

# "Of all cooperative enterprises

is the most important and gives the greatest returns."

– William J. Mayo, M.D., 1919

▲ Public health does public good • 08

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# Letter from the secretary-treasurer

This issue of Mayo Clinic Alumni magazine provides a glimpse into public health endeavors by Mayo Clinic and its alumni. I say glimpse because the public health efforts have been vast. The stories in this issue provide a look back at some of the early efforts of the Mayo brothers and their father and a snapshot of current efforts. While the focus of public health has evolved from garbage collection and milk quality to opioid stewardship, healthcare disparities and much more, the commitment is as strong as it was when Dr. Charlie oversaw public health in Rochester. Students and trainees at Mayo Clinic take note of the rich history and current efforts and perpetuate the values of public health in their own work around the world. I'm proud to be part of the tradition of service in public health matters.

Another aspect of Mayo's rich history is welcoming the next generation into our professions. Assisted by your generosity, the Alumni Association gives stethoscopes (alumniassociation.mayo.edu/product/fund-a-stethoscope) to first-year medical students of Mayo Clinic Alix School of Medicine and gives diploma frames (alumniassociation.mayo.edu/products/fund-a-diplomaframe) to Mayo Clinic Graduate School of Biomedical Sciences students as they complete their theses. These gifts help to reinforce the recipients' connection to Mayo Clinic and its values. We appreciate your help in our continuing to be able to offer these gifts to the new physicians and scientists from the Mayo community.



M. Molly Mc MAhon, M.D.

M. Molly McMahon, M.D. (ENDO '87) Secretary–Treasurer Mayo Clinic Alumni Association Division of Endocrinology, Diabetes, Metabolism, and Nutrition Mayo Clinic in Rochester

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"Of all cooperative enterprises **public health is the most important** and gives the greatest returns."

> – William J. Mayo, M.D., 1919, address on "Socialization of Medicine and of Law" to the Minnesota and Wisconsin State Bar Association



Father and sons — William Worrall Mayo, M.D., is flanked by his sons William J. Mayo, M.D., and Charles H. Mayo, M.D., in 1910.

ccording to the American Public Health Association, public health promotes and protects the health

of all people and their communities. While healthcare institutions and providers treat people who are ill, public health aims to prevent people from getting sick or injured. Public health focuses on population health instead of the individual patient.

Mayo Clinic's public health endeavors date back to the early days of William Worrall Mayo, M.D., and his sons, William J. Mayo, M.D., and Charles H. Mayo, M.D.



Countless Mayo Clinic physician and scientist alumni, both those at Mayo Clinic and those around the world, have worked in public health and made significant contributions to population and community health. In this issue of Mayo Clinic Alumni magazine, we shine a light on a selection of individuals doing that work.

The Mayo Clinic Opioid Stewardship Program team took on the formidable task of standardizing opioid prescribing practices across multiple locations and creating policies and workflows for the treatment of patients with opioid use disorder. This program, now in its eighth year, is measuring its progress and focusing on how to screen for and help patients who may have opioid use disorder. This Herculean undertaking has resulted in what Mayo Clinic believes to be the most comprehensive opioid stewardship program in the U.S. The public health effects of these efforts cannot be overestimated, and Mayo wants to help other healthcare organizations do the same.

Also included are stories about two Mayo Clinic physicians involved in public health — one for patients at higher risk for HIV transmission and one for immigrants and refugees who may not be well served by healthcare systems. Two other features focus on Mayo Clinic alumni who work for the Centers for Disease Control and Prevention. They're among the thousands of CDC professionals working for the nation's health protection agency to save lives and protect people from health threats.

We extend gratitude to all alumni working in public health around the world. •

# To protect & advance the health of the people

A LOOK AT DR. CHARLIE'S **PUBLIC HEALTH INVOLVEMENT** IN ROCHESTER









(Previous spread) Left: Charles Horace Mayo, operating room, 1913–1922. Top: Charles H. Mayo, M.D., and nurse Alma Knight tend to a baby, 1936. Right: Institute Hills, 1930s. (Above) Charles H. Mayo, M.D., and William J. Mayo, M.D., in the first operating room at Saint Marys Hospital, 1904.



# Father & sons' involvement in **public health**

## 863

William Worrall Mayo, M.D., arrives in Rochester as an examining surgeon for Civil War draftees.

#### 1865

Rochester City Board of Health forms for vital statistics information and collection and disposal of garbage; Dr. W.W. Mayo is first medical health officer.



esidents past and present of Rochester, Minnesota, owe a debt of gratitude to **Charles H. Mayo, M.D.** — Dr. Charlie. Not only for the expected reasons but also for the unexpected, including milk regulations, vaccination clinics and streets free of garbage.

In addition to his service to Mayo Clinic patients, Dr. Charlie served as Rochester's health officer for a quarter century — 1912 to 1937 — promoting scientific methods to control the spread of disease and helping to place Rochester in the forefront of the public health movement in the Upper Midwest. Dr. Charlie led the way to provide free smallpox vaccinations; organized garbage collection and disposal; advocated for and oversaw the first milk control ordinance and food safety ordinance, including pasteurized milk; introduced school health, dental, prenatal and well-baby clinics; and established procedures for handling bodies of the deceased.

#### FAMILY HISTORY OF COMMITMENT TO PUBLIC HEALTH

During the pioneer days, there were no ongoing public health services. Instead, efforts were directed at specific problems of immediate

#### 1866

Rochester passes its first public health ordinance, eliminating manure piles.

## 869

Rochester City Council authorizes Board of Health to take measures to care for persons with **smallpox** and prevent the spread of contagious diseases at city's expense.

#### 1872

Minnesota becomes fourth state to establish a state board of health (preceded by Massachusetts, Virginia and California).

#### 1883

Minnesota requires all towns, villages and cities to establish local boards of health, establishing a system for coordinated action on a statewide basis. concern to the community and its leaders — typically a communicable disease epidemic. In 1863, Rochester and the surrounding area were threatened by a smallpox outbreak. The city's mayor appointed three aldermen to serve on a smallpox control committee, likely to give city officials the authority to quarantine families exposed to smallpox and isolate cases of the disease.

Two years later, **William Worrall Mayo, M.D.,** was appointed as Rochester's first medical health officer. He also served on the city's first board of health from 1884 to 1887. The senior Dr. Mayo served intermittently as chair or secretary of the city health board for several decades. Dr. Mayo's elder son, William J. Mayo, M.D. — Dr. Will also served as secretary or health officer of the Rochester Board of Health and was a member of the Minnesota State Board of Health from 1892 to 1899.

#### **DR. CHARLIE'S TURN**

In 1900, Governor John Lind appointed Dr. Charlie to the Minnesota State Board of Health — a role he held for two years. A decade later, during a scarlet fever outbreak in the state, many in Rochester were worried about the epidemic and effect it would have on businesses and the clinic. Another local physician had been recruited to serve as part-time health officer. He defended himself from angry complaints about lack of progress in advancing public health matters, including milk and meat regulations, saying that dairy farmers and butchers had threatened to fire him if he stepped on their toes.

Dr. Charlie said, "Give me the job. They won't try to fire me."

In the middle of the night, a delegation of concerned Rochester citizens awakened Dr. Charlie and insisted he assume the position of city health officer immediately. Legend has it that he was sworn in wearing his nightshirt and dressing gown.

Dr. Charlie immediately introduced strict quarantine measures to put an end to the scarlet fever epidemic. The Mayo brothers paid for a deputy city health officer to assist Dr. Charlie.

## 1892–1899

William J. Mayo, M.D., serves as member of the Minnesota State Board of Health, and secretary or officer of Rochester Board of Health at various times.

### 900-1902

**Charles H. Mayo, M.D.,** serves on Minnesota State Board of Health. **1911** Dr. W.W. Mayo dies. **1912** Dr. Charlie sworn in as Rochester health officer.



 $Charles\,H.\,Mayo,\,M.D., in\,an\,operating\,room\,at\,Saint\,Marys\,Hospital\,between\,1913\,and\,1922.$ 

Holmes School, Rochester, early 1900s.

# 1913

Examinations of school children begin for early detection of contagious diseases.



### **1914**

Dr. Charlie appoints Gertrude Booker Granger, M.D., as deputy health officer — first woman as health officer in Rochester.

#### 1916

Ordinance passes to put garbage collection under city health officer.



Charles H. Mayo, M.D., and nurse Alma Knight tend to a baby, 1936.



Mayo Clinic Alumni



#### extolls the virtues of milk and pasteurization.

#### MOOVE-MENT TO PASTEURIZATION

Dr. Charlie won a local battle to require the pasteurization of milk.

A state inspector had declared Rochester milk to be the dirtiest in the state for a town its size, and Dr. Charlie was convinced that many of the ailments he saw in the clinic were due to consumption of infected milk. Encouraged by the Women's Civic League, he persuaded the city council to pass an ordinance providing for the inspection of dairy herds and milk plants to ensure cleanliness. To better understand the processes involved in milk production, Dr. Charlie established a dairy farm at his Mayowood home. He became convinced that compulsory pasteurization was necessary and proposed a city ordinance requiring dairies to comply.

