

Dr. Mina Hosseinipour (left) at one of the UNC-Malawi Project sites in Lilongwe, Malawi. Pictured with her are two of her Clinical Study Coordinators, Cecelia Kanyama (center) and Nasinuku Saukila (right). | Photo provided by Dannette Smith Cook



Dr. Mina Hosseinipour did not know her research would positively change the trajectory of the worldwide HIV epidemic when she graduated with a bachelor's degree from the University of Kentucky in the early 1990's. In fact, it wasn't until she was a resident in internal medicine at Baylor College of Medicine that she decided to pursue a career in infectious diseases.

This led her to The University of North Carolina (UNC), a world leader in the field of infectious diseases, where she completed her fellowship and a concomitant Master's of Public Health. During her third and final year of fellowship, she headed to Africa to work with the UNC Malawi Project: a cooperative between the Lilongwe Ministry of Health and UNC to initiate the HIV Prevention Trials Network (HPTN) Study 052.

This landmark study showed that in couples in which one partner is HIV positive and the other is HIV negative (so-called "discordant couples"), early anti-retroviral treatment (ART) in the affected partner causes a marked drop in infection rates of the non-infected partner. This study was truly a game-changer, recognized by the prestigious

scientific journal *Science* as their "Breakthrough of the Year" in 2011. The study was originally designed to enroll thousands of discordant couples to treat and track over a period of 5 years. However, after periodically reviewing preliminary data, the NIH stopped the study early. It appeared that the results were so profound that it was imperative to offer treatment to all patients meeting the enrollment criteria. These results changed the trajectory of HIV therapy through the addition of new treatment guidelines to "scale-up ART." In fact, the results were so impressive that they prompted Dr. Hosseinipour's boss and the lead author on the study, Dr. Myron Cohen, to conclude in an interview that "it makes you actually believe that you can actually see the beginning of an epidemic, and the end of an epidemic, in one lifetime."

In addition to this prestigious research, Dr. Hosseinipour has also co-authored a study showing reduction in transmission of HIV from infected mothers to their offspring when treated with ART while pregnant.

So here we are, with a new paradigm of "treatment as prevention" and celebrating one million babies born HIV negative to an

HIV positive mother through the initiatives of PEPFAR. It is truly a new era for prevention and treatment of HIV around the globe. Dare we say, "The Downfall of an Epidemic?"

Dr. Hosseinipour and your correspondent were medicine residents together at Baylor College of Medicine in Houston. Your correspondent is pleased and proud to share an interview with Hosseinipour regarding both her remarkable career and her role in changing the face of the HIV/AIDS epidemic.



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Interview: Turning the Tide on an Epidemic

A Native Kentuckian Changes the Deadly Trajectory of HIV Infection | Dannette Smith Cook, M.D.

Tell us a little bit about the work you did that earned *Science* journal's Breakthrough of the Year Award in 2011.

I initially went to Lilongwe, Malawi to start the HPTN 052 study that led to the "breakthrough" of the year. The breakthrough demonstrated that early antiretroviral therapy can reduce HIV transmission to a negative partner by 96%. My work on the research protocol largely included developing the research protocol with our chair (Myron S. Cohen) and then building the local team, training, recruiting discordant couples, and supervising the implementation of the study. Much of the recruitment included building partnerships with local organizations that perform lots of HIV testing, as well as establishing our own testing activities. Our site was the leading enrolling site, and we put 251 couples on the study.

How has that seminal paper affected the direction of research in HIV/AIDS since its publication two years ago?

On an international scale, the WHO has issued a guideline for the management of discordant couples largely stating that with-in all such couples, the HIV infected member should be offered treatment. More broadly, the HPTN 052 study supported earlier initiation of ART for the general population and the latest (2013) WHO guidelines support initiation of ART at CD4 of 500 cells (rather than 350). Research now focuses on how earlier treatment (or universal treatment of HIV infected patients) will reduce HIV transmission on a population level. Countries, like Malawi, have used the "treatment is prevention" message as a strong rationale to expand ART treatment to all HIV positive pregnant women as this provides a maternal health benefit to the mother, as well as a prevention benefit for the infant and any HIV negative partner they might have.

Is treatment of infected partners at higher CD4 counts to prevent transmission to non-infected partners now considered standard of care?

It is now the WHO recommendation (as well as IAS, DHHS, etc) but some countries have not yet moved to 500 cells, due to cost considerations and whether or not the health care infrastructure can accommodate the increased number of patients that would need care. [WHO- World Health Organization, IAS- International AIDS Society, DHHS- Department of Health and Human Services]

Infection rates in Malawi according to UNAIDS stands at 10%. Remarkably, they describe a 55% drop in the 10 years between 2001 and 2011. How often do you estimate infection rates? Do you attribute the marked drop in infection rates to more widespread availability of ART?

The Malawi Ministry of Health conducts HIV prevalence estimates alongside UNAIDS annually. This is largely based on an epidemiology program called "SPECTRUM" that uses inputs from regularly collected data to estimate the prevalence. In rural South Africa, there was a study that clearly demonstrated that HIV incidence decreased according to population coverage of ART (Tanser, et al.). Malawi has even higher coverage than seen in this article, so I suspect that many of the reductions are due in part to increased ART coverage. There may be increased condom use among known positives that could also contribute to the reduction (among other factors).

In what amount of time would you expect to see a drop in infection rates with new guidelines?

I suspect the trajectory of reduction in new infections will be somewhat slower than with the initial roll out, as the change is modest to go from 350 to 500 [CD4 Cell Counts], as compared to the initial situation where no one was on therapy to the current rates of approximately 60% coverage of those in need at the 350 threshold.

You also co-authored another study showing decrease in vertical transmission rates in infants whose HIV infected mothers were given anti-retroviral treatment for at least 12 weeks prior to delivery. Do pregnant women in Malawi frequently make it to delivery without pre-natal care? How can you target (especially HIV infected) pregnant women for pre-natal care prior to 28 weeks of pregnancy? Were the CD4 counts in the study participants also liberalized up to a CD4 count of 500? [PMTCT-Prevention of Mother to Child Transmission of HIV]

Ninety percent of Malawian women attend at least one antenatal visit, although most do not present until the mid-to-late second trimester or even in the third trimester (average 26 weeks). So for PMTCT, it is important to start early in pregnancy to optimally reduce transmission to the infant. Malawi pioneered an approach of treating all HIV positive pregnant women regardless of CD4 cell count at the initial visit in which they were identified as positive. (Option B+) This has resulted in over a 700%

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Tell me about the impact on economic and social development that the HIV/AIDS epidemic has had in Malawi. UNAIDS discusses the increased impact on women as well as the devastation in fields that employ women such as teachers and healthcare workers (HCW).

Certainly, several areas have been affected by the HIV epidemic including teachers, healthcare workers, military, and police. With respect to HCW and teachers, the numbers required to provide services is well below requirements; up to 70 or 80% of positions in government facilities are unfilled according to the different health care cadres. And education is the backbone for the future. Despite the AIDS epidemic, Malawi had enormous population growth (2.8% per annum), such that the need for these positions will be even more important. This population growth is a major barrier to development in Malawi.

Is your institution able to target rural populations as well? What are the different barriers to care between rural and urban affected populations?

Yes, our programs target some rural communities, as we extend our catchment area to 50km from our facility. This includes rural communities. Distance to health facilities becomes a larger barrier for rural communities.

What have been some of the roadblocks to healthcare for people infected with HIV/AIDS in Malawi. Are patients able to obtain the medications they need? Who provides the medications for those that cannot afford the drugs?

The ART has been free since 2004, so that ART drug cost is not a barrier. However, the transport costs to get to clinics are difficult for the rural poor. The ART program, (funded through the Global fund with a parallel procurement system) has safeguards to prevent stock-outs. For general health care in Malawi, all govern-

ment hospitals and clinics are free. However, for medications that are not provided through the Global Fund, medications are frequently out of stock, and patients will depart clinics without these medications. Also, if they are admitted to the hospital, there are common stock-outs of essential medications and supplies. In these scenarios, patients would go without. [The Global Fund to Fight AIDS, Tuberculosis, and Malaria]

You mentioned that you are able to provide ART through your clinic to patients, but once they are hospitalized they may not have access to many of the medications they need. Is that ART as well as antibiotics, etc? Does the act of being hospitalized become a marker for increasing mortality? Stated in another way, when an elderly person falls and breaks a hip, no matter what their health capacity was prior to the break, their incidence of all-cause mortality rises significantly during the year after the break. Do you see a "this is the beginning of the end" scenario when your patients ultimately do need hospitalization?

ART would still be available to the patient, as they can either get an emergency supply through the hospital clinic, the ART clinic, or they can take their own. I don't think the same holds entirely with our HIV infected patients, as usually the problem is largely reversible if they can get through the acute period. But, that gives me a research idea to evaluate the outcomes of patients who have had admissions and what follows thereafter.

I remember the day I ruled out a career in Infectious Diseases. I have vivid memories of one particular patient who died from an AIDS-related illness. Unfortunately, sometimes we were just too late to make a difference, especially in the early days of ART. I know you must have had experiences during residency just like that, but somehow you decided to face it head on. I am curious about that. Was there a particular patient that affected your decision to go into Infectious Diseases?

While I won't target a particular patient, I was rather struck by how, as an intern in 1995/96, there was complete hopelessness to HIV, but by the time I was in my third year as a resident and ART was now more available, the number of dying AIDS patients on my service was lower. By going to the HIV clinic, I could see the hope and reality of HIV treatment. I see the exact

same phenomenon in Africa. When I arrived in 2001, death was the reality for HIV patients. Now, my clinic is a lot of healthy people going about their usual lives. Imagine if your patient had survived, if you had reversed his course.... going from a bedridden state, to walking with a cane, to coming into your office with his new born baby. It is transformative.

What is the typical lifespan of someone who has received optimal treatment of HIV now? What are the causes of mortality for patients with HIV today?

I haven't taken care of HIV infected patients in the US for some time now, but life expectancy for most HIV infected patients in care (I clarify "in care") actually approaches that of HIV uninfected individuals. And the spectrum of illnesses faced by HIV infected patients is similar to that of any aging population, including cardiovascular disease, liver disease, and renal disease.

Grassroots & Citizen Involvement in HIV.

I know that UNAIDS has several NGO's on its program coordination board. Personally, I see the integration of the field of HIV/AIDS with citizen diplomacy as being not only an early vanguard of that type of arrangement, but also a model of cooperation and mutual respect. Could you touch on the role that these types of groups have played in your field? You mentioned that some of these groups can be helpful because they provide access to medications outside the "usual channels". That certainly reflects influence at a very local level. What about higher up in the policy making and funding choices you see in the field?

Certainly community advocacy groups are a part of the HIV campaign and make their voices heard, particularly at the World AIDS conference. But, more of the meetings and conferences that I attend focus on the science of HIV. Our research groups have community constituency groups that are part of the scientific process, so that we remain actively engaged in the needs of community. On a local level in Malawi, our site has a community advisory board and an active community program in charge of education. For most policy decisions in which I'm involved, we really focus on the technical aspect of decision-making, and then the decisions are presented to the wider range of stakehold-

ers. This ensures that decisions can remain evidence-based, rather than appealing to particular groups.

Do you see large international agencies as a help or a hindrance in trying to provide medical care and social support for Malawians affected with HIV? In what ways?

I think they are helpful because they increase the human workforce and often provide supplies in a way that does not go through the inefficient (and often corrupt) systems of the Malawi government channels.

Tell me what you like about living in Malawi (or Africa in general) (Many Patterson students go on to international careers, often in developing countries, or in places that no one else has an interest in going!)

Well, as an expatriate, you have a pretty good quality of life in the sense that you can live securely and can afford to hire staff to help with the garden, cleaning, cooking, or child care. The community is also geared to have immediate social circles, usually with other expats also living abroad. It is sometimes unfortunate how easy it is to integrate with the other expats, as it limits your interactions with Malawians. But, I've been in Malawi long enough that I have some Malawi social circles as well, and you end up feeling like you live in a small town.

What about living and working in Malawi keeps you there?

I think the work is the big component. The range of activities from teaching, research, clinical care, and policy development makes for continued excitement and challenges.

Dr Hosseinipour, thank you so much for sharing your insights with us. It is truly difficult to fathom the progress that has been made in the last 12 years since you arrived in Malawi. Congratulations and best wishes to you and the UNC-Malawi Project. 🇺🇸🇲🇼

Dr. Dannette Smith Cook is a first year Master's Candidate in Diplomacy at The Patterson School. She is certified in internal medicine by The American Board of Internal Medicine and a Fellow in the American College of Physicians. Dr. Cook is a practicing hospitalist in Somerset, Kentucky.