenia including: how to operationalize and reach consensus for a single definition of sarcopenia for research and clinical use; how to best measure muscle mass; and the identification of the precise biological pathways in muscle that predispose individuals to mobility loss in old age. Here I highlight ways in which our research group is addressing all of these issues.

First, to operationalize the definition of sarcopenia, we have collated and analyzed data from dozens of cohort studies of older adults and smaller randomized trials of particular patient populations (such as HIV positive individuals and those recovering from hip fracture). Our early efforts resulted in the first data-based definition of sarcopenia, which was published as a series of papers in the Journals of Gerontology Medical Sciences in 2014. Since then, we have complete additional analyses to refine our work. The major results of these papers, and the implications of the results, will be discussed at a Position Development Conference in the Fall of 2018. This conference will involve an Expert Panel reviewing and voting on a series of statements about defining sarcopenia that should clearly identify areas of consensus to move the field forward, and highlight any outstanding controversies that merit additional attention to resolve.

Second, we have recently used a novel, non-invasive method to assess muscle mass in older adults, and examined this measure with adverse health outcomes in older adults, called d3-creatine dilution. Older methods to approximate muscle mass rely on relatively limited and expensive imaging devices (such as computed tomography (CT), magnetic resonance imaging (MRI), or dual energy x-ray absorptiometry (DXA)). The newer d3-creatine dilution method does not require participants to travel to a clinical center for assessment and is easier to use in the field. In addition, other approximations of muscle mass (by CT, MRI or DXA) are only weakly associated with poor outcomes in older adults (such as falls, mobility limitation and disability) while our preliminary data suggested that muscle mass assessed by d3-creatine dilution is strongly related to these outcomes. Thus, this new measure may have important uses in clinical and research settings.

Finally, we are about to embark on the development of a new cohort study of older men at women at risk of mobility limitation called SOMMA, the study of mobility, muscle and aging. Lead by a team of outstanding Principal Investigators (Steve Cummings, CPMC; Steve Kritchevsky, Wake Forest; Anne Newman, University of Pittsburgh; and Russ Hepple, University of Florida), SOMMA will be run by the San Francisco Coordinating Center. This study will recruit about 1000 older men and women for complete characterization of physical performance and changes in mobility, and these participants will all undergo a muscle biopsy. We will then investigate the link between key biological properties and pathways in muscle tissue (such as autophagy, oxidative stress, and mitochondrial function) to declining performance and disability. Our hope is that the SOMMA study will identify new therapeutic targets that will ultimately prevent mobility problems in older adults.
Accomplishments: Conference Presentations

**Langlais, Crystal**

**Rodriguez, Luis**


**Eng, Chloe**
Memory change after stroke: has the relationship weakened in recent years? Society for Epidemiology Research Meeting. Baltimore, MD. June 2017

**Engmann, Natalie**


**Abdiwahab, Ekland**
Abdiwahab, EA; Tahir, P; Hiatt, RA. Social Gradient in Cancer Incidence and Mortality: A Systematic Review. Poster presentation at: American Society for Preventive Oncology Annual Meeting; 2018 March 12; New York, NY.

**Demb, Joshua**

**Wannier, Rae**

**Dang, Kristina Van**

**Ackley, Sarah**
Multiple exposures, reinfection, and risk of progression to active tuberculosis. Society for Epidemiology Research Meeting. Baltimore, MD. June 2018.

**Mehrotra, Megha**

**Kalapatapu, Rajkumar**
Passed the 10-Year Maintenance of Certification Psychiatry Exam in February 2018 administered by the American Board of Psychiatry and Neurology, A Member Board of the American Board of Medical Specialties

**Rodriguez, Luis**
NIH-NIDDK F31 Ruth L Kirschstein Predoctoral Individual National Research Service Award to Promote Diversity in Health-Related Research. Race/Ethnic Specific Association Between

**Langlais, Crystal**
Association of Cancer Research Meeting, Chicago, IL, April 2018.

**Irish, Amanda**
Use of remote sensing data and machine learning to predict roof type for indoor residual spraying campaigns. Society of Epidemiology Research Meeting, Baltimore, MD, June 2018

**Mooney, Alyssa**

**Epstein, Adrienne**

**Abdiwahab, EA**
Abdiwahab, EA; Ospina-Romero, M; Filshtein, T; Brenowitz, WD; Kobayashi, LC; Mayeda, ER; Glymour, MM. Association Between Cognitive Change and Cancer Incidence: findings from the Health and Retirement Study. Poster presentation at: Society for Epidemiologic Research Annual Meeting; 2018 June 21; Baltimore, MD

**Wannier, Rae**

**Dang, Kristina Van**

**Ackley, Sarah**
Multiple exposures, reinfection, and risk of progression to active tuberculosis. Society for Epidemiology Research Meeting. Baltimore, MD. June 2018.