According to "The Doctors Mayo" by Helen Clapesattle, "Dr. Mayo wanted to make Rochester dairy farms observe rules almost as strict as those in his own operating room. He wanted the milkmen to wash their hands with antiseptic soap before entering their cow barns, to wear spotless clothing, handle the milk in special cooling rooms, pasteurize every drop of it, and have it graded regularly by an employee of the city health department."

This 1925 proposal wasn't welcomed by the cities' milk distributors, who said it would drive them out of business. During a contentious five-hour debate, Dr. Charlie reminded the council members that their job was to safeguard the health of the city, not the pocketbooks of the dairy farmers, according to Clapesattle's book. The bill passed by a single vote.

#### 1920-1922

Six-week program in home nursing introduced for local women.

#### 1921

City passes regulation for storage of food in restaurants, stores and vehicles. Rochester physicians begin weekly public health talks open to the public.

1921

1922 City hires public health nurse.





Downtown Rochester, 1931.

1923

disposal plant.



1925 Pasteurized milk ordinance passes.

#### 1928

Mayo pediatricians organize and staff well-baby clinics at health department.



A state inspector had declared Rochester milk to be the dirtiest in the state for a town its size, and Dr. Charlie was convinced that **many of the ailments he saw in the clinic were due to consumption of infected milk.** 

#### **REFUSE REUSE**

Another of Dr. Charlie's initiatives in Rochester was garbage collection. An ordinance that passed in 1916 required garbage collection to fall under control of the health officer, with garbage collectors appointed by the city council. The cost per home for waste pickup was 10 cents per week. Prior to that, waste was thrown in streets and alleys and picked up occasionally.

In 1920, Dr. Charlie donated to the city a 30-acre farm in southeastern Rochester, with \$5,000 in hogs, pens, feed and wells. Edible waste from the garbage collection was fed to the farm's hogs. When the hogs were sold for slaughter, the income was returned to the city's health program to defray costs. This system lasted until 1953.

Many public health initiatives were introduced during Dr. Charlie's

tenure as city health officer, including appointing the first woman as a health officer in the city. Dr. Charlie hired Gertrude Booker Granger, M.D. (I '98, died 1928), as full-time deputy health officer. She'd been the third physician and first woman to join the Mayo brothers' practice in 1898, responsible for eve exams and refractions. She served as deputy health officer for two years, working with Dr. Charlie on the 1917 passage of the city ordinance for the inspection of milk, dairies, dairy herds and bottling/pasteurizing plants. Dr. Booker Granger played an important public health role during the 1918 influenza pandemic, advocating for masking, isolation and other safety measures.

Dr. Charlie resigned as city health officer in 1937 and died two years later. •

#### 1930 Community prenatal clinics begin.

#### 1931

Sexually transmitted diseases clinics begin.

#### 1932-1937

Dr. Charlie serves as president of Minnesota Public Health Association.

#### 1937

Rochester Board of Public Health and Welfare forms; Dr. Charlie resigns as city health officer.

#### 1939

Drs. Charlie and Will die.



# Good stewards

MAYO CLINIC OPIOID STEWARDSHIP PROGRAM

> enjamin Lai, M.B., B.Ch., B.A.O. (FM '15), Department of Family Medicine and chair of Mayo Clinic's Opioid Stewardship Program, frequently lectures and publishes about opioid use disorder and gets email from physicians and other colleagues who hear his presentations:

"Opioid addiction has ruined my family and was responsible for taking the life of a family member."

"I lost someone close to a drug overdose. The start of their drug use was prescription medication when they were young."

"A good friend died from an opioid overdose. I still think about them and am so saddened by this epidemic taking such a toll on so many lives."

"**My son has addictions.** He drove under the influence, and his passenger was killed. He's in a rehab unit in prison. Our only hope is that it has been a wake-up call for him."

Those are comments from colleagues at Mayo Clinic. But the stories aren't that different from Dr. Lai's experience in "the real world". After completing residency at Mayo Clinic, he worked in a rural town in northern California. He was one of few primary care providers taking care of very sick and medically underserved patients.



"At Mayo Clinic, no matter where you go, the providers practice under one set of guidelines and communicate one primary message — 'We'd love to help you get the help you need."

– Benjamin Lai, M.B., B.Ch., B.A.O.

"The majority of them were on opioids and other controlled substances," he says. "I quickly realized that many of my patients were prescribed astronomical amounts of opioids and that if I continued that, I would perpetuate the problem. I educated myself about opioid stewardship and spearheaded developing institutional guidelines. I had a passion for the work, and we had positive outcomes tapering patients off of opioids while addressing their pain and functional limitations through nonpharmacologic and nonopioid treatment options."

When Dr. Lai returned to Mayo Clinic in Rochester in 2018, it was natural for him to get involved with the Opioid Stewardship Program. "My time practicing in 'the real world' helped to prepare me for this important work."

#### WHEELS IN MOTION

Dr. Lai returned to Mayo Clinic at a good time to get involved with opioid stewardship. Two years prior in 2016, the Centers for Disease Control

#### Steps to the OSP

#### Developing the Mayo Clinic Opioid Stewardship Program required:

- Understanding providers' prescribing habits
- Establishing prescribing guidelines for common surgical procedures
- Standardizing prescribing limits
- Monitoring patients taking opioids for chronic pain
- Providing written, video and audio materials to educate providers and patients about appropriate opioid use
- Ensuring compliance with changing requirements in the states where Mayo provides care
- Instituting required education about proper use of opioids and management of opioid use disorder at all levels including medical students, residents and fellows, nurses, advanced practice providers, pharmacists and continuing medical education
- Engaging at state and national levels to share experience and advocate for evidence-based approaches to address the epidemic
- Including institutional policies about prescribing practices in the EHR
- Encouraging co-prescribing of naloxone for patients at higher risk for overdose
- Developing screening protocols for patients at risk for opioid use disorder
- · Creating policies and workflows for treatment of patients with opioid use disorder
- Ensuring community partnerships for comprehensive addiction treatment services

and Prevention issued "Prescribing Opioids for Chronic Pain". The report indicated that opioids were being overprescribed and provided guidelines for prescribers.

Mayo Clinic leaders took note and wanted to make meaningful contributions to this complex issue that affects providers, patients and the institution. Halena Gazelka, M.D. (ANES '10,

PAIN '11, PLM '15), Department of Anesthesiology and Perioperative Medicine at Mayo Clinic in Rochester, was named chair of a 40-member multisite, multidisciplinary committee aimed at developing institutional policies, procedures, workflows, tools, patient and provider education, and compliance oversight practices that



Estimated percentage of U.S. healthcare institutions that **have opioid stewardship programs** despite most states having passed laws since 2016 on prescribing limitations, prescribing naloxone and checking the Prescription Drug Monitoring Program. Mayo Clinic hopes to influence change.



Opioid Stewardship Program members Julie Cunningham, associate chief pharmacy officer, Mayo Clinic in Rochester; Halena Gazelka, M.D., former chair; Casey Clements, M.D., Ph.D. (EM '12), Department of Emergency Medicine, Mayo Clinic in Rochester; Benjamin Lai, M.B., B.Ch., B.A.O., chair; Jenna Lovely, senior manager, pharmacy, Mayo Clinic in Rochester.

ensured opioids were being prescribed in a safe format within state, federal and regulatory guidelines.

Dr. Gazelka formed teams to address short-term prescribing, longterm prescribing, education and tool development, and electronic health record-related issues.

Within the first year, Mayo Clinic surveyed its providers about their opioid prescribing habits, understanding of CDC guidelines, enrollment in the Prescription Drug Monitoring Program and opinions on standardizing opioid prescribing across the practice. The survey revealed wide variation in opioid prescribing after surgical discharge and 94% support for standardized opioid prescribing.

A survey of surgical patients showed that 63% of opioids prescribed after a surgical procedure went unused and that 87% of patients didn't dispose of unused medication. Unused opioids present the problem of later inappropriate use by the patient, giving or selling the medication to others, or the medication being stolen from the original patient. By 2017, each Mayo Clinic location had developed an opioid stewardship program and, by 2018, the individual programs had merged into a single institutional program. Developing enterprise prescribing guidelines required reviewing and consolidating CDC and five states' legislation.

"It was challenging to work with state-specific guidelines and educate accordingly within the context of enterprise standards, but we did it," says Dr. Gazelka.

#### **THE NITTY-GRITTY**

For short-term prescribing, the team developed specialty- and procedure-specific recommendations for opioid prescribing after surgery. The resulting guidelines include daily supply and general morphine milligram equivalent (MME) maximum recommendations. For easy reference, the Mayo Clinic prescribing guidelines are located in AskMayoExpert, the institution's knowledge management database. The short-term prescribing guidelines were introduced in orthopedic surgery in August 2017 and to other departments in 2018.

Results in the months immediately after implementation in orthopedic surgery showed a 50% decrease in opioid prescribing for total hip and total knee arthroscopy. Further patient surveys showed that the fewer opioids patients were prescribed, the fewer they took. Most patients reported reasonable pain control with the reduced prescribing guidelines.

"Providers were worried about the potential effect on patient satisfaction scores and burden of increased need for refills, but neither of those concerns has panned out," says Dr. Gazelka.

Mayo's guidelines no longer allow opioid monotherapy. Patients are

prescribed NSAIDs, acetaminophen, topical agents and other alternatives, with opioids as the last option. Most patients get no more than two days' worth of opioids, and patients are no longer advised to "stay ahead of the pain."

The team that focused on chronic opioid prescribing for noncancer pain similarly developed guidelines after reviewing information from national societies, federal agencies, federal and state regulatory bodies, and providers.

To kick off the work of developing education and tools, the team conducted a survey that showed

# LISTENING WITHOUT JUDGMENT

An astute surgeon saved this patient's life, not with the scalpel but with the art of direct and honest conversation. **Nafisseh Warner, M.D.** (MED '12, ANES '16, PAIN '17), Department of Anesthesiology and Perioperative Medicine at Mayo Clinic in Rochester, wrote **"A Surgeon Saved My Life: A Story of Addiction,"** published in the April 2020 issue of Mayo Clinic Proceedings. The article explains an encounter Dr. Warner had with an individual who was aware of her work in opioid prescribing optimization and who wanted to share his story. The following is excerpted from Dr. Warner's article.

"Please call me. I need to share my personal experience with opioids. I want to contribute." This line immediately caught my attention on opening my e-mail on a busy Monday morning. The writer was an established and successful medical professional from a regional health care facility and was aware of my research involving the optimization of perioperative opioid prescribing.

... He was first exposed to opioids in early adulthood after a motor vehicle accident in which he experienced multiple traumatic orthopedic injuries. This necessitated a long hospital stay during which he received opioid-based pain management. Unbeknownst to him at the time, this experience would set the stage for a lifelong struggle.

... He struggled with chronic pain and addiction. His opioid prescriptions were renewed, often without question. After all, he was a high-functioning individual with true pathology and no obvious red flags for addiction. As time passed, he began to notice some providers seeming suspicious, or worse yet, judgmental. ... The anticipation of asking for a refill was mentally and emotionally exhausting, even when his pain was at its worst.

... "The cravings for opioids consumed me, making me do things I would never dream of doing. At work, I would search the procedural suites for pills

that almost one-third of Mayo Clinic providers weren't aware of the CDC guidelines. The survey and focus groups identified gaps in safe prescribing practices, use of screening practices, use of the Prescription Drug Monitoring Program and knowledge about naloxone prescribing. Almost all of the providers saw the need for a consistent approach to opioid prescribing.

The tools the team developed were and continue to be communicated in a variety of ways and are available in AskMayoExpert; mandatory computer-based "Every practice struggles with this. We hope others can incorporate practices we've developed at Mayo Clinic to prevent creating the next opioid-dependent or opioid use disorder patient."

- Benjamin Lai, M.B., B.Ch., B.A.O.



left lying around. ... If I saw pills readily accessible in someone else's home that I was visiting, I would quickly grab a few of them without a second thought. Nothing else mattered."

The patient was referred to a spine surgeon for ongoing lower back pathology. After reviewing the patient's medical record, the surgeon took a seat next to him. He asked about his pain, his opioid use, his ongoing struggles with identity. Most importantly, he listened without judgment. Then the surgeon said something that no one else had ever told him: "You are addicted to opioids. This is a life-threatening condition, but you can beat this if you seek help from a professional as soon as possible."

The patient was shocked at the truth in his surgeon's words. ... The surgeon immediately referred him to an addiction specialist, who ultimately prescribed buprenorphine-naloxone therapy as part of medication-assisted treatment of opioid use disorder. ...

"In order to combat opioid addiction, it is essential that medical specialists never underestimate the importance of recognition," the patient shared with me. ... An astute surgeon saved this patient's life, not with the scalpel but with the art of direct and honest conversation.

All medical professionals, including surgeons, must be equipped with the tools to recognize addiction, address it as a serious medical problem, and refer to the appropriate resources for help. Although there are validated tools to help in the recognition of opioid use disorder, the principal focus must remain on establishing meaningful relationships with our patients. The best therapy is often the simple act of sitting and listening. We need to restore humanity to our interactions. We must remove the stigma that surrounds opioid addiction and be willing to discuss this openly with our patients. If we don't ask, we may never know.

#### **GET MAYO CLINIC PROCEEDINGS ONLINE**

Mayo Clinic alumni have free online access to Mayo Clinic Proceedings. Log on to the Alumni Association website (alumniassociation.mayo.edu). Under Resources, select Mayo Clinic Proceedings. Today, the Opioid Stewardship Program is ostensibly the **most comprehensive opioid stewardship program in the U.S.** — the result of thousands of hours of effort and institutional investment.

education modules; CME content; and an opioid stewardship intranet site that includes policies, workflows, research, and provider and patient education material.

Messaging for patient education materials was standardized and includes information about opioids in general, treatment of acute pain, long-term effects of opioid use and Mayo Clinic's decision to change opioid prescribing practices. The materials include a video that explains pain management for hospitalized patients at admission messaging that being pain-free isn't a reasonable or safe expectation and that multimodal therapy will be used. A similar video was created for the outpatient setting. Messaging also is delivered to the public through media in communities where Mayo Clinic has a presence.

The electronic health record team makes sure providers have easy access to patients' clinical data including opioid use history, risk factors and safety assessments; the state's Prescription Drug Monitoring Program database; opioid prescribing guidelines; and Mayo Clinic care practice models. Providers can see when a patient has been prescribed more opioids than CDC guidelines recommend, been prescribed a bad drug combination, gotten inappropriate refills and had urine drug screens.

#### **EVIDENCE OF CHANGE**

In 2022, Dr. Lai took over leadership of the Opioid Stewardship Program. Today, the program is ostensibly the most comprehensive opioid stewardship program in the U.S. the result of thousands of hours of effort and institutional investment.

Results to date include:

- All regions in the Mayo Clinic practice achieved a 5% or greater decline in the number of patients discharged with an opioid prescription between 2018 and 2022.
- In the Midwest practice, all regions have achieved

a 5% or greater decline of hospital discharges with an opioid prescription of greater than 100 MME.

- The number of Mayo Clinic patients on high doses of opioids (90 MME daily dose) and not prescribed naloxone has decreased. Patients who are at higher risk of overdose are co-prescribed and educated about naloxone.
- The number of patients who are prescribed both opioids and benzodiazepines — a combination that's deemed unsafe and puts patients at significantly higher risk of overdose — has decreased.
- The number of opioid prescriptions issued with a provider review of the state Prescription Drug Monitoring Program database has increased. Prescribers are encouraged to review the database to check patients' refill patterns to ensure they aren't getting multiple prescriptions from multiple prescribers.

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## A look at the opioid epidemic

#### Prevalence

patients say they've been prescribed more opioids than needed. **2 in 5** patients say their physician talked to them about the risk of opioid addiction. patients say their physician or pharmacist told them what to do with leftover opioids.

# More than **50%** of people who have opioid use disorder say they got their initial opioids from a **friend or relative for free**.



## 3 weeks

In 2015, the CDC reported the amount of opioids prescribed was enough for every American to be medicated around the clock for 3 weeks.

### Impact

**136** Americans die from a **drug overdose** every day.

**100k**+ **Number of deaths** involving drugs in both 2021 and 2022.

# Opioids are the **leading cause** of **accidental death** in adults **younger than 45**.



People who have opioid use disorder have 12x more emergency room visits and healthcare costs 8x higher than the average.

"The Opioid Stewardship Program team developed and implemented guidelines for practice and prescribing in multiple settings, communicated and educated about them, and tracked metrics on prescribing practices," says Dr. Lai. "In the stage we're in now, we're determining if the guidelines are working and sharing that information with department and division chairs so they can take steps to address outlier prescribing. We're focusing on patients who use opioids chronically and may be vulnerable to or have opioid use disorder. That includes educating providers about how to screen patients, which resources to offer them and how to prescribe

naloxone — now available as an over-the-counter nasal spray — for patients at risk for overdose. We also recommend medication to treat opioid use disorder — buprenorphine, methadone and naltrexone."

The 2023 Consolidated Appropriations Act removed the federal requirement for healthcare providers to submit a notice of intent to prescribe medications such as buprenorphine to treat opioid use disorder. Ninety percent of patients who have opioid use disorder who quit without medication therapy will return to use within a year. According to **Holly Geyer, M.D.** (I '11), Division of Hospital Internal Medicine at Mayo Clinic in Arizona and the Opioid Stewardship Program lead at Mayo Clinic in Arizona, these medications help to reduce cravings and withdrawals, improve function, prevent illness and illegal activity, enable the individual to participate in treatment and reduce mortality.

Dr. Geyer emphasizes the need for all providers to be alert for opioid use disorder. "Opioid stewardship means using the right drug for the right patient for the right indication at the right dose and the right route for the right length of treatment with the right patient screenings and referrals. The American Medical Association estimates that between 3% and 19% of patients who ever encounter an opioid will develop dependency

### Opioid stewardship education

The Federal Medication Access and Training Expansion (MATE) Act requires that DEA-registered providers complete a one-time new training requirement for eight hours of education related to substance use disorder management when they apply for or renew their DEA registration.

Mayo Clinic School of Continuous Professional Development offers more than 40 hours of clinically relevant continuing education on safe opioid prescribing and management, addiction management and related topics, including the following resources that can be found at **ce.mayo.edu/online-education**:

- Opioid Treatment Best Practices DEA Requirement
  Online CME Course
- Ending the Crisis: Guide to Opioid Addiction and Safe Use Audiobook
- Opioid Best Practices Online CME Course
- Mayo Clinic Talks Podcast: Opioid Edition
- Mayo Clinic Opioid Conference: Evidence, Clinical Considerations and Best Practice 2024
- Pain Management for the Non-Pain Specialist 2024

"Ending the Crisis: Mayo Clinic's Guide to Opioid Addiction and Safe Opioid Use" can be found at **store.alumniassociation.mayo.edu** or in person in the Alumni Store on the Rochester campus. The book represents the collective knowledge of the members of the Mayo Clinic Opioid Stewardship Program. It is the only book on the market on the topic of opioids, pain and addiction written expressly for patients and families.



"Opioid stewardship is a partnership between you and the patient. It's important that you help the patient understand that challenging conversations on the topic of opioids are never about you versus them as a patient. It's about you and the patient versus the toxicities of the drug."

– Holly Geyer, M.D.



### Mayo Clinic Opioid Stewardship Program leadership



BENJAMIN LAI, M.B., B.CH., B.A.O. DEPARTMENT OF FAMILY MEDICINE

- Enterprise chair
- Mayo Clinic in Rochester lead
- Mayo Clinic Health System Southeastern Minnesota lead
- Mayo Clinic Health System Iowa lead



HOLLY GEYER, M.D. DIVISION OF HOSPITAL INTERNAL MEDICINE • Mayo Clinic in Arizona lead



TINA ARDON, M.D. (FM '13) DEPARTMENT OF FAMILY MEDICINE • Mayo Clinic in Florida lead

or addiction. These aren't small numbers, and risk factors can drive them up. It is important that an opioid stewardship program include the protocols, procedures, tools and workflows necessary to screen for and treat patients with opioid use disorder."

Dr. Geyer says that Mayo Clinic leaders take the program very seriously but ultimately defer to the physician's clinical judgment. "Opioid stewardship is a partnership between you and the patient. It's important that you help the patient understand that challenging conversations on the topic of opioids are never about you versus them as a patient. It's about you and the patient versus the toxicities of the drug."

#### SUPPORT FOR OTHERS

Opioid stewardship programs are not as ubiquitous as one might think. It is estimated that only 23% of U.S. healthcare institutions have programs despite most states having passed laws since 2016 on prescribing limitations, prescribing naloxone and checking the Prescription Drug Monitoring Program. Follow-up studies have shown that the introduction of state guidelines resulted in a less than 1% change in the number of patients receiving opioid prescriptions, less than 2% change in the number of patients receiving non opioid pain treatment and a negligible effect on the number of days of supply of opioid doses prescribed.

"These statistics show that doing the minimum required for prescribing isn't enough and doesn't provide the change that is needed," says Dr. Geyer. "We believe we can all do better for patients. This includes screening them, educating them, offering them opioid alternatives, targeting functionality as the end goal of treatment regimens and listening to them when they approach us with opioid-related complications. Our state-of-the-art Opioid Stewardship Program is evidence of that.

"Healthcare providers have a responsibility to prescribe opioids judiciously, and healthcare systems have a role to monitor opioid prescribing trends to optimize



JASON DAUFFENBACH, D.O. (PMR '14) PAIN MEDICINE

Mayo Clinic Health System
 Southwestern Minnesota lead



GLENN KAUPPILA, D.O. (FM '14) FAMILY MEDICINE • Mayo Clinic Health System Northwestern Wisconsin lead



ERIN MORCOMB, M.D. (FM '16) FAMILY MEDICINE • Mayo Clinic Health System Southwestern Wisconsin lead

safety and minimize harm. There is still a long way to go, and providers are hungry for standardization and accountability in their institutions. We believe Mayo Clinic is uniquely positioned as a trusted healthcare leader to support other healthcare institutions in meeting external and internal expectations and in their goals and requirements for opioid prescribing, monitoring and reporting. Already, we've helped a number of institutional members of the Mayo Clinic Care Network."

Dr. Lai adds that Mayo's program could be of substantial value to taking a healthcare organization from no stewardship to full engagement. "Every practice struggles with this. "We believe **Mayo Clinic is uniquely positioned as a trusted healthcare leader to support other healthcare institutions** in meeting external and internal expectations and in their goals and requirements for opioid prescribing, monitoring and reporting."

- Holly Geyer, M.D.

We hope others can incorporate practices we've developed at Mayo Clinic to prevent creating the next opioid-dependent or opioid use disorder patient. Ten years from now, I'd like to be out of a job in this area of medicine. That's not realistic we still have a lot of work to do. It's important to not only have guidelines but also the resources and training for providers to feel comfortable having conversations with patients with a unified voice. At Mayo Clinic, no matter where you go, the providers practice under one set of guidelines and communicate one primary message — 'We'd love to help you get the help you need.'" •

# Research makes right

PUBLIC HEALTH RESEARCH TO IMPROVE EQUITY & OUTCOMES



2024 • Issue 1

# Meaningful mission, clinical passion

BRINGING TELE-PREP TO MAYO CLINIC PATIENTS

ary Jo "MJ" Kasten, M.D. (INFD '92), Division of Public Health, Infectious Diseases and Occupational Medicine at Mayo Clinic in Rochester, is on a mission. She wants to make HIV preexposure prophylaxis (PrEP) more available and easier to adhere to. Working with HIV patients is her clinical passion.

"The first blood test for HIV was introduced in my final year of medical school in the mid-1980s," she says. "When I was a resident, many of the people I worked with didn't want to care for HIV patients, perhaps because of fear or because we didn't have treatment to offer. Today, HIV is treatable no one has to die from it. We can even prevent it with PrEP."

When Mayo Clinic opened an HIV clinic in 1992, Dr. Kasten started working in it. She also is the medical director for the PrEP clinic at the Aliveness Project in Minneapolis. In 2020, she received Mayo Clinic innovation grant funding to develop a tele-PrEP program. The project was waylaid by the pandemic but is back on track.

#### **PrEP NOW**

HIV PrEP is a once daily oral medication that's highly effective at minimizing the risk of acquiring HIV through sexual transmission and is part of a nationwide strategy to eliminate HIV transmission. The Centers for Disease Control and Prevention recommends PrEP for people at higher risk of acquiring HIV. It's estimated that 1 in 4 gay or bisexual men and 1 in 200 heterosexual people would be eligible for and potentially benefit from taking HIV PrEP. In many parts of the U.S., PrEP is available only through HIV providers, creating a significant barrier to access especially in rural areas.

Retention of PrEP patients at the HIV clinic at Mayo Clinic in Rochester has been negatively affected by the need for patients to return every three months for clinic visits and lab tests. Dr. Kasten and others believe that PrEP can be successfully implemented by telemedicine, as it's done at some other medical facilities.







"PrEP is a vital part of preventive care for patients at high risk of acquiring HIV. I contribute to caring for people who some would like to ignore, which makes it an even more meaningful mission to me."

– Mary Jo "MJ" Kasten, M.D.

"Currently, visits involve discussing the patient's risks and getting blood work and other lab tests," says Dr. Kasten. "In some parts of the country, clinics allow patients to self-collect their throat, rectal and blood samples, send them to a lab for testing and have video visits to maintain their PrEP prescriptions."

A prepandemic survey of PrEP patients in the Mayo Clinic Section of Infectious Diseases revealed that 37% had stopped taking PrEP for reasons including lack of flexibility with in-person appointments, cost, and problems with clinic distance from home and time away from work. Comments included the following:

- "I would love to get back on PrEP, but it's nearly impossible. I had to take off work and appointments were running late, so I had to leave before I was seen. The system is broken. Fix it."
- "The appointments are short and could mostly be done through the patient portal. I feel like it's a waste of my time, and the only appointments available are in the afternoon, which is terribly inconvenient."
- "Consultant was empathetic and sensitive. The nurses were fantastic."
- "I live 45 minutes away from the Rochester clinic. The appointments aren't very considerate of my time or work commitments."
- "Online and mail-in is the wave of the future. These things are happening at significantly less resourced institutions."


It takes a village: Elitza Theel, Ph.D. (CM '12), and Matthew Binnicker, Ph.D. (CM '06), Mayo Clinic Division of Clinical Microbiology; Christina O'Connor, certified HIV pharmacist; and Joseph Yao, M.D. (I '87), Mayo Clinic Division of Clinical Microbiology, assisted Mary Jo "MJ" Kasten, M.D., and the tele-PrEP project with STI study design and validation, data interpretation, patient surveys and patient education materials. Not pictured: Maryam Mahmood, M.B., Ch.B. (INFD '18), Division of Public Health, Infectious Diseases and Occupational Medicine.

### **PrEP THEN**

To move toward being able to offer tele-PrEP, Dr. Kasten and colleagues have worked with partner organizations and Mayo Clinic Laboratories to validate mail-in sexually transmitted infection tests. The results showed excellent correlation between self-collected and provider-collected samples, with self-collection of STI tests having greater sensitivity. These validations are the steps necessary to offer virtual PrEP visits. Dr. Kasten estimates tele-PrEP visits will be available in 2024.

Patients in Mayo's HIV clinic were queried about their ability to follow instructions and correctly selfcollect specimens:

- Confidence in doing self-collection rectal swab 76%
- Confidence in doing self-collection throat swab 90%

"Patients will be able to self-collect samples for syphilis, gonorrhea and chlamydia," says Dr. Kasten. "The blood tests they'll need can be done at a time convenient for the patient at our lab or a local lab. Patients can have a video or phone visit for follow-up care. "Tele-PrEP will expand access to people in medically underserved and rural communities. Many family physicians in small communities don't have PrEP on their radar and could partner with Mayo Clinic experts in HIV medicine to serve their patients. With tele-PrEP, we can deliver patient-centered care to many more patients and improve retention in care and adherence to HIVprevention measures."

After tele-PrEP is introduced, Dr. Kasten and her team will compare the recruitment of new PrEP patients and retention rates of PrEP patients for two years and survey patients about their satisfaction with face-to-face and virtual visits.

"I went into medicine because I like people, am interested in science, and grew up in a social justice family and community where making a difference is important," says Dr. Kasten. "PrEP is a vital part of preventive care for patients at high risk of acquiring HIV. I contribute to caring for people who some would like to ignore, which makes it an even more meaningful mission to me." •



# A global village **'in our backyard'**

# STUDYING HEALTHCARE DISPARITIES

FOR IMMIGRANTS & REFUGEES

rene Sia, M.D. (INFD '99), can relate to the immigrant experience. One of eight children in her family and the only one to pursue healthcare, she completed medical school and residency in the Philippines. To become licensed in the U.S., she had to repeat residency. She then completed a fellowship in infectious diseases at Mayo Clinic in Rochester. Dr. Sia says she encountered cultural differences between the two countries.

"Racial discrimination influences how I look at things and helps me be empathetic to the experiences of other immigrants and refugees," says Dr. Sia, Division of Public Health, Infectious Diseases and Occupational Medicine at Mayo Clinic in Rochester. "I was inspired to want to help others by observing my mother, who was the person friends called for advice about Chinese medicines. I've long been interested in global health. Sometimes global health means going to other countries. But we have a global village in our backyard in Rochester."

Five years after completing her fellowship at Mayo Clinic, Dr. Sia learned about tuberculosis-related concerns among students - most of whom are immigrants and refugees - at Hawthorne Adult Education Center in Rochester. Several cases of active TB had been diagnosed, creating an environment of fear and stigma. Hawthorne serves a large foreign-born population and offers programming including learning the English language, getting a General Educational Development (GED) or high school equivalency credential, and starting college. Hawthorne learners represent more than 70 languages. Recent emigration from regions of the world where TB is endemic elevates the risk for reactivation of the disease. Despite the public health system having policies and processes for evaluating and treating TB, Hawthorne learners weren't getting tested or treated. Attempts at voluntary TB screening had resulted in very low participation rates. Dr. Sia became involved in getting to the bottom of the problem.

"We needed to listen to the affected population and figure out the barriers to testing and treatment," she says. "We received NIH funding to look into the problem

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"I think I have greater perspective because I wasn't born and raised in the United States. Immigrants and refugees have a lot to contribute to our country.

# I consider the opportunity to work with them to be a gift."

- Irene Sia, M.D.



Irene Sia, M.D., (third from left) with her parents and siblings, mid-1980s.

and develop solutions. That meant partnering with the community for the long term. We approached the situation as research partners with the community, not as a service provider. Our goal wasn't to deliver TB treatment — the public health and healthcare systems do that. Instead, our goal was to determine why the existing system wasn't working well. To have an effect, you can't always apply what you think you know to a population that may not relate to it. You have to sit down with community members to learn about their experiences and health priorities."

NIH funding supported the establishment of the Rochester Healthy Community Partnership. Partners include Mayo Clinic researchers, community organizations, medical centers, public health agencies, schools and universities. The partnership's primary aim is to improve health through community-based participatory research, education and civic engagement. Community-based participatory research uses collaborative research methods that engage community members, uses local knowledge in understanding health problems and the design of interventions, and equitably involves researchers and community partners in all aspects of research.

"We've developed an effective community-based research infrastructure and are experienced in designing and carrying out programs with community partners who help identify health priorities in and solutions for their communities," says Dr. Sia. "We have a strong track record of engaging research participants from minority populations who remain underrepresented in clinical trials, programs and initiatives aimed at improving health among these populations."

A 2016 comprehensive evaluation conducted by the University of New Mexico showed that the success of the Rochester Healthy Community Partnership is largely due to continuous and active community leadership and effective leveraging of resources.

### LET'S TALK ABOUT TB

Dr. Sia's team developed a community-based participatory research approach for the Hawthorne TB situation. Research identified that fear and stigma about TB were barriers to testing, which opened the door to talking with involved parties about those concerns.

The team conducted TB screening opportunities at Hawthorne, each preceded by a brief education session in classrooms, with a video that was developed and tested at Hawthorne by the partnership. Facilitators described testing procedures, answered questions and left sign-up sheets in classrooms. The discussions created an atmosphere of open dialogue about TB. Names from the sign-up sheets were shared with the TB clinic to determine those who were eligible for on-site screening. More than 618 tests were completed between 2009 and 2017, with 121 positive results. Of those, 101 completed evaluation at the TB clinic; none were determined to have active disease. Seventy-two patients started medication for latent infection at no cost to them.

This intervention has been sustained due to the participatory, adaptable framework and ownership by stakeholders.

"We work with immigrant groups in the community to identify priorities or barriers to health and healthcare and, importantly, work together through research on how to improve," says Dr. Sia. "We created methods to explore this research approach and implement interventions in a participatory manner."

# **STORIES FOR CHANGE**

In another project, Dr. Sia's team and the Rochester Healthy Community Partnership are exploring whether digital storytelling interventions for chronic diseases such as diabetes could be effective among individuals who don't speak English as their primary language.



Irene Sia, M.D. (right), and her academic partner Mark Wieland, M.D. Their work was the first to describe participatory development of a culturally and linguistically appropriate digital storytelling intervention to improve Type II diabetes management among immigrants and refugees.

Racial and ethnic minorities in the U.S., including immigrants and refugees, are more likely to have suboptimal diabetes outcomes. According to Dr. Sia, culturally tailored storytelling has been used as an effective intervention method to target health behavior changes. In this community-based participatory research project, the storytelling intervention development was derived through an equitable partnership that empowers communities, promotes understanding of culturally pertinent issues and targets multifaceted health barriers.

The Rochester Healthy Community Partnership surveyed Somali and Latino immigrant and refugee community members who had Type II diabetes to assess diabetes attitudes, knowledge and behaviors; and conducted focus groups to allow community members to share experiences with medication management, glucose self-monitoring, physical activity and nutrition. Survey participants reported a high burden of disease, negative perceptions of diabetes and multiple barriers to optimal diabetes management. The focus groups revealed that acceptance of a diabetes diagnosis often took several visits to healthcare providers and repeated testing. Participants talked about the pain and anxiety they experienced with glucose testing and injections. In some cases, a self-care activity was considered counter to cultural traditions or norms. Family responsibilities, work and the expense of healthy food also were identified as barriers to self-care.

From the focus groups, team members identified candidates to serve as authentic storytellers. The eight who were selected — four each from the Somali and Latino communities — participated in four and a half days of workshops to create deeply personal, powerful stories about their experiences with diabetes self-management. The narratives included information, communication and persuasion to encourage behavior change — a technique that may be particularly effective in populations with strong oral traditions. Two video packages were created — one in each language and both with English language subtitles. The videos included an introduction, four personal stories and a concluding educational message.

**Mark Wieland, M.D.** (I '08, CMR '09), chair, Division of Community Internal Medicine, Geriatrics, and Palliative Care at Mayo Clinic in Rochester and Dr. Sia's academic partner, says this work was the first to describe participatory development of a culturally and linguistically appropriate digital storytelling intervention to improve Type II diabetes management among immigrants and refugees.

Ninety-six percent of participants in the storytelling intervention reported increased confidence about managing their diabetes, and 92% reported that the video motivated them to change a specific behavior in their self-management. Participants also showed improvement in glycemic control post-intervention. Drs. Sia and Wieland recently completed an NIH-funded randomized clinical trial of the storytelling intervention with 455 participants. Results of that study showed improvements in diabetes control.

"The groups who participated in this research came from different continents with different linguistic and cultural experiences, but their knowledge about and attitudes, perceptions and behaviors related to diabetes were very similar," says Dr. Sia. "Many participants share a common lived experience of low socioeconomic position, immigration and limited English proficiency. The systemic barriers they face are probably more significant than the cultural barriers to healthy behaviors. It's important that we keep this in mind when we develop interventions to improve health."

### **'A GIFT'**

The work of Dr. Sia and the Rochester Healthy Community Partnership has included myriad other research projects, including obesity prevention and cancer screening, over two decades of teamwork.

"My expertise isn't in physical activity, nutrition and diabetes but, rather, is in engaging with communities. We work with community partners and build relationships and trust with them," says Dr. Sia. "Our aim is that our research studies will inform policies and practices to sustain change in public health. We're celebrating 20 years of these efforts in the community — 20 years of developing trust.

"I may be more empathetic to things the immigrants and refugees I work with have experienced although my experience doesn't compare to theirs. I think I have greater perspective because I wasn't born and raised in the United States. Immigrants and refugees have a lot to contribute to our country. I consider the opportunity to work with them to be a gift." • "Sometimes global health means going to other countries. **But we** have a global village in our backyard in Rochester."

- Irene Sia, M.D.





# Disease detectives

SERVING TO PROTECT THE PUBLIC HEALTH



# "We have to be ready to respond

to outbreaks, describe what's going on and identify the agents at play."

– Julian Villalba Nunez, M.D.

# CDC INVESTIGATOR

# **Microscopic focus** on ID pathology

ulian Villalba Nunez, M.D. (PPTH '22), is a disease detective. He leads the human diagnostic pathology team at the Infectious Diseases Pathology Branch reference laboratory at the Centers for Disease Control and Prevention in Atlanta, Georgia. He says he's always had an inquisitive mind, been scientifically oriented and wanted to help people.

The Infectious Diseases Pathology Branch (IDPB) is the primary unit in the CDC responsible for conducting investigations of infectious diseases of unknown etiologies and identifying new or previously unrecognized pathogens. The group provides histopathologic, immunohistochemical, molecular, microbiologic and electron microscopic evaluation of tissues from patients with confirmed or suspected infectious diseases and epidemiologic support for investigations.

In a typical case, the branch gets a request from a state's department of health to investigate the cause of



# "We're the group that will identify a pathogen now that will cause a pandemic in the years to come."

– Julian Villalba Nunez, M.D.

a deceased patient's illness. The state's medical examiner had performed an autopsy, looked at tissue, and suspected a viral or infectious agent but couldn't identify it or didn't have the capabilities to test it.

As a clinical consultant and staff pathologist, Dr. Villalba works with the health department and medical examiner and requests tissue samples. When the formalin-fixed paraffin-embedded tissue blocks arrive, IDPB histotechnologists cut a thin tissue sample that will be examined by Dr. Villalba and other IDPB pathologists. Dr. Villalba may order a molecular assay or another stain if he suspects a viral disease. He reports back to the state's department of public health about the case's diagnosis.

Dr. Villalba's team also stands at the ready to identify agents involved in disease outbreaks. Among the outbreaks the branch has worked on in the past 30 years are Hantavirus (*Sin nombre* virus), Zika virus, Chikungunya virus, *Mycobacterium marinum* skin infections associated with fish markets, *Exserohilum* infections, leptospirosis, dengue hemorrhagic fever





A digitally colorized electron microscopic image shows mpox virus particles from a human skin sample in a 2003 outbreak. Animals imported from Ghana introduced mpox virus to the U.S. when they infected prairie dogs that were sold as pets and subsequently infected humans.

The Infectious Diseases Pathology Branch is the primary unit in the CDC responsible for **conducting laboratory studies and investigations of infectious diseases** of unknown etiologies and identifying new or previously unrecognized pathogens.

and mpox. A 2023 investigation focused on a multinational outbreak of fungal meningitis among people who had procedures under epidural anesthesia in two clinics in Mexico. Several people died from the infection.

The Infectious Diseases Pathology Branch evaluates more than 2,400 cases each year on average for diagnostic testing or research projects, and maintains relationships with public health departments, academic medical centers, medical examiner offices, pathologists and global partners in the process. It is the only CDC branch that studies pathology.

"We contribute to public health, science and patient care and help millions of people based on what we describe to our partners around the world," says Dr. Villalba. "We have to be ready to respond to outbreaks, describe what's going on and identify the agents at play. We have the longest list of tissuebased infectious disease assays in the world. If we don't have an assay for a particular agent, we develop one."

Dr. Villalba, who is from Venezuela, has long had an interest in infectious diseases, global health, epidemiology and epidemics. While training in medical microbiology and anatomic and clinical pathology at Massachusetts General Hospital in Boston, he completed two stints of elective training at the CDC and became interested in its work in public health. He joined the CDC after completing a fellowship in pulmonary pathology at Mayo Clinic in Rochester, Minnesota.

"Much like Mayo Clinic, the CDC puts the needs of patients around the world first," says Dr. Villalba. "We disseminate our work through CDC and other scientific publications. For all of the cases we receive and evaluate, we issue reports that can lead to clinical management decisions. Very few places in the world do the kind of surveillance pathology that we do that can influence practice and policy."

Dr. Villalba notes that work by the Infectious Diseases Pathology Branch was instrumental when the CDC described SARS-CoV-1 in 2003, giving the CDC a head start when SARS-CoV-2 emerged and caused the COVID-19 pandemic. "We're the group that can identify a pathogen now that will cause a pandemic in the years to come." •



"I help facilities with outbreaks to determine what is making patients sick, how it's being transmitted and **how to put measures in place to control it**."

– Belinda Ostrowsky, M.D.

CDC EMBED

# **Boots on the ground** to combat ID outbreaks

n 1991, Belinda Ostrowsky, M.D. (I '95), was a fourth-year medical student rotating in infectious diseases at Mayo Clinic in Rochester from the State University of New York at Stony Brook School of Medicine. During her first clinical case while rounding with Walter
Wilson, M.D. (M '71, I '73, INFD '74, CM '75), the Edward C. Rosenow, III, M.D., Professor of the Art of Medicine, the patient said, "Are you the detective who'll figure out what's wrong with me?"

As it turns out, Dr. Ostrowsky was that detective — is that detective. She's a field medical officer in the Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, stationed



Belinda Ostrowsky, M.D., is a field medical officer in the Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, stationed in New York.

in New York. After internal medicine residency at Mayo Clinic in Rochester, she completed an infectious diseases fellowship at Beth Israel Deaconess Medical Center in Boston, Massachusetts, and an Epidemiology Intelligence Service fellowship at the former National Center for Infectious Diseases of the CDC.

The EIS trains disease detectives to step up at a moment's notice to investigate public health threats.

"The CDC has people embedded in different roles all over the U.S., but only a handful like me are embedded in health departments in this field," says Dr. Ostrowsky, who investigates healthcare-associated infectious disease outbreaks in congregate healthcare facilities including hospitals and nursing homes. "I help facilities with



"I'm part of a big team of people that is determined to **stay one step ahead of the bugs** so it's safe out there for my loved ones and yours."

– Belinda Ostrowsky, M.D.

outbreaks to determine what is making patients sick, how it's being transmitted and how to put measures in place to control it. I work with resistant bacterial and fungal infections such as carbapenem-resistant Enterobacterales and *Candida auris* — two pathogens that have made the news in recent years. I provide education to healthcare workers to further patient safety and make changes in practice in a constructive way. I also instruct CDC trainees and health department staff while I'm on the job, allowing me to train the next generation.

"The frontline workers, public health department and CDC partner for the good of patients and healthcare facilities. This can involve testing and moving patients and implementing challenging control measures. I am privileged to go to facilities to help them recognize the patterns they may not see. There's been no shortage of pathogens and problems to solve in the last few years."

Dr. Ostrowsky, who also is a clinical associate professor at Montefiore/Albert Einstein College of Medicine in Bronx, New York, said training at Mayo Clinic instilled in her intellectual curiosity and the ability to focus on the big picture — essential skills for a disease detective.

"I'm one step removed from the individual patient, but I make an impact on a larger scale," she says. "We use what we do with one facility to help multiple facilities, helping many patients at the same time by protecting and improving the lives across a large and vulnerable population."

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"Public health and infectious diseases are exciting fields, with constant new

*twists*. We know how to look critically for outbreak investigations, apply the principles of infection control and collaborate among organizations."

– Belinda Ostrowsky, M.D.

Dr. Ostrowsky notes that, despite public health and infectious diseases being in the forefront of news in recent years, it has become more challenging to recruit physicians to these specialties. In 2022, 44% of infectious diseases programs didn't fill their intended positions in the national fellowship match. Contributing factors may include lower salaries compared to other fellowship-trained specialties; lack of exposure to the specialty during medical training; and concerns about work-life balance, given the specialty's efforts during the pandemic and other high-profile disease outbreaks.

"Public health and infectious diseases are exciting fields, with constant new twists," she says. "We know how to look critically for outbreak investigations, apply the principles of infection control and collaborate among organizations. Those relationships were key when we were challenged to work across the spectrum of care for COVID-19 response, including rolling out widespread vaccinations."

Dr. Ostrowsky chaired the 2023 Infectious Diseases Week Meeting on behalf of the Society for Healthcare Epidemiology of America, which attracted more than 10,000 healthcare providers dedicated to improving infectious diseases care, including public health, infectionprevention and control, and antimicrobial stewardship.

"The intellectual curiosity I honed at Mayo Clinic allows me to look, listen and analyze to figure out how the pieces fit together and how we can explain it to the involved parties to make sure the intended message is imparted and acted on," says Dr. Ostrowsky. "It's rewarding work that gives back to the community. When my father had medical issues that led him to a nursing home, my personal and professional lives collided. I'm part of a big team of people that is determined to stay one step ahead of the bugs so it's safe out there for my loved ones and yours." •

# The mystery of the S. marcescens outbreak

Belinda Ostrowsky, M.D., was part of a CDC team that was called upon to investigate an outbreak of *Serratia marcescens* bacterium at a tertiary care hospital in the late 1990s. Twenty-six surgical ICU patients had acquired the bloodstream infection over nine months.

The team was charged with defining the extent of the problem, identifying the source and risk factors, and implementing control measures. They reviewed the facility's pharmacy procedures, infection control policies, and practices in the surgical ICU. The team found that rates of this infection elsewhere in the hospital were unchanged — only surgical ICU patients were affected. Most of the affected patients had received fentanyl.

"This case was probably the closest I have been to feeling like fictional teen detective Nancy Drew in my career," says Dr. Ostrowsky. "The case was very much active when we arrived on the scene."

As part of the investigation, Dr. Ostrowsky and her team reviewed medical records to determine which personnel had contact with the affected patients. They found that one respiratory therapist had contact with all or most of the patients.

Separate from the CDC investigation, another employee had reported seeing a respiratory therapist crouched down by a patient's bedside, appearing to manipulate an IV line. Cultures of that patient's IV fentanyl medication grew the same Serratia marcescens bacterium identified in the case patients.

The respiratory therapist was asked to provide a hair sample to check for fentanyl, and the test was conclusive for use of the drug. The team concluded that, most likely, the therapist had reused a needle to remove some of the drug from patients' IV bags, introducing the bacteria.

"This was in the early days of the opioid crisis when fentanyl was a lesser known drug, and less was known about the potential for its abuse," says Dr. Ostrowsky.

After the respiratory therapist was terminated, there were no additional cases of the bacteria in the hospital for two years.

"Although my interest in infectious diseases started at Mayo Clinic, I was convinced this was my calling after investigating this challenging outbreak."

"This case was probably the closest I have been to feeling like fictional teen detective Nancy Drew in my career. **The case was very much active when we arrived on the scene**."

- Belinda Ostrowsky, M.D.



Serratia marcescens. Source: Sinhyu, Getty Images.



# Mayo Clinic Children's Center achieves recognition for quality surgical care

ayo Clinic Children's Center has been verified as a Level 1 Children's Surgery Center by the American College of Surgeons Children's Surgery Verification Quality Improvement Program.

The program was developed to improve the quality of children's surgical care by creating a system that allows for a prospective match of every child's individual surgical needs with a care environment with optimal pediatric resources. Verified centers must meet criteria outlined in Children's Surgery Verification standards by ensuring that children facing surgery receive care under a multidisciplinary program with quality improvement and safety processes, data collection and appropriate resources provided to them as patients at the hospital.

The Children's Surgery Verification Program is based on other nationally recognized American College of Surgeons quality improvement programs that have measurably improved surgical quality, prevented complications, reduced costs and saved lives.

"Every day, our team at the Mayo Clinic Children's Center provides the highest quality care to pediatric patients who have the most complex and heart-wrenching illnesses, from congenital anomalies to pediatric oncology," says **Randall Flick, M.D.** (ANES '95), medical director of Mayo Clinic Children's Center. "We are incredibly proud of the ACS's verification of our team's hard work transforming children's lives and operating at the forefront of healthcare's capability."

To become a verified center, Mayo Clinic Children's Center met essential criteria for staffing, training and facility infrastructure, and protocols for care, ensuring its ability to appropriately care for children who are surgical patients. The center also participates in a national data registry that yields semiannual reports on the quality of its processes and outcomes, thus identifying opportunities for continuous quality improvement.

# Mayo Clinic researchers identify link between gut bacteria, preclinical autoimmunity & aging in rheumatoid arthritis

A lthough the bacteria in the intestine are helpful for digesting food and fighting infections, they have long been suspected to play an essential role in triggering rheumatoid arthritis.

Mayo Clinic researchers discovered that an abundance of specific gut bacteria is responsible for the triggering of an immune response before the clinical symptoms of rheumatoid arthritis appear.

"As we age, our gut bacteria and their byproducts change, which impacts our immune system," says senior author **Veena Taneja, Ph.D.** (IMM '98), Department of Immunology at Mayo Clinic in Rochester. There is a known link between imbalances in gut bacteria, aging and rheumatoid arthritis, but it is challenging to prove this connection in humans. "This research sheds light on the complex relationship between gut microbiota and rheumatoid arthritis."

Dr. Taneja explains that it is difficult to determine if gut microbiota is the cause of the disease in patients because an autoimmune response precedes the onset of clinical symptoms in patients by one to 10 years.

"The gut microbiome may hold the key to understanding healthy aging and how to avoid chronic diseases and may lead to earlier diagnosis and treatment," says Dr. Taneja.

Using a preclinical model, the researchers determined that the gut bacteria *Eggerthella lenta* causes an autoimmune response before the onset of the clinical symptoms of rheumatoid arthritis. In that



response, the immune system produces autoantibodies that target and attack the body's tissues and cells instead of foreign invaders such as bacteria and viruses.

This same microbe also reduces amino acids including arginine, citrulline and tryptophan metabolites to levels more similar to that of much older people who see a gradual deterioration of their immune system due to aging.

In addition to their other findings, researchers noted a connection between *Eggerthella lenta* and higher levels of these autoantibodies in female patients with rheumatoid arthritis, highlighting the importance of considering gender-specific factors in the disease.

This biomarker may help diagnose severe rheumatoid arthritis and assess its progression. The research suggests that clinicians could use measurements of metabolic byproducts induced by these gut bacteria as a marker for the severity of the disease. In familial cases and people harboring rheumatoid arthritis-susceptible genes, the researchers say that sequencing bacteria, autoantibodies and metabolites — especially in healthy females — may help predict the likelihood of their developing rheumatoid arthritis.

Researchers will study whether targeting *Eggerthella lenta* with antibiotics or specific genes and metabolites can affect preclinical autoimmunity in rheumatoid arthritis. They also are exploring the link between *Eggerthella lenta* and its effect on aging. Mayo Clinic pioneers approach to ovarian cancer vaccine

ayo Clinic research is biomanufacturing an experimental cell-based ovarian cancer vaccine and combining it with immunotherapy to study a "one-two punch" approach to halt disease progression in ovarian cancer patients.

This research begins with a blood draw from women with advanced ovarian cancer whose tumors have returned after standard surgery and chemotherapy. White blood cells are extracted from the blood, biomanufactured to become dendritic cells and returned to the patient. Dendritic cells act as crusaders that march through the body, triggering the immune system to recognize and fight cancer.

"We're building on an earlier phase 1 clinical trial that showed promising results in terms of survival after the dendritic cell-based vaccine," says **Matthew Block, M.D., Ph.D.** (MDPH '05, IMM '05, I '08, CI '10, HEMO '11), Division of Medical Oncology at Mayo Clinic in Rochester and a co-principal investigator. "Of the 18 evaluable patients in the phase 1 study, 11 had cancer return, but seven of them — 40% — have been cancer-free for almost 10 years. We typically expect 90% of patients in this condition to have the cancer return."



Matthew Block, M.D., Ph.D.

Mayo Clinic's pioneering approach, developed in the lab of Keith Knutson, Ph.D. (IMM '05), Department of Immunology at Mayo Clinic in Florida and the Andrew A. and Mary S. Sugg Professor of Cancer Research, equips the vaccine with bits of proteins that unleash an immune response. The vaccine is targeted to harness Th17 immunity. In ovarian cancer, Th17 cells are linked to reduced immune suppression and improved survival. By driving a Th17 immune response, the vaccine aims to redirect the immune system's efforts to fight cancer.

"To our knowledge, nobody else has ever deliberately tried to make a Th17 immune response using a cancer



vaccine. It targets a new part of the immune system that fights infection and activates a defense mechanism," says Dr. Knutson, a co-principal investigator on the study. "We want to learn if that immune response is more helpful to ovarian cancer patients who have relapsed than other types of immune responses."

The vaccine will be given in combination with a checkpoint inhibitor immunotherapy drug to

> Jonathan Leighton, M.D

# Jonathan Leighton, M.D., elected president, American College of Gastroenterology

onathan Leighton, M.D. (GI '94), Division of Gastroenterology and Hepatology at Mayo Clinic in Arizona, is the 2023–2024 president of the American College of Gastroenterology, a medical organization representing more than 19,000 clinical gastroenterologists and other specialists in digestive diseases. Dr. Leighton is a fellow of the ACG and was elected to its board of trustees in 2013.

Dr. Leighton, the Barry M. and Virginia S. Weinman Honored Investigator in Gastroenterology Research, has held Mayo Clinic leadership positions including chair of the Division of Gastroenterology and Hepatology at Mayo Clinic in Arizona, director of the Inflammatory Bowel Disease Clinic, and a member of the Mayo Clinic in Arizona Executive Operations Team. Dr. Leighton is a professor of medicine in the Mayo Clinic College of Medicine and Science.

Dr. Leighton's clinical interests include inflammatory bowel disease, colorectal neoplasia and diseases of the

small bowel. His research includes new devices for imaging the small bowel — including capsule endoscopy and balloon enteroscopy — and new technologies for detecting colon polyps and colon cancer. Dr. Leighton's other research interests include new therapies for inflammatory bowel disease and biomarker discovery for ulcerative colitis and Crohn's disease.

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identify and kill stealthy tumors that don't respond to cell therapy alone. Preclinical research by Dr. Knutson's team in mouse models suggests that the combination of the immunotherapy drug and Th17-targeting vaccine creates a synergistic effect that strengthens the immune system's ability to target and kill ovarian cancer cells.

"What's exciting about this research is that it allows us to study why tumors have recurred. We will investigate what turned on the immune response and what caused it to wane," says Dr. Block. "We hope to learn whether there is a complementary effect in which the two interventions work together better in ovarian cancer patients than either of them alone."

The aim of the vaccine is to prevent ovarian cancer tumors from returning. The latest research also seeks to understand why some ovarian cancer tumors evade the body's immune response.

Mayo Clinic's Center for Regenerative Biotherapeutics is leading the biomanufacturing efforts across all its campuses with an approach that helps ensure the safety, identity, strength and purity required of commercialgrade medicines.

Clinical trials for cell-based ovarian cancer vaccines would be difficult, if not impossible, at Mayo Clinic without its biomanufacturing facilities. Once white blood cells are extracted from the patient, they must be transferred to the lab within hours to be grown and prepared for biomanufacturing.

"Manufacturing of an ovarian cancer vaccine is personalized and targeted to each patient's unique immune profile," says Dr. Knutson. "It is absolutely essential to our research to have biomanufacturing facilities on site, near the patient, in case we need to make adjustments based on each patient's individual tumor that could better kill cancer cells."

Dr. Block says that's what makes this research unique from a scientific standpoint. "The study participant can walk over to the lab, have their blood drawn and, within hours, their specimens can be transferred to the on-site facility where the process of biomanufacturing the vaccine begins. That would not be possible with an outside manufacturer."

Mayo Clinic will begin biomanufacturing the ovarian cancer vaccine for a phase 2 clinical trial in Rochester, with plans to expand the biomanufacturing capabilities to Florida and Arizona.

The results of the phase 2 clinical trial will determine whether the cell-based ovarian cancer vaccine will advance to later-stage biomanufacturing and clinical trials. Mayo hopes to then work with an industry collaborator to license the technology and bring it to market to expand patient access around the world.

# Mayo Clinic awards named professorships

Mayo Clinic awarded named professorships — the highest academic distinction at Mayo Clinic.

# Yogish Kudva, M.B.B.S. (I '95, ENDO '98)

Dr. Richard F. Emslander Professor II

- Division of Endocrinology, Diabetes, Metabolism, and Nutrition; Department of Internal Medicine
- Mayo Clinic in Rochester

# Jann Sarkaria, M.D. (RADO '97)

William H. Donner Professor

- Department of Radiation Oncology
- Mayo Clinic in Rochester

**Win-Kuang Shen, M.D.** (I '86, CV '90, CVEP '91) John M. Nasseff Sr. Professor of Cardiology in Honor of Dr. Burton Onofrio

- Division of Heart Rhythm Services, Department of Cardiovascular Medicine
- Mayo Clinic in Arizona

# Michael Stewart, M.D. (OPH '99)

Knights Templar Eye Foundation, Inc. Professor of Ophthalmology Research

- Chair, Department of Ophthalmology
- Mayo Clinic in Florida

# 2023 Distinguished Mayo Clinic Investigator awards recognize Andre Terzic, M.D., Ph.D. & Neill Graff-Radford, M.D.

he Distinguished Mayo Clinic Investigator Award is presented to individuals whose research careers demonstrate evidence of great distinction, high distinguished scholarship, creative achievement, and excellence in education and administrative responsibilities.

Andre Terzic, M.D., Ph.D. (CV '92), Department of Cardiovascular Medicine at Mayo Clinic in Rochester and the Marriott Family Director, Comprehensive Cardiac Regenerative Medicine for the Center for Regenerative Biotherapeutics and a Marriott Family Professor of Cardiovascular Research, has spent more than 30 years at Mayo Clinic and has fundamentally advanced medicine, from cardioprotection and heart regeneration to disease-profiling and precision therapy. Dr. Terzic's work has had a major influence on the understanding of heart disease causes and cures. He and his team are credited with decoding molecular circuits of cardioprotection, advancing cardiac regenerative medicine, programming cell fate decisions, and resolving patterns of disease and aging.

Most notable in his career is the establishment of the Mayo Clinic Center for Regenerative Biotherapeutics. Dr. Terzic spearheaded and guided the center from its beginning to its current leadership in the field of regenerative medicine. Dr. Terzic served as the inaugural Michael S. and Mary Sue Shannon Family Director for Regenerative Biotherapeutics at Mayo Clinic from 2011 to 2021.

**Neill Graff-Radford, M.D.** (N '89), Department of Neurology at Mayo Clinic in Florida and the David Eisenberg Professor, has spent 34 years at Mayo Clinic and has made a substantial impact on the understanding and treatment of neurological disease. His contributions to research include brain-behavior relationship studies; biomarker development for Alzheimer's disease; molecular genetic studies; clinical-pathological research; substantial impact on the understanding, treatment and prevention of normal pressure hydrocephalus and Lewy body disease; and the development of the largest brain bank for neurodegenerative disorders in the world, with more than 10,000 specimens.

Dr. Graff-Radford has led the charge in developing widely accepted norms for neuropsychological data for





Andre Terzic, M.D., Ph.D., and Neill Graff-Radford, M.D., are presented with the 2023 Distinguished Mayo Clinic Investigator Award by Gregory Gores, M.D. (I '83, GI '86), former Executive Dean of Research.

African Americans and continues to contribute to diversity, equity and inclusion through his work in research with underserved populations. Dr. Graff-Radford and his team have received funding for more than 20 years to recruit and follow minority patients in clinical trials; published 38 peer-reviewed papers on the genetics, neuropsychology, imaging and biomarkers of underserved populations; and provided free medical evaluations to more than 550 African American patients. Mayo Clinic researchers shine light on ovarian cancer

study published in the Journal of Clinical Oncology explored the use of fluorescence-guided surgery to treat epithelial ovarian cancer, the most common type of ovarian cancer. Fluorescence-guided surgery uses fluorescence imaging to light up cancerous tissue, giving surgeons a better view of tumors and cancer cells and making cancer removal more thorough and accurate.

"For ovarian cancer, we have evidence that removing as much of the tumor as possible at the time of surgery can improve a patient's overall survival and help prevent the disease from progressing," says **Kristina Butler, M.D.** (GYNP '11, GYNO '14), Department of Medical and Surgical Gynecology at Mayo Clinic in Arizona and one of the study authors.

The phase 3 study evaluated the safe and effective use of pafolacianine — a fluorescent drug that targets a folate receptor that may be overexpressed in ovarian cancer with a type of fluorescence imaging called intraoperative near-infrared imaging (NIR).

The 109 study participants had been diagnosed with folate receptorpositive epithelial ovarian cancer or suspected of having the disease. Before fluorescence-guided surgery, patients received an injection of contrast dye that made their cancer glow. Patients received a 60-minute infusion of pafolacianine one hour before surgery.

During the surgical procedure, all suspicious visible lesions were documented for all patients using white light and palpation. Patients were then randomly assigned to be evaluated a second time using NIR or to proceed directly to surgery to remove the lesions.

In the second evaluation, the care team used NIR fluorescence imaging to identify lesions not visible under white light. Surgeons removed all visible lesions. Before completing surgery, surgeons reimaged the areas from which lesions were removed to ensure no visible lesions remained.

For both study groups, lesions were sent to a laboratory where pathologists evaluated the tissues for cancer. Pathologists weren't told whether lesions had been identified using white light or NIR fluorescence imaging. The lab results confirmed that NIR fluorescence imaging helped surgeons identify tumors that weren't visible under white light.

"This technology can be used with newly diagnosed patients, patients who have already had chemotherapy and patients with recurrent ovarian cancer," says Dr. Butler. "It opens up opportunities that did not exist before."

The Food and Drug Administration approved the fluorescent drug used in this study for use in surgery.



Kristina Butler, M.D.

Dr. Butler says some drugs used in fluorescence-guided surgery can cause noncancerous tissue, such as lymph nodes or necrotic tissue, to glow. This makes it difficult to determine which tissue is cancerous. And some drugs have a high rate of side effects, including nausea and vomiting.

Experts at Mayo Clinic have been at the forefront of the effort to bring new fluorescent drugs into clinical research. Dr. Butler and her team hope to next evaluate aminolevulinic acid hydrochloride, an agent currently approved for fluorescence-guided surgery of high-grade gliomas that is metabolized intracellularly and accumulates in cancer cells. The team aims to learn in clinical trial how this orally administered drug may be applicable to ovarian cancer resection in its ability to target cancerous tissue.

# Obituaries

Christopher Allan, M.D. (PATH '71), died July 25, 2023. Richard Belatti, M.D. (ANES '78), died Oct. 23, 2023. Richard Dobbs, M.D. (S '57, ENT '59), died Sept. 28, 2022. Donald Feeney, M.D. (U '63), died Sept. 9, 2023. Gary Gitnick, M.D. (I '68, GI '69), died Nov. 4, 2021. John Kelly Jr., M.D. (N '77), died Aug. 18, 2023. Mark Kimpel, M.D. (OPH '92), died May 4, 2023. John Kovach, M.D. (ONCL '76), died Oct. 5, 2023. James Monge, M.D. (S '62), died Jan. 14, 2024.

Gerardo Neuwirth, M.D. (PD '63, PDA '65), died Oct. 25, 2023. Donald Paarlberg, M.D. (OR '71), died Sept. 18, 2022. Edward Renner, M.D. (M '73), died April 2, 2022. James Reynolds, M.D. (I '60), died Dec. 16, 2023. James Scott-Miller, M.D. (S '56, OR '59), died Nov. 28, 2023. Jerral Seibert, M.D. (I '61, DERM '64), died Oct. 30, 2023. William Sibley III, M.D. (S '62), died June 2, 2023. Harold Stine, M.D. (RD '72), died Jan. 15, 2024.

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### ABOUT THE MAGAZINE

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