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MYTHS AND FACTS ABOUT
Prostate Cancer

Dermatological Issues and Mental Health:
THE CONNECTION

UPDATE ON Premenstrual Dysphoric Disorder

THERAPEUTIC PLASMA EXCHANGE FOR SEPSIS AND SEPTIC SHOCK | PAGE 50

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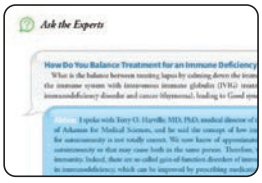

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Artificial Intelligence in Healthcare Moves from New to Normal

THANKS TO human ingenuity, new ideas about and innovative methods for practicing medicine continually push the industry forward. In previous generations, brilliant minds solved medical problems and propelled society into an age where doctors could prevent disease with vaccinations, treat disease with penicillin and preserve life with blood banks. Curiosity, innovation and hard work resulted in effective ways to save lives.

But until recently, diagnosis and treatment were limited to what humans could see, test and interpret. From blood tests to PET scans, testing modalities were dependent upon human interpretation, and even the best and brightest clinician was limited. Thanks to artificial intelligence (AI), that's changing, and it's changing fast.

More and more, AI is being accepted and embraced as a partner in healthcare. In fact, clinicians are increasingly willing to utilize AI as long as safeguards are firmly in place. As we discuss in our article "How AI Is Changing the Face of Healthcare" (p.18), AI is augmenting the clinical team by reviewing test results, interpreting health data and coming up with diagnostics faster than humanly possible. With capacity for predictive analytics and streamlining administrative workflow, AI is making healthcare more targeted and efficient.

The advent of AI and its ability to improve medical efficiency is well-timed for an industry experiencing staffing shortages. Our article "Technological Advancements in Cardiology: Improved Monitoring" (p.22), discusses the way AI-augmented cardiac remote patient monitoring (RPM) devices provide real time patient data, helping to bridge the gap between patient need for continuous care and the ongoing shortage of cardiac physicians. AI-powered RPM devices facilitate early detection and prompt intervention. It also brings cardiac care to rural communities that feel the most pronounced effects from the ongoing physician shortage.

And yet, not every change in healthcare is due to AI; some changes come from adapting and adjusting when established systems no longer work. With regard to care delivery, the fee-for-service model may have worked in the past, but it may not be the best choice going forward. We discuss this shift in our article "Rethinking Care Delivery: The Promise and Practice of Value-Based Care" (p.26). While fee-for-service focuses on volume, value-based care focuses on collaboration among care teams to support comprehensive patient care that drives positive outcomes. It emphasizes outcomes over volume, and rewards the quality of the care rather than the amount of care provided.

As always, we hope you enjoy the additional articles in this issue of *BioSupply Trends Quarterly*, and find them both relevant and helpful to your practice.

Helping Healthcare Care,

Patrick M. Schmidt
Publisher

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Our mission is to serve as the industry's leading resource for timely, newsworthy and critical information impacting the biopharmaceuticals marketplace, while providing readers with useful tips, trends, perspectives and leading indicators on the topics pertinent to their business.

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HHS Cuts Funding for mRNA Vaccine Research

The U.S. Department of Health and Human Services (HHS) has begun a coordinated wind-down of its mRNA vaccine development activities under the Biomedical Advanced Research and Development Authority (BARDA), including the cancellation and descoping of various contracts and solicitations. The decision follows a comprehensive review of mRNA-related investments initiated during the COVID-19 public health emergency.

"We reviewed the science, listened to the experts and acted," said HHS Secretary Robert F. Kennedy, Jr. "BARDA is terminating 22 mRNA vaccine development investments because the data show these vaccines fail to protect effectively against upper respiratory infections like COVID and flu. We're shifting that funding toward safer, broader vaccine platforms that remain effective even as viruses mutate."

The wind-down affects a range of programs, including:

- Termination of contracts with Emory University and Tiba Biotech.
- Descoping of mRNA-related work in existing contracts with Luminary Labs, ModeX and Seqirus.
- Rejection or cancellation of multiple pre-award solicitations, including proposals from Pfizer, Sanofi Pasteur, CSL Seqirus, Gritstone and others, as part of BARDA's Rapid Response Partnership Vehicle and VITAL Hub.
- Restructuring of collaborations with DoD-JPEO, affecting nucleic acid-based vaccine projects with AAHI, AstraZeneca, HDT Bio and Moderna/UTMB.

