



# TAKING ON HIV AND ORAL HEALTH

EMBARKING ON A NEW STUDY OF PEOPLE LIVING WITH HIV, DR. TEMITOPE OMOLEHINWA HOPES TO BUILD DATA ON AN UNDERSTUDIED ISSUE

OPPOSITE: Dr. Temitope Omolehinwa (GD'14, GD'17, D'20), Assistant Professor of Oral Medicine, is leading a new clinical study of people living with HIV to examine the impact of therapies on their oral health.

DR. TEMITOPE OMOLEHINWA (GD'14, GD'17, D'20) got into dentistry wanting to be a clinician, not conduct research. But over the past several years, the pull of research has been impossible to resist.

"I couldn't help myself," says Dr. Omolehinwa, Assistant Professor of Oral Medicine at Penn Dental Medicine. "I saw trends in the clinic and I wanted answers."

She's on the cusp of launching an investigation — her first as a principal investigator — that aims to provide answers to the many questions that surround the oral health, systemic health, and treatment of people living with HIV. Funded with \$3.75 million over five years by the National Institutes of Health's National Institute of Dental and Craniofacial Research (NIH/NIDCR), the longitudinal study will result in a robust database that Dr. Omolehinwa and others will mine for clues to offer better care to those who are HIV-positive.

"Over the years I have had patients saying to me, 'If you ever move on with a study, please count me in,'" says Dr. Omolehinwa, who is director of the Medically Complex Care (MCC) Clinic at the School, which serves more than 700 people with HIV. "They're very interested in being a part of whatever efforts will advance HIV care. I'm glad we're now working to make that happen."

## **DRAWN TO RESEARCH**

During her dental education at the University of Lagos in Nigeria, Dr. Omolehinwa received a strong background in clinical dentistry. She derived satisfaction from clinical practice. "I really enjoy the hands-on nature, and not being able to predict my day-to-day," she says.

To enhance her skills, she came to Penn Dental Medicine in 2012 as an oral medicine resident. Around the time that she was interviewing for her residency, the School had recently launched its Doctor of Science



in Dentistry (DScD) Program, created to prepare students for careers as dentist-scientists in academic dentistry, pairing clinical care with either basic science or clinical research.

Open and eager to learn, Dr. Omolehinwa entered that program in 2013 concurrently with her residency training, studying under Dr. Sunday Akintoye, Associate Professor and Director of the oral medicine research program. Akintoye had coincidentally also attended Dr. Omolehinwa's alma mater, the University of Lagos, and he returned there through a Fulbright fellowship in 2015.

Dr. Akintoye recalls that Dr. Omolehinwa "captured the attention of different faculty members by her depth of knowledge and enthusiasm for oral medicine."

Despite her fondness for clinical work, her research project for her DScD degree was firmly based in basic science. It examined the effects of hypoxia, or a lack of oxygen, on mesenchymal stem cells and the role it played in osteonecrosis of the jaw (ONJ), a condition

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— DR. SUNDAY AKINTOYE

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sometimes caused by radiation therapy when targeted to the oral cavity, and one that Dr. Akintoye's lab has long investigated.

"I like to try everything," she explains.