**Mehrotra, Megha**

**Mooney, Alyssa**
Accepted Received a post-doctoral fellowship position with the California Policy Lab at UC Berkeley.

**Demb, Joshua**
American Society of Preventive Oncology Conference Travel Award, New York, NY. March 2018.
PhD Student presentations at SER conference, Baltimore, MD

Chloe Eng, 2nd year PhD student presenting on “Memory change after stroke: has the relationship weakened in recent years.” Asks if post stroke cognitive change has become less common – if so could this contribute to recent declines on dementia incidence.

Megha Mehrotra, 3rd year PhD student and Dr. Daniel Westreich, Associate Professor at UNC and Megha’s committee member. Megha’s poster was on: “Practical Transportability: a Virtual Twins approach for variable selection.”

Luis Rodriguez, 3rd year PhD student and Dr. Patrick Bradshaw, Assistant Professor at UCB and Luis’ committee member. Luis is presenting his research on “Diabetes and Cardiovascular disease mortality among women with and without breast cancer.”
**PhD Student UPDATE**

Caroline Tai, PhD presented her dissertation last June on “Integrating Genetics into Population-Based Studies.”

Shown here with her committee members Drs. Thomas Hoffmann, John Witte and Elad Ziv.

After graduation, Dr. Tai took a position as a biostatician at Evidation Health.

**Kristen Aiemjoy, PhD** presented her dissertation last June on “Defining Diarrhea: Validating and improving symptoms-based measures of pediatric diarrhea.”

Shown here with her committee members Drs. Jeremy Keenan, John Neuhaus and Ben Arnold.

Dr. Aiemjoy is now a post-doc working at Jason Andrews at Stanford on typhoid sero-epidemiology in Nepal.

**Kathryn Ray, PhD** presented her dissertation last June on “Mass antiobiotic interventions – How can we assess the impact on gut microbiome at the community level?”

Shown here with her committee members Drs. Susan Lynch and Tom Lietman.

Dr. Ray is working with the F.I. Proctor Foundation in expanding their Data Coordinating Center for upcoming clinical trials.
**Natalie Engmann, PhD** presented her dissertation last April on “Breast density, body mass index, and breast cancer risk: Implications for clinical and public health settings.”

Shown here with her committee members Dr. Robert Hiatt and Dr. Karla Kerlikowske.

Dr. Engmann is now an Associate Health Economist in the Evidence for Access Group at Genentech.

**Joshua Demb** receiving the American Society of Preventive Oncology (ASPO) Travel award for having one of the top abstracts at the conference held in New York in March 2018.

**PhD students Josh Demb, Kristina Dang, Megha Mehrotra, Luis Rodriguez and Chloe Eng** after admiring Josh’s SER poster on the recession and cancer screening behaviors. Joined by alumnus **Elizabeth Rose Mayeda** (now Assistant Professor at UCLA) and **MAS student Monica Ospina**.
UPCOMING EVENTS

Monday, August 20 & 21, 2018
12:00 – 1:00 pm, MH 1407
Guest lecture: Chuck Huber, PhD
Senior Statistician, State Corp. LT
Missing Data and Multiple
Imputation (8/20) and Multilevel/
Longitudinal Modeling (8/21)

Friday, September 7, 2018
12:00 – 2:00 pm, MH 2700
Welcome lunch for incoming PhD ETS
students.

Friday, September 14, 2018
12:30 – 2:00 pm
Dissertation research presentation by
Sarah Ackley
Modeling vaccine preventable
disease in California.

Monday, October 1, 2018
12:00 – 3:00 pm
Guest lecture by Melinda Power, ScD
George Washington University
TBD re: Marginal Structural Models

Friday, October 19, 2018
9:30 – 12:30 pm
Guest lecture by Tarik Benmarhnia,
PhD, UCSF
TBD re: Attribution Measures

Monday, November 5, 2018
12:00 – 3:00 pm
Guest lecture by Susan Athey,
Economist, Stanford University
TBD: Causal Forests: Integrating
Causal Thinking into Machine
Learning Methods

Wednesday, January 16, 2018
Guest lecture by Chanelle Howe, PhD,
MPH, Brown University
TBD re: Selection Bias

What are these PhD students up to?

Answers, from top to bottom
Luis Rodriguez with his wife,
Cecilia and daughters,
Samantha and Paula.

Rae Wannier presenting her
abstract “Modeling the
impact of trachoma MDA on
GU chlamydia using
transmission models” at the
Society of Epidemiologic
Research conference held
in Baltimore, MD.

Alumnus, Dr. Eugenie Poirot
with Thelma Madeline
Roullet born December 7,
2017. Congratulations
Eugenie!