While some final-stage contracts (e.g., Arcturus and Amplitude) will be allowed to run their course to preserve prior taxpayer investment, no new mRNA-based projects will be initiated. HHS has also instructed its partner, Global Health Investment Corp., which manages BARDA Ventures, to cease all mRNA-based equity investments. In total, this affects 22 projects worth nearly $500 million. Other uses of mRNA technology within the department are not impacted by this announcement.

The move signals a broader shift in federal vaccine development priorities. Going forward, BARDA will focus on platforms with stronger safety records and transparent clinical and manufacturing data practices. Technologies that were funded during the emergency phase but failed to meet current scientific standards will be phased out in favor of evidence-based, ethically grounded solutions such as whole-virus vaccines and novel platforms. ❖

U.S. Department of Health and Human Services. HHS Winds Down mRNA Vaccine Development Under BARDA, Aug. 5, 2025. Accessed at www.hhs.gov/press-room/hhs-winds-down-mrna-development-under-barda.html.

FDA Requires Major Changes to Opioid Pain Medication Labeling

The U.S. Food and Drug Administration (FDA) is requiring safety labeling changes to all opioid pain medications to better emphasize and explain the risks associated with their long-term use. Changes follow a public advisory committee meeting in May that reviewed data showing serious risks when opioids are used over long periods.

The updated labeling reflects data from two large FDA-required observational studies, which provided new data on how long-term opioid use can lead to serious side effects. FDA decided to require the following safety labeling changes to help healthcare professionals and patients make treatment decisions rooted in the latest evidence:

- Clearer risk information: A summary of study results showing the estimated risks of addiction, misuse and overdose during long-term use.
- Dosing warnings: Stronger warnings that higher doses come with greater risks, and that those risks remain over time.
- Clarified use limits: Removing language that could be misinterpreted to support using opioid pain medications over indefinitely long duration.
- Treatment guidance: Labels will reinforce that long-acting or extended-release opioids should be considered only when other treatments are inadequate.
- Safe discontinuation: A reminder not to stop opioids suddenly in patients who may be physically dependent, as it can cause serious harm.
- Overdose reversal agents: Additional information on medicines that can reverse an opioid overdose.
- Drug interactions: Enhanced warning about combining opioids with other drugs that slow down the nervous system — now including gabapentinoids.
- More risks with overdose: New information about toxic leukoencephalopathy — a serious brain condition that may occur after an overdose.
- Digestive health: Updates about opioid-related problems with the esophagus.

FDA has also required an additional prospective, randomized, controlled clinical trial to examine the benefits and risks of long-term opioid use, and will be closely monitoring the progress of the clinical trial to ensure its timely completion. ❖

U.S. Department of Health and Human Services. FDA Requires Major Changes to Opioid Pain Medication Labeling to Emphasize Risks, July 31, 2025. Accessed at www.hhs.gov/press-room/hhs-winds-down-mrna-development-under-barda.html.

University of Toledo Receives NIH Funds for Fungal Infection Research

A University of Toledo immunologist has received a federal grant to study how a type of cell unexpectedly discovered in the oral cavity helps the body fight off fungal infections. The cells, called megakaryocytes, are predominantly present in bone marrow where they produce blood platelets crucial for blood clotting.

Recent research led by Heather Conti, PhD, an associate professor in the College of Natural Sciences and Mathematics, found those cells also were present in the tongue, and they seem to play a key role in the immune response to a common but potentially dangerous fungal infection. "Others have shown megakaryocytes in the lungs, but no one had previously described them in the oral mucosa," Dr. Conti said. "We were seeing that they respond to the fungal infection. They expand and they make things that are involved in clearing that infection. They appear to have an important role."

Those findings, published last year in the journal *Mucosal Immunology*, form the basis of Dr. Conti's new project, which received a three-year $473,632 grant from the National Institute of Dental and Craniofacial Research earlier this spring.

Dr. Conti's NIH-funded project is specifically focused on studying how oral megakaryocytes interact with Candida and with a cytokine called interleuken-17. Though interleuken-17 is beneficial in the context of clearing fungal infections, it also is believed to play a major role in the development of several autoimmune diseases. As such, it and similar cytokines are increasingly being targeted with next-generation inhibitors to alleviate the symptoms of autoimmune disorders such as psoriasis.

With autoimmune disorders on the rise — and some species of Candida showing resistance to current antifungal medications — decoding the body's immune response against fungal infections is increasingly important. "Any time we better understand the immune response against the fungus and how we can take advantage of that, it means less antifungal usage," Dr. Conti said. "Those medications are toxic, and infections don't always respond."

While focused specifically on oral fungal infections, Dr. Conti's research has the potential to unlock more secrets about the immune system in general. "This adds to our knowledge of what interleuken-17 is doing in the body," she said. "This is a new cell that interleukin-17 talks to, and we'll be able to understand better what that means not just in the oral cavity, but throughout the body as well." ❖

Linkhorn, T. NIH Funds New Research Into How Our Bodies Fight Fungal Infections. The University of Toledo news release, June 17, 2025. Accessed at news.utoledo.edu/index.php/06_17_2025/nih-funds-new-research-into-how-our-bodies-fight-fungal-infections.

NIH Changes Terms and Conditions Governing Federal Grants

The National Institutes of Health (NIH) announced a significant change to the terms and conditions governing federal funding applicable to all NIH grants, cooperative agreements and other awards, including future awards.

The new terms require awardees to certify that they do not operate or promote diversity, equity and inclusion (DEI) or diversity, equity, inclusion and accessibility (DEIA) programs in violation of federal anti-discrimination laws. Awardees also must refrain from participating in any "discriminatory prohibited boycott," defined as refusal to do business with Israeli companies or companies doing business in or with Israel. Additionally, they may not engage in conduct prohibited by Section 2(b) of Executive Order (EO) 14190 of Jan. 29, 2025, regarding "radical indoctrination" in public education (referred to as "discriminatory equity ideology").

Specifically, by accepting federal funding under this change, recipients certify that:

1) They do not and will not during the term of the financial assistance award operate any programs that advance or promote DEI, DEIA or discriminatory equity ideology in violation of federal anti-discrimination laws;

2) They do not engage in and will not during the term of this award engage in a discriminatory prohibited boycott.

This changes the existing civil rights terms listed in Section 4.1.2 of the federal Grants Policy Statement (GPS) that reference the Civil Rights Act of 1964, prohibiting discrimination on the basis of race, color or national origin; Title IX of the Educational Amendments of 1972, prohibiting discrimination on the basis of sex; Section 504 of the Rehabilitation Act of 1973, prohibiting discrimination based on physical or mental disabilities; the Age Discrimination Act of 1975, prohibiting discrimination on the basis of age; and EO 13166 of Aug. 11, 2000, prohibiting discrimination against people with limited English proficiency.

The new requirement "supersedes" Section 4.1.2 of the GPS, while Section 4.1.2 "will be updated to incorporate this standard term and condition of award." In addition, at least portions of Section 4.1 will remain as "civil rights requirements do not apply to foreign and international organizations." ❖

Bourque, D, Hartsfield, SB, Martin, SH, Merrill, RJ, and Werner, MJ. NIH Announces Significant Changes to Federal Grant Terms, Conditions on Civil Rights. Holland & Knight Healthcare Blog, April 24, 2025. Accessed at www.hklaw.com/en/insights/publications/2025/04/nih-announces-significant-changes-to-federal-grant-terms.

2026 Proposed Payments: Outpatient Settings and Physician Offices

By Bonnie Kirschenbaum, MS, FASHP, FCSHP

THIS YEAR, several pieces of legislation being debated will significantly impact practices' revenue streams, operations and clinical services. Therefore, it will be imperative to work in sync with finance/revenue cycle teams to determine strategies for negotiating. The outpatient prospective payment system (OPPS) and physician fee schedule (PFS) are the two predominant fee schedules for services in outpatient arenas and follow a calendar year schedule beginning Jan. 1. The following proposed OPPS/PFS rules have been released for comment and will be finalized later this fall. Paying attention to them will provide insight into your strategic planning moving forward into a year that will be reeling under budget cuts passed by congress.

Changes for 2026

Changes for determining payment rates are included, as well as requirements for quality reporting programs for hospital outpatient, rural emergency hospitals, ambulatory surgery centers (ASCs) and overall hospital quality star rating. Hospital price transparency is emphasized, and several requests for information have been introduced.

Proposed 2026 increased fee payment rates rose 2.4 percent but are reduced by two percent for hospitals failing to meet quality reporting requirements. ASC payments increase by 2.4 percent when quality requirements are met. (Note: The cancer hospital payment adjustment policy provides individual estimated percent increases in 2026 OPPS payments to each cancer hospital.) Following are highlights of 2026 OPPS/ASC proposed rules:

• *Controlling unnecessary increases in outpatient services volume in excepted off-campus PBDs.* This applies the PFS equivalent rate for any healthcare common procedural coding system codes assigned to drug administration services ambulatory payment classification when provided at an off-campus provider-based department (PBD) excepted from section 1833(t)(21) of the Act (i.e., site neutral payments). Rural sole community hospitals would be exempted.

• *Drugs, biologicals and radiopharmaceuticals.* The proposed packaging threshold is $140 per day based on average sales price (ASP). Passthrough payments will continue to be paid at ASP+6%. SI G status will expire for 28 products on Dec. 31, 2025, 52 products will expire during 2026 and 41 products with SI G status will continue throughout 2026. SI K separately payable products also remain at ASP+6%. Biosimilars are exempted from the OPPS daily threshold when their reference products are separately paid to allow for separate payment even if it's below the threshold for as long as the reference product remains separately paid. IRA requires qualifying biosimilar payment at ASP+8%. See actual payment rates posted on the CMS website in the Addendum B[1] or quarterly ASP tables.[2]

• *Non-opioid policy for pain relief.* Payment for non-opioids is available in both OPPS and ASC settings. Actual payment amounts are published in the quarterly ASP pricing files, as well as in Addendum B.

• *Medicare PFS.* This proposed PFS rule impacts several aspects of pharmacy, as well as the overall financial health of the healthcare system and how various segments must adhere to it. The final rule will be published late fall following the comment period and revisions, if any.

• *Proposed shift to prevention and wellness: physician pay.* Physicians and collaborative agreement services provided by pharmacists are also affected. Reimbursements for nearly 9,000 billing codes mostly associated with specialty care decline 2.5 percent due to different data sets used to calculate their value. Primarily, this affects billing code rates associated with services such as surgery, diagnostic imaging, outpatient care, pain management and orthopedics. Specialties such as radiologists, cardiologists and gastroenterologists may see lower payments for a substantial number of common codes. With a goal of boosting primary care, there is less of a pay difference since the proposal exempts billing codes frequently used. It wouldn't apply to services that can't be performed more speedily with practice, such as visits, behavioral health, certain maternity care and telehealth. Quality measures are affected, too. Ten not directly improving patient health outcomes are deleted, while five new are added to focus on the prevention of chronic disease. The Medicare Diabetes Prevention Program then allows more Medicare beneficiaries (at no cost) to access coaching, peer support and practical training in strategies to delay or prevent the onset of type 2 diabetes for people with prediabetes.

• *Chronic disease management: a new five-year payment model launching Jan.*

1, 2027. The mandatory Ambulatory Specialty Model (ASM) is focused on specialty care for beneficiaries with heart failure and low back pain. It aims to enhance the quality of care and reduce low-value care by improving upstream chronic disease management. Participants will be accountable for their performance, generating savings. ASM rewards specialists who detect signs of worsening chronic conditions early, enhance patients' function, reduce avoidable hospitalizations and use technology that allows them to communicate and share data electronically with patients and their primary care providers.[3]

• *Medicare telehealth services.* Proposed permanent adoption of pandemic-era waivers defining direct supervision includes virtual presence via audio/video real-time communications technology. It extends its waiver allowing federally qualified health centers and rural health clinics to bill for telehealth services through 2026, and streamlines how services are added to the Medicare telehealth services list by removing distinctions between provisional and permanent status. Reviews will focus only on whether a service can be provided via real-time, two-way audio-video. A temporary policy allowing teaching physicians to supervise residents virtually in all settings ends, requiring in-person presence during key parts of care in metropolitan areas, while keeping the rural exception.

• *Autologous cell-based immunotherapy and gene therapy payment.* Preparatory procedures for tissue procurement required for manufacturing autologous cell-based immunotherapy or gene therapy are included in the payment of the product itself. Effective Jan. 1, 2026, any preparatory procedures for tissue procurement required for manufacturing an autologous cell-based immunotherapy or gene therapy that were paid for by the manufacturer will be included in the calculation of the manufacturer's ASP.

• *Drugs payable under Medicare Part B.* For ASP, categories are drugs given incident to a physician's service, covered durable medical equipment and other drugs specified by statute (e.g., certain vaccines). Payment limits for most separately payable drugs is based on ASP+6%. Payment limits are published in the ASP pricing file or Not Otherwise Classified pricing file. The calculation of ASP involves a number of factors, including price concessions and bona fide service fees, both of which are under review. Refer to pages 423-440 in the published rule for details.

For maximum fair price (MFP), the Medicare Drug Price Negotiation Program requires negotiation of MFP for certain high-expenditure, single-source drugs payable under Medicare Part B and covered under Part D. CMS reached agreement on a negotiated price for all 10 selected drugs covered under Part D for 2026, the initial price applicability year. Units of selected drugs sold at MFP are included in the calculation of the manufacturer's ASP. Other pricing metrics could include wholesale acquisition cost less than ASP for a single source drug or biological; ASP widely available at market. price or average manufacturer price (AMP); and selected drugs 106 percent of MFP. Payment limits are published on the ASP drug pricing file, updated quarterly.[2]

• *Skin substitute reimbursement.* The proposed 2026 PFS would pay for skin substitutes as incident-to-supplies at a flat rate of $125.38 per square cm to reduce spending and curtail potential fraud and abuse. If approved as a biological, payment typically is ASP+6%. If approved as a device or regulated under 361 (human cells and tissues), payment is "incident to" supply.

• *Meshing PFS with IRA.* This rulemaking proposes to update policies in both Medicare Part B and Part D. In Part B, it proposes to describe the identification of payment amount benchmark quarter in certain instances along with the calculation of Part B rebate amounts. In Part D, it clarifies the calculation of a Part D rebate amount, and proposes methodology for removing units of a Part D 340B rebatable drug by using prescriber and contract pharmacy national provider identifiers to determine 340B claim eligibility. It also establishes a 340B data repository for Part D claims where 340B covered entities would need to submit claims-level data beginning on or after Jan. 1, 2026. Third-party administrators could submit some data elements on behalf of covered entities. A voluntary start would transition to a mandatory reporting structure. ❖

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Implementing AI in the Physician's Office

By Amy Scanlin, MS

WHEN ENTERING "Top Benefits of AI in Physician's Offices" into ChatGPT, the response highlights the increasingly rapid growth of this burgeoning technology. From expanded access to patient care, faster and more efficient office workflows, streamlining automated tasks and the creation of personalized care plans, not to mention its potential for diagnostic support, artificial intelligence (AI) in physician offices is here to stay.

The Benefits of AI

Experts have written extensively about AI's potential in diagnostics, but many find AI's ability to improve administrative efficiency offers a fantastic initial application for this powerful technology. Enhanced capabilities take the place of time-consuming administrative tasks and enable a greater focus on one-to-one patient care.

In fact, a 2024 American Medical Association (AMA) survey showed nearly two-thirds of physicians reported using AI in their practices, a 78 percent increase from the year prior. Documentation of billing codes, creating discharge instructions, translation services and transcription and charting are among the most common uses. More than half of respondents said the reduction in administrative burdens was the biggest opportunity for AI in their practices.[1]

Concerns Remain

Concerns for this technology as barriers for entry remain, however, including data privacy, poor integration with electronic health records, dispensing incorrect information, liability and employee training requirements.

The design of AI tools such as ChatGPT lack the robust privacy requirements of platforms designed for healthcare information. Furthermore, because AI uses historical datasets for training, these tools may incorporate erroneous information or biases into their algorithms. They may also exclude current clinical recommendations or new findings. In one well-documented example, developers shut down a chatbot designed to support the management of eating disorders when it dispensed diet and exercise tips to users. The weight loss information dispensed by the chatbot was reportedly not part of the data on which the tool was meant to be trained.[2] This cautionary tale highlights the importance of human oversight with the use of any technology.

The learning curve for AI's use may be steep. After all, medical schools only recently introduced AI into their curricula. In some cases, staff may also be uninterested or uncomfortable learning how to incorporate AI, concerned it will take over their jobs. The time required to effectively use AI can also be cumbersome, taking away from important daily duties. That being said, many with higher levels of data literacy and health informatics are jumping at the opportunity to incorporate AI methods so they can take advantage of the ability to streamline tasks.

AI's Entry Point: Chatbots

Incorporating chatbots into office functionality can be an easy entry into the world of AI. Chatbots are computer programs or software that simulate human-like conversations. Used by anyone with an Internet-enabled computer or smartphone, 10 percent of AMA survey respondents reported adding patient-facing chatbots to their medical practices.

From a patient standpoint, chatbots can act like virtual assistants and enable scheduling appointments, link those to the patient's own digital calendar,

and send prescription and refill reminders. Chatbots help patients triage their symptoms through text chats to determine whether a condition warrants medical attention and, if so, where the nearest treatment facility is located. Many patients find chatbots easier to navigate than their own patient portals or telehealth appointments. That makes them an attractive proposition from a provider standpoint. The ability for a bot to respond to patient administrative needs, with the patient's consent, saves time and lowers costs, allowing staff to focus on responsibilities that require problem-solving, emotional intelligence, interpersonal skills and judgment.

Chatbots have a relatively low cost of entry for medical practices, with fees ranging from approximately $150 to $400 monthly. Custom-designed chatbots can cost tens of thousands to upwards of $100,000. The market for chatbots continues to grow, with estimates reaching $1.2 billion by the year 2032.[2]

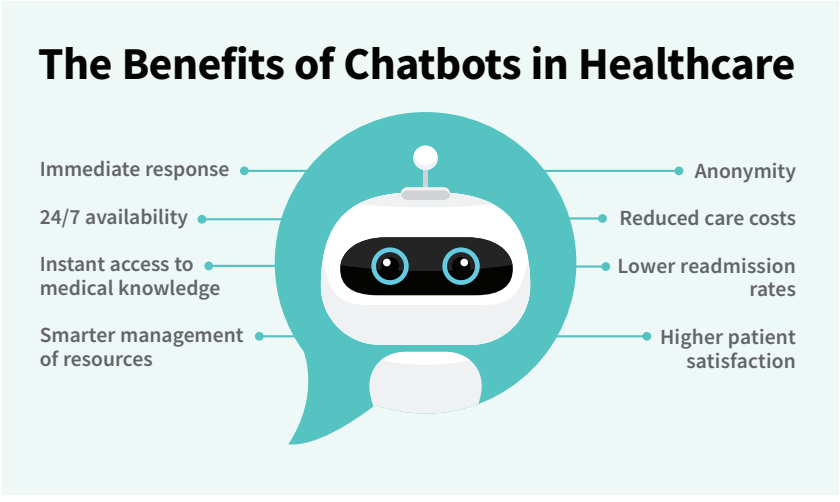
Despite chatbot's growing success, many caution that more research is required before they are standardized in medical practices, particularly given the concerns for data privacy. Although the level of required privacy between chatbot hosts and their users is dependent upon the types of conversations held, providers must be vigilant in choosing chatbot software and hosts whose security practices align with their own accepted data integrity practices. Similarly, providers should inform patients about their data privacy, explaining data collection and storage, and whether responses can be tracked and linked to other online data.[2]

Realizing AI's Full Potential

Chatbots are just one opportunity to incorporate AI efficiencies into medical practices. Billing, coding and generation of patient discharge sheets are the biggest uses of AI per the AMA survey.[1]

Automated billing and coding software can improve invoicing and collections, thanks to the elimination of manual transcription errors. Natural language processing (an AI language model using human-like speech) can listen to patient/provider conversations, enter information into the patient's electronic health record, and then search for and identify relevant information to assign billing codes for the patient's visit. Additionally, AI-created customized patient discharge sheets can translate lengthy provider instructions into actionable summaries for greater patient understanding and improved compliance.

Back to the power of AI in diagnostics, AI can also facilitate research into difficult-to-diagnose conditions and treat them, including rare diseases. Providers can scan large data sets quickly to find similar symptoms and speed the process of diagnosis, including identifying examples of treatments that have been effective in similar cases.[1]



The Future Is Near

Clinical trials looking at the efficacy of AI and chatbots are underway, including their potential to support medical adherence, improve sleep and improve diabetic foot care, as well as many others. And no wonder, with the enthusiasm for AI's power and its seemingly limitless potential. Regulatory requirements also continue to be debated, an important consideration for nearly half of the AMA respondents who stated improved regulatory oversight would increase their trust in adopting AI.[1]

As more and more medical practices incorporate this new technology, adherence to safety and data privacy is imperative, as is focusing attention on that much-needed human approach that makes the practice of medicine such a meaningful discipline. ❖

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Research

Study Finds No Connection Between Antibiotic Use and Autoimmune Disease in Children

A groundbreaking retrospective cohort analysis of more than four million children conducted at Sungkyunkwan University in South Korea offers compelling evidence that there is no significant association between early antibiotic exposure and heightened risk of autoimmune diseases in children.

In the study, researchers leveraged the comprehensive South Korea National Health Insurance Service-National Health Insurance Database, a mother-child linked insurance claims database that allowed researchers to identify cohorts of children born between April 2009 and December 2020 whose mothers received antibiotic prescriptions during pregnancy or while breastfeeding. After tracking these children's health outcomes longitudinally for more than seven years, the study encompassed data on diagnoses of multiple autoimmune diseases, including type 1 diabetes, juvenile idiopathic arthritis, inflammatory bowel diseases (such as ulcerative colitis and Crohn's disease), systemic lupus erythematosus and Hashimoto's thyroiditis.

The statistical analyses employed adjusted for a wide range of potential confounders, including maternal health conditions, socioeconomic factors and delivery methods, to isolate the specific effect of antibiotic exposure. Findings revealed no significant increase in the overall incidence of autoimmune diseases among children exposed to antibiotics either prenatally or during early infancy. And, this null association persisted across diverse autoimmune conditions studied and held true even when stratified by the timing and extent of antibiotic use.

These results stand in contrast to earlier studies that reported a possible link between early antibiotic exposure and autoimmune risk. According to the researchers, such discrepancies likely reflect differing research methodologies, population characteristics and the complexities inherent in immune system development. They caution against oversimplified conclusions, suggesting that genetic susceptibility, indication for antibiotic treatment, environmental factors and microbiome diversity all interplay in nuanced ways that require further exploration. ❖

New Study Finds No Connection Between Antibiotic Use and Autoimmune Diseases in Children. Bioengineer, Aug. 22, 2025. Accessed at bioengineer.org/new-study-finds-no-connection-between-antibiotic-use-and-autoimmune-diseases-in-children.

Advisory Panel

HHS Reinstates Childhood Vaccine Safety Task Force

The U.S. Department of Health and Human Services (HHS) has reinstated the Task Force on Safer Childhood Vaccines, a long-dormant federal panel created by Congress to oversee the safety and quality of children's vaccines. According to HHS, the task force will work with the Advisory Commission on Childhood Vaccines to make recommendations for developing, promoting and refining childhood vaccines that result in fewer and less severe adverse reactions than current vaccines. It will also look at ways to support vaccine safety research and improve adverse reaction reporting.

"By reinstating this task force, we are reaffirming our commitment to rigorous science, continuous improvement and the trust of American families," said National Institutes of Health (NIH) Director Jay Bhattacharya, who will serve as chairman of the group. "NIH is proud to lead this effort to advance vaccine safety and support innovation that protects children without compromise."

The task force was originally created by Congress under the National Childhood Vaccine Injury Act of 1986, but was disbanded in 1998. HHS said the group, which will also include representatives from the Centers for Disease Control and Prevention and the U.S. Food and Drug Administration, will send its first report to Congress within two years. ❖

Dall, C. HHS Revives Childhood Vaccine Safety Task Force. Center for Infectious Disease Research and Policy, Aug. 15, 2025. Accessed at www.cidrap.umn.edu/childhood-vaccines/hhs-revives-childhood-vaccine-safety-task-force.

Research

Study Finds Lymphoma Accelerates Aging of Immune Cells and Tissues

A new study led by a team of researchers at Moffitt Cancer Center reveals lymphoma can accelerate the biological aging of the immune system and other tissues, providing new insight into how cancer reshapes the body beyond tumor growth.

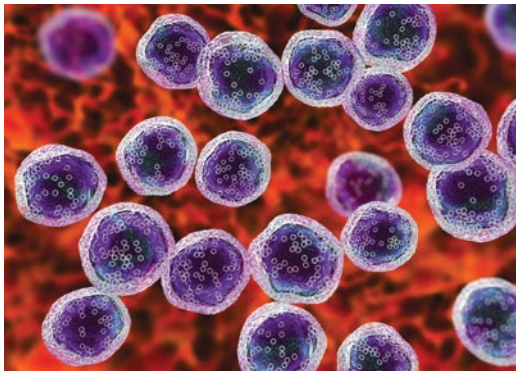
The study, published in *Cancer Cell*, shows B cell lymphoma rapidly transforms young T cells, which are key immune fighters, into a state resembling those of T cells in much older individuals. These changes included increased inflammation, impaired protein balance and altered iron regulation. The effects were not limited to immune cells. Markers of aging also appeared in the blood vessels, kidneys and intestines.

"Cancer doesn't just grow in isolation; it has widespread effects on patients. We found that lymphoma alone, without treatment, is enough to provoke systemic signs of aging," said John Cleveland, PhD, senior author and chief scientific officer at Moffitt. "This helps explain why many cancer patients experience symptoms typically associated with aging."

The findings challenge the long-held belief that accelerated aging in cancer patients is primarily caused by treatments like chemotherapy or radiation. While those therapies are known to age cells, this study shows the cancer itself can push immune and tissue systems into an aged state.

"Our results also suggest there may be opportunities to reverse some cancer-driven aging effects," said Rebecca Hesterberg, PhD, the study's lead author and a researcher in Moffitt's Department of Tumor Microenvironment and Metastasis. "By understanding the biology, we can begin to think about interventions that not only treat the cancer but also protect or even restore healthy immune function."

Researchers discovered lymphoma-exposed T cells accumulated excess iron, making them resistant to a type of cell death called ferroptosis. They



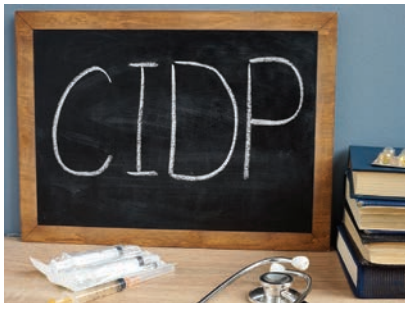
also exhibited defects in protein quality control, a hallmark of aging. Some of these changes were reversible when tumors were eliminated in animal models, pointing to new therapeutic opportunities.

The study underscores the importance of understanding how cancer interacts with aging biology. ❖

Moffitt Study Finds Lymphoma Accelerates Aging of Immune Cells and Tissues. Moffitt Cancer Center news release, Aug. 22, 2025. Accessed at www.moffitt.org/newsroom/news-releases/moffitt-study-finds-lymphoma-accelerates-aging-of-immune-cells-and-tissues.

Research

Argenx Is Conducting a Phase IV Study to Assess Efgartigimod Ph20 SC to Treat Adult CIDP Patients



Argenx is conducting a Phase IV clinical study titled "A Study to Assess Adults with CIDP Transitioning From IVIG to Efgartigimod PH20 SC" to evaluate how adults with chronic inflammatory demyelinating polyneuropathy (CIDP) transition from intravenous immune globulin (IVIG) treatment to efgartigimod PH20 SC. Efgartigimod PH20 SC, a biological treatment administered via subcutaneous injection, is designed to replace the current IVIG treatment, potentially offering a more accessible and less-invasive option for patients.

In the interventional study that follows a single-group model without masking, participants will transition from IVIG to efgartigimod PH20 SC to assess their adjustment over approximately 17 to 19 weeks. Originally begun on Dec. 10, 2024, with its primary completion and estimated full completion dates yet to be announced, this latest study update was submitted on Aug. 14, 2025, indicating ongoing recruitment and progress.

If successful, efgartigimod PH20 SC would provide an alternative to existing CIDP treatments. ❖

Tipranks. Argenx's Promising CIDP Treatment