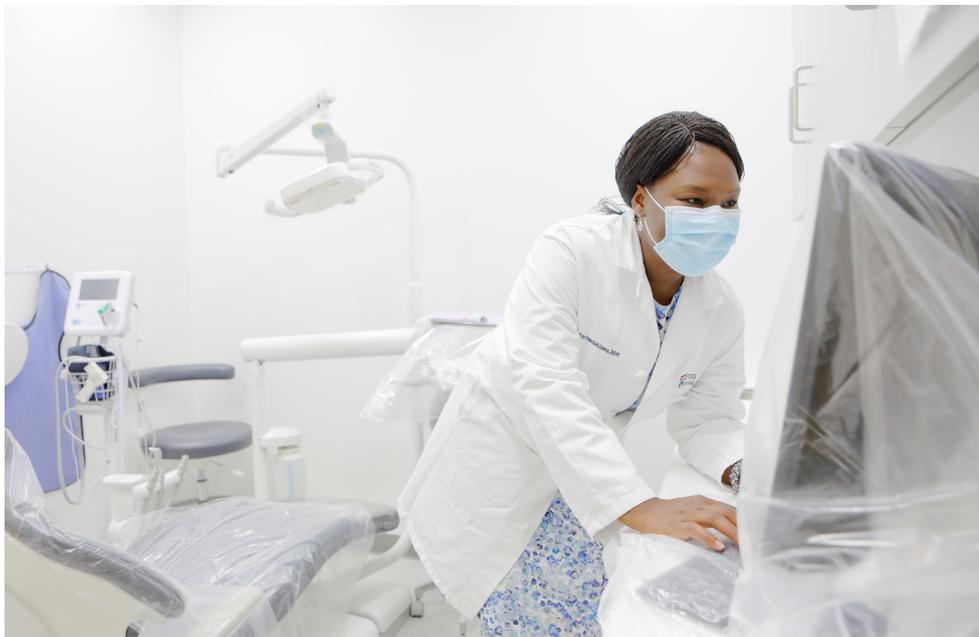
Her commitment to her laboratory work earned her the prestigious Lester Burket Research Award from the American Academy of Oral Medicine for best research project in basic science in 2014.

After earning her DScD and being hired to the Penn Dental Medicine faculty in 2017, Dr. Omolehinwa was ready to once again focus in on her clinical care and teaching. In addition to heading the MCC Clinic, she now also serves as Director of the Medically

Complex Patient Fellowship Program.

"I have watched her evolve into an effective teacher, rising clinician-scientist, and a good mentor to the dental students and residents," Dr. Akintoye says. "Her effective teaching style, strong clinical skills, and research background will make her a star in the oral medicine profession."

Through her close and careful clinical care, Dr. Omolehinwa found herself making note of curiosities and trends she wanted to pursue. Among several papers she crafted to present and study those questions, she pulled together a retrospective study of HIV patients she saw in the MCC Clinic, a



project that brought her into collaboration with Dr. Mel Mupparapu, Professor of Oral Medicine, as well as Dr. Akintoye.

Antiretroviral therapies (ART), though lifesaving, come with side effects, and many researchers believe systemic diseases, such as dyslipidemia, diabetes, and hypertension, are among the “side effects” associated with the drugs. “I was thinking a lot about the connection between these conditions, the chronic inflammation of these patients, the medications they were on, and their oral health,” Dr. Omolehinwa says.

She presented the findings of her retrospective study at the School’s Research Day in 2019, which showed that about 62% of patients living with HIV undergoing treatment at Penn Dental Medicine had at least one non-communicable disease, with cardiovascular conditions being the most prevalent.

Her study caught the attention of Dr. Patricia Corby, who had been hired earlier that year as the School’s Associate Dean of Translational Research and shortly thereafter opened the School’s Center for Clinical and Translational Research. Dr. Corby saw potential in the project — and in Dr. Omolehinwa.

“I see Temitope as the ideal trainee,” Dr. Corby says. “Besides being very smart and having an outstanding work ethic, she

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had the strengths to write the grant following our very high standards, was always humble enough to ask the right questions, was responsive with feedback while also expressing her opinion when she disagreed with any of our guidance.”

With the help of Dr. Corby and her team, led by Kira Nightingale, the Director of Research Operations for the Center, Dr. Omolehinwa poured her time and energy into crafting a grant proposal to prospectively study the connections her earlier study had illuminated, responding to a call from the NIH for studies on HIV and comorbidities.

“I joke with Pat Corby that she must have moved here because of me,” Dr. Omolehinwa laughs. “I just soaked up everything I could from her background in clinical and translational research. She expanded my way of thinking.”

## LINKED CONDITIONS

Despite being a junior researcher with limited experience in such projects, the grant was quickly funded. This fall, Dr. Omolehinwa, along with partners and collaborators have been completing preparations for the study, which will begin enrolling patients in late November. Collaborating on the project are Drs. Akintoye and Mupparapu as well as Dr. Vincent Lo Re, Associate Professor of Medicine at Penn Medicine; Kelly Jordan-Sciutto, Vice-chair and Professor in Penn Dental Medicine’s Department of Basic and Translational Sciences; members of Dr. Corby’s team, as well as biostatisticians from Penn Medicine.

The study aims to enroll patients not only from the Penn Dental Medicine clinic, but also at Penn Presbyterian Medical Center and the NIH-funded Penn Center for AIDS Research (CFAR). It will include a total of 350 participants, a number the researchers foresee no problem in reaching. “To avoid bias, we need to make sure we’re seeing patients besides those who are having frequent oral evaluations so we get a mix of different populations,” Dr. Omolehinwa says.

From her retrospective study and care in the MCC clinic, Dr. Omolehinwa has seen that patients with HIV are at risk for oral health challenges. Though most of her patients are consistent with their ART regimen, she has seen “rampant caries,” or dental cavities, in spite of good oral hygiene. And, curiously, many of these caries occur at the root, where the tooth meets the gums, rather than on occlusal surfaces, which come into contact with food more frequently.

“Since some patients are on a lot of medications, and others are not on as many, we’re asking ourselves whether the drugs they’re on have anything to do with this increased risk for developing dental caries,” she says.

Though one might think that inflammation associated with HIV infection could trigger oral inflammatory problems, such as periodontitis, Dr. Omolehinwa and others have noted that their patients living with HIV on ART don’t have significant periodontitis. They do, however, tend to have dry mouth, which can lead to other concerns, such as thrush.

Meanwhile metabolic conditions — including vascular diseases, diabetes, dyslipidemia, and osteoporosis — plague patients whose HIV infection is well controlled on ART. Researchers believe these conditions owe to HIV’s chronic activation of the immune system, possibly exacerbated by ART. Dr. Omolehinwa suspects that patients’ saliva, which may be altered by which drugs they’re taking, could be responsible for the unusual caries patterns, and could feed back into systemic disease, as dental caries is also an infectious disease.

### SCIENCE-BACKED ANSWERS

The study that Dr. Omolehinwa is launching aims to draw links between what medications patients are taking, what is happening in their oral cavity, and what conditions are affecting their whole body. Within this cohort of people living with HIV, she and her colleagues will be following two groups of patients: those with non-communicable diseases, like the metabolic conditions, and those without non-communicable diseases.

Participants in the study will be tracked over years, receiving baseline and follow-up measures of oral health, general health, bone density, oral and systemic inflammation biomarkers, and more. “Patients will be seen every six months, taking a close look at mucosal tissues and dental status, including caries rates, periodontal assessments, and oral cancer screenings,” Dr. Omolehinwa says. “We will also be collecting oral samples, such as saliva and oral swabs, as well as blood samples.”

In addition, the researchers will be collecting a broader range of data, including quality-of-life measurements, cognitive functioning, and mental health screenings.

With this data, Dr. Omolehinwa hopes to test her hypothesis that the severity of oral diseases, such as caries and periodontitis, is associated with ART-driven changes affecting not only systemic health but also oral health due to salivary function changes, such as dry mouth, in patients with chronic metabolic conditions.

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“The question is, is all this low-grade persistent inflammation a result of HIV infection, or is it a direct effect of the drug, or both?” Dr. Omolehinwa says. “The truth is we don’t know.”

The study is longitudinal, observational, and not interventional, but is tailored toward cataloging data that will inform a variety of translational research projects in years to come.

“I really see this as a study that will keep evolving,” she says. “We’re setting up a large database with this specific cohort, and we’re looking into proteomics, genomics, microbiome information, and much more. We’re already getting requests from other investigators interested in collaborating with us as we get started. In the immediate near term, we’re focusing on oral health, but there is a lot of potential for collaboration in the context of this study with the comprehensive type of data we’re collecting.”

As the study gets off the ground, Dr. Omolehinwa is already looking toward plans to extend the grant, continuing to reap information that will allow for the development of future interventional trials aimed at improving the oral and overall health of those living with HIV for years to come — and which may cement Dr. Omolehinwa’s dual identity as both clinician and researcher.

“We can answer questions in the clinic but a lot of times we need to go beyond what we’re seeing in the dental chair,” she says. “I’m a firm believer in translational research and clinical research. I think a combination of both is important to get a full picture.”

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— By Katherine Unger Baillie