

MIT Center for Biomedical Innovation **BioACCESS Seminar** on *Meeting the Challenge of Ensuring Global Access to Insulin*

February 19, 2019 // 3:00 PM – 4:30 PM

Location: 68-181 (MIT Campus), 31 Ames Street, Cambridge, MA

Diabetes is characterized by elevated blood glucose levels, leading to numerous health complications, as well as detrimental socioeconomic burden as a result of both direct (e.g. medication, glucose testing) and indirect (e.g. productivity loss, lifestyle changes) costs. Globally, the number of adults with diabetes has increased from 108 million in 1980 to 422 million in 2014, with the number of type 2 diabetics expected to rise to 511 million by 2030. An increase in the projected demand for insulin, required for all type I and 20-30% of type II diabetic patients, will exacerbate already existing barriers hindering sustained access. This is especially concerning in low- and middle-income countries, where prevalence has been rising more rapidly. China and India alone account for close to 45% of the total diabetes burden today.

This seminar aims to:

- Convene a community interested in improving access to healthcare in resource-limited settings
- Explore the supply-side and demand-side barriers hindering sustained access to high-quality, affordable diabetes management, especially insulin
- Identify areas ripe for innovation to inform the design of cost-effective interventions aimed at improving population health

-Agenda-

3:00 – 3:10 PM	Introduction to MIT CBI, BioACCESS, and Framing of the Seminar MIT Center for Biomedical Innovation
3:10 – 4:10 PM	Presentations Dr. Veronika J. Wirtz <i>Associate Professor, Department of Global Health, Boston University School of Public Health & Director, World Health Organization Collaborating Center in Pharmaceutical Policy</i> Access to care for diabetes with focus on insulin: a health system lens The prevalence of diabetes has increased rapidly over the last four decades, from 108 million in 1980 to 422 million in 2014, in particular in low- and middle-income countries. Patients affected by diabetes in low- and middle-income countries tend to be diagnosed at younger age. The increasing burden of diabetes has large social and economic consequences at household, community and country level. Many countries

lack resources including effective policies to create a conducive environment for prevention and high quality of care. This presentation will highlight the key factors that influence access to medicines for diabetes, including trade, manufacturing and market authorization as well as financing, procurement and medicine prescribing.

Dr. A.J. Kumar

Chief Scientific Officer, Jana Care

Jana Care: A breakthrough diagnostic platform to tackle chronic diseases

Jana Care builds point-of-care tests for the diagnosis and management of chronic diseases. These tests include HbA1c and glucose, which are important tests for diabetes. In addition to diagnostic tests, Jana Care provides digital management programs through the Habits apps to empower patients to make lifestyle changes and better adhere to their medical care programs. Jana Care's devices are used in over 1,000 clinics in India and are used in screening programs at major events like the Kumbh Mela. Over 200,000 patients have benefited from our tests for screening, diagnosing, and monitoring diabetes. Our technology addresses a key gap in diabetes care in emerging economies where approximately 50% of diabetics are undiagnosed.

Alex Abramson

PhD Candidate, Langer Lab, MIT

An insulin pill that delivers – Microinjection in the gut

Biomacromolecules transformed our capacity to effectively treat diseases; however, their rapid degradation and poor absorption in the gastrointestinal (GI) tract generally limits their administration to parenteral routes. An oral biologic delivery system must aid in both localization and permeation to achieve systemic drug uptake. Inspired by the leopard tortoise's ability to passively reorient, we developed an ingestible self-orienting millimeter scale applicator (SOMA) that autonomously positions itself to engage with GI tissue and deploys milliposts fabricated from active pharmaceutical ingredients directly through the gastric mucosa while avoiding perforation. We show that the drug in our device remains stable for 16 weeks at 40°C, removing the need for refrigeration. We also conduct in vivo studies in rats and swine supporting the materials and method's safety and, using insulin as a model drug, demonstrate that the SOMA delivers similar API plasma levels to subcutaneous millipost administration.

Dr. Amy Moran-Thomas

Alfred Henry and Jean Morrison Hayes Career Development Assistant Professor of Anthropology, MIT

An anthropology of medical technologies amidst a global diabetes epidemic

According to the International Diabetes Federation, diabetes now kills more people each year than AIDS and breast cancer combined, and the majority of these deaths take place in contexts of scarcity. Yet many of the key technologies for treating diabetes—such as insulin assemblages and glucose measurement technologies—were initially designed for use in affluent contexts. This talk presents an ethnographic perspective on the growing mismatch between imagined users of these therapies and

those who need them today for survival. Exploring some societal and historical dimensions of how these technologies are circulating in the world today, this presentation takes an anthropological perspective to reflect on how realities of new users and global equity issues might be better taken into account in the design phases of developing diabetes care technologies.

4:10 – 4:30 PM

Q&A / Discussion

-Presenter Biographies-

Dr. Veronika J. Wirtz

Veronika J. Wirtz, MSc, PhD is an Associate Professor in the Department of Global Health at the Boston University School of Public Health, where she is also Director of the World Health Organization Collaborating Center in Pharmaceutical Policy. Her research focuses on health system strengthening and program evaluations of medicines access and utilization. Between 2014 and 2016 she was the Co-Chair of The Lancet Commission on Essential Medicine Policies which published its report Essential Medicines for Universal Health Coverage in Fall 2016. She has worked as a technical advisor for various international organizations, among them the World Health Organization, the Pan American Health Organization, the World Bank, the Global Fund to fight AIDS, Tuberculosis and Malaria. She is a Visiting Professor of the National Institute of Public Health (INSP), Mexico where she was a faculty member between 2005 and 2012. She received her training as a pharmacist from Albert-Ludwigs-University in Freiburg, Germany and her Master in Clinical Pharmacy and PhD from the University of London, UK.

Dr. A.J. Kumar

A.J. Kumar is the Chief Scientific Officer at Jana Care, where he leads the research team to create new, affordable point-of-care diagnostics tests for chronic diseases. A.J. received a B.S. in physics at Stanford and then spent 2 years in rural South Africa with the Peace Corps. Upon returning to the U.S., he completed his PhD in applied physics at Harvard and worked on the development of a point-of-care test for sickle cell disease while under the guidance of Prof. George Whitesides. He has served as a consultant on diagnostics for companies and on a scientific advisory board on protein diagnostics for the Bill and Melinda Gates Foundation. He is passionate about harnessing new technologies to improve human health for all.

Alex Abramson

Alex Abramson is a PhD Candidate in Chemical Engineering at MIT studying under Professor Robert Langer. His research focuses on developing ingestible robotic capsules for oral biologic drug delivery and other therapies. Alex has worked closely with Novo Nordisk pharmaceuticals and

gastroenterologist Giovanni Traverso to develop a commercially viable and safe oral insulin pill with a comparable efficacy to subcutaneous injections. His work, published in *Science*, has received considerable press coverage from such news outlets as the *New York Times*, NPR and *Wired*. He is also involved in the public health sector and has performed research on quantifying the quality of life impact that innovations in the biomedical space have on patients worldwide.

Dr. Amy Moran-Thomas

Amy Moran-Thomas is a cultural anthropologist, interested in the human and material entanglements that shape global health and medicine in practice. She received her PhD in Anthropology from Princeton University in 2012, and held postdoctoral fellowships at Princeton and Brown University before coming to MIT as Assistant Professor of Anthropology in 2015. She teaches classes at MIT about health and society, technology and culture, and “the social lives of medical objects.” Her forthcoming book, *Traveling with Sugar: Chronicles of a Global Epidemic* (UC Press, October 2019), offers a humanistic account of the global diabetes epidemic.

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Meeting the Challenge of Ensuring Global Access to Insulin

Seminar Report

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Dr. Veronika J. Wirtz

Associate Professor, Department of Global Health, Boston University School of Public Health & Director, World Health Organization Collaborating Center in Pharmaceutical Policy

Access to care for diabetes with focus on insulin: a health system lens

The prevalence of diabetes has increased from 4.7% to 8.5% between 1980 and 2014, with 1 in 11 adults affected but 1 in 2 adults with diabetes undiagnosed. As of 2015, diabetes was directly responsible for 1.6 million deaths, while another 2.2 million deaths were attributed to high blood sugar. More than 75% of people with diabetes live in low-and-middle income countries. Trends in diabetes prevalence are largely driven by changes in population size, age structure and in risk factors, many of which are modifiable. China, India and US are countries with the largest number of patients with diabetes. Amongst the diabetic population, approximately 90% have type II, 20-30% of which take insulin, while the rest are insulin-dependent type I.

Global responses in the form of international agreements and strategies, such as the *Sustainable Development Goals* and *WHO Global Action Plan for the Prevention and Control of NCDs*, have focused attention on the increasing burden of diabetes but little actionable progress has been made. From a health systems lens, it is important to understand the different parts of a health system and how to design them through evidence-informed and societally-driven choices to reach desired performance metrics (e.g. efficiency, quality, access). Health systems are broader than just healthcare, they also include commercial and social determinants, public policies, and more.

A study using standardized, nationally representative data from Service Provision Assessments conducted in 2013–2015 across 5 countries shows that diabetes services are less available compared to those for CVD and COPD. Another study shows that across all world bank income groups, the proportion of households with participants with known diabetes who might not be able to afford insulin is systematically higher than those who take metformin, glibenclamide, and gliclazide. Looking at inequalities within countries, a study in Kenya shows that poorer households pay more for medicines than wealthier households. Issues of pricing are not unique to LMICs alone, even in the US a significant number of patients cannot access medicines due to high costs.

NCDs have not received the same attention in global health as infectious diseases, accounting for a mere 2% of development assistance for health between 2000-2017. Nevertheless, interesting strategies can be learned from successes in delivering HIV care: generic medicines to lower costs, reducing distance between patients and dispensing units by making the primary care level in communities the principle access point, task shifting to allow nurses and community health workers to deliver care, standardizing treatment guidelines and aligning procurement lists to reduce variability in the quality of care, and simplification of treatment regimens to once-a-day combination tablets with support tools to improve adherence. Challenges with delivering diabetes care remain, including low competition in the insulin market, specialist centers as the main access points, lack of qualified human resources, disjoint standards, and device-intensive procedures.

The aim of the Addressing the Challenge and Constraints of Insulin Source and Supply (ACCISS) Study is to improve access to insulin for those in need around the world¹. This requires a clear understanding of the barriers that prevent people from accessing affordable insulin. Since 2015, ACCISS has been looking into issues around insulin price and availability, which are preventing access to this life-saving medicine for 1 in 2 people in need. Phase I of the study focused on identifying the barriers to access to insulin and creating interventions based on this evidence. Phase II, starting in 2018, focuses on piloting these tools and interventions at a country level while continuing to work globally to address inequities and inefficiencies in the insulin market. The ACCISS study is led by Margaret Ewen at Health Action International, David Beran from Geneva University Hospitals and the University of Geneva and Richard Laing from Boston University. Several “profiles” have been developed to highlight unique dimensions of this complex problem: biosimilar insulin and regulatory landscape, patents, trade, prices, tariffs and taxes, as well as the manufacturing market.

Effectively addressing the global burden of diabetes requires effort in the following three areas: prevention, diagnosis, and treatment. Health system “innovations” are needed to enable adequate financing in resource poor settings, simple and low-cost technology, and community-focused delivery of care. From a health equity perspective, focusing on the poor and most vulnerable people is necessary to reduce suffering, poverty and promote development.

Dr. A.J. Kumar

Chief Scientific Officer, Jana Care

Jana Care: A breakthrough diagnostic platform to tackle chronic diseases

Jana Care builds point-of-care tests for the diagnosis and management of chronic diseases. NCDs are a leading cause of deaths and socio-economic burden globally, accounting for close to 7/10 deaths globally. LMICs are disproportionately affected, with 75% of NCD deaths occurring in those regions, leading to an estimated cumulative economic loss of \$7 trillion between 2011-2025. The WHO recommends cost-effective interventions to reduce the burden of NCDs, especially through programs integrated into the primary care level.

¹ <http://haiweb.org/what-we-do/acciss/about-acciss/>

Jana Care has developed several tools aimed at improving diagnosis and supporting behavior change. Specifically, these include the **Aina** smart-phone based diagnostic platform that performs various assay types (immunoassay, enzymatic or chemical-affinity) and the **Habits** behavior coaching app that enables personalized disease management to improve treatment outcomes. Aina is a portable, smartphone connected lab system that performs fingerstick blood tests within minutes. Its multi-test capabilities include HbA1c and blood glucose (diabetes), creatinine (kidney), NT-proBNP (heart failure), lipid profile (heart), and hemoglobin (anemia). The Aina system is CE marked and registered for sale in the European Union, emphasizing the importance of ensuring quality despite developing a system at a lower price point that better meets the needs of patients in India. It has been validated for accuracy and precision based on globally accepted ISO and CLSI guidelines for in-vitro diagnostic devices. The Aina system comes in different designs – Aina mobile and Aina station – to suit various needs within the healthcare system (e.g. at-home / remote testing and clinic-based tests). The system's cloud connectivity and data tracking allows for the triage of patients based on risk levels to provide the most appropriate treatment at the suitable level of the healthcare system. A dashboard allows patients and caregivers to track progress and changes in risks.

The Habits app is aimed at incentivizing positive behavior change to better manage NCDs. Various versions of the app have been developed and customized for patients with traditional type 2 diabetes, gestational diabetes, and congestive heart failure. The diabetes coach is based on a landmark study, the Diabetes Prevention Program (DPP), and was developed in collaboration with the Global Obesity Centre of the Madras Diabetes Research Foundation. Content on the app is localized and curated to specific geographies, including a food database reflective of different diets across regions and languages. The diabetes coach allows users to learn through interactive lessons and tips on various topics, track activities by recording blood glucose, meals, and exercise, and receive support through an automatic AI chat to reduce the likelihood of hyperglycemia and hypoglycemia events.

A dedicated app also exists for gestational diabetes mellitus (GDM), which affects 5–30% of pregnancies worldwide. Women with GDM are 7X more likely to develop diabetes later in life and children born to GDM mothers are more likely to develop obesity and diabetes in the future. The habits clinical dashboard provides insight into individual disease management and population health trends on the state of care. For example, overlaying prevalence of high-risk diabetics on a geographic map points to the influence the built-environment can have on disease progression. It also allows for easy remote monitoring of patient health and two-way communication to ensure follow-up. Jana Care places importance on data security and ensuring user protection, in line with international standards. Security measures include user authentication, data security (e.g. encryption), 24/7 monitoring of logs, infrastructure (e.g. hosted by Amazon Web Services with back-ups), and IT governance (e.g. ISO standards for quality management systems).

Currently, Jana Care devices are used in over 1,000 clinics in India and are used in screening programs at major events like the Kumbh Mela. Over 300,000 patients have benefited from tests for screening, diagnosing, and monitoring diabetes.

Alex Abramson

PhD Candidate, Langer Lab, MIT

An insulin pill that delivers – Microinjection in the gut

For decades, researchers have sought to provide oral delivery of therapies instead of injections. In fact, research in ingestible macromolecules started in 1922, the same year as the first insulin injection. Delivery of therapies through injections often implies the need for trained professionals, while causing discomfort to patients, generating waste, and perpetuating stigma. Insulin is the only life-saving therapy for type 1 diabetics to control their blood glucose and lower glycosylated hemoglobin levels, as well as the most effective therapy for 20-30% of type 2 diabetics. A challenge remains with the low bioavailability and high variability of oral biologics. Additionally, delivery of macromolecules orally is limited by rapid degradation and poor absorption in the gastrointestinal tract. Studies have shown that patient and healthcare professional preference for oral delivery leads to delays in initiating insulin therapy by up to 7 years and reduces quality of life in ways that can lead to poor adherence.

As described in a recent paper published in *Science*, an ingestible self-orienting system for oral delivery of macromolecules was presented². To overcome the challenges associated with oral biologic delivery, the system aids with localization, safe and efficacious actuation, permeation, and release of clinically relevant dose size to achieve systemic drug uptake. Inspired by the leopard tortoise's ability to passively reorient, the Langer Lab has developed an ingestible self-orienting millimeter scale applicator (SOMA) that autonomously positions itself to engage with GI tissue and deploys milliposts fabricated from active pharmaceutical ingredients directly through the gastric mucosa while avoiding perforation. They show that the drug in the milliposts remain stable for 16 weeks at 40°C, removing the need for refrigeration. They have also conducted in vivo studies in rats and swine supporting the materials and method's safety and, using insulin as a model drug, demonstrate that the SOMA delivers similar API plasma levels to subcutaneous millipost administration. Use of the SOMA device have not lead to tissue damage or abnormalities from stomach injections, while cost of production are comparable to traditional syringes for insulin injection. This demonstrates the potential such a device could have for overcoming cold-chain issues, while improving the patient experience and adherence.

Dr. Amy Moran-Thomas

Alfred Henry and Jean Morrison Hayes Career Development Assistant Professor of Anthropology, MIT

An anthropology of medical technologies amidst a global diabetes epidemic

This presentation provides an anthropological and cultural perspective to the global diabetes epidemic. While there are multiple dimensions to the discussion, the focus was on insulin in particular and associated medical technologies (e.g. glucose monitors). The research presented bridges the anthropology of health and environment (chronic disease; ecological and agricultural change;

² Abramson et al., *Science* 363, 611–615 (2019)

metabolism and nutrition) with ethnographic studies of science and technology (medical devices; global health chemicals; epigenetic debates; online health communities; technology and kinship). In the context of diabetes and insulin, reflections were made from a decade of community-based research in Belize and work in other communities.

Many of the key technologies for treating diabetes - such as insulin assemblages and glucose measurement technologies - were initially designed for use in affluent contexts and therefore often neglect the unique social, economic, cultural, and environmental contexts of low-and-middle income countries. In some communities, healthcare providers are hesitant to prescribe insulin due to the risk of patients rationing or overdosing. The need for refrigeration prevents a reliable and sustained supply of quality medicines. Lack of standardization between glucose monitors and test strips leads to a complex supply chain, with new models and features that reduce compatibility. In aggregate, the physician-patient relations are largely shaped far beyond the clinics where these encounters occur, in distant laboratories and facilities that may not have insight into the realities faced by many communities that need such devices to survive.

This has led to a growing mismatch between imagined users of these therapies and those who need them today for survival. There needs to be a more deliberate effort to collaboratively rethink “innovation” beyond slight enhancements to existing technologies. With a substantial number of new diabetics located in low-and-middle income countries, the talk focused on how to better consider the needs of these users and ways to better embed principles of global equity in the design and deployment phases of diabetes care technologies.

Examples were shared of efforts aimed at promoting equitable design: DIY glucometer developed in the MIT Little Devices Lab and turning silk into diabetes test strips. Just as there is a cold chain, access to care also requires a “care” chain to provide peer support, consultation on managing diabetes, promoting adherence, ensuring follow-up, and responding to other needs of patients. Maintenance of systems is just as important as the initial development and deployment of technologies, especially as the care of NCDs is chronic as well and requires continuous effort and attention.

Discussions

The four presentations outlined above were followed by an interactive dialogue between the audience and panel of speakers. Topics from the discussion are summarized in the following points:

- Understanding the impact of patents and standardization in medical devices on access.
- Evaluating tradeoffs between incentives to innovate and making medical products affordable.
- Measuring overall health system costs, not just the production of insulin and medical devices.
- Assessing the influence of different insurance systems (e.g. universal coverage vs. private plans vs. pay by performance) on the accessibility and affordability of insulin.
- Understanding unique considerations of communities to design appropriate innovations.
- Framing access to healthcare as being broader than just health alone; it also includes commercial determinants of health amongst other topics.
- Assessing the role of public-private partnerships in the NCDs space.
- Measuring the relative impact of different intervention in health systems.
- Using quality data to better identify, evaluate, and overcome barriers to access.
- Understanding disparities both between and within countries.

Forward Looking

The barriers preventing access to insulin and diabetes management are multidimensional and complex. They span the healthcare value chain and can most effectively be tackled by bringing together a community of professionals with diverse expertise and shared aspirations to make access to healthcare more equitable. This event was aimed at initiating a discussion and is the inaugural session of the *BioACCESS Global Health* seminar series. Future events will focus on various geographies, disease types, and parts of the healthcare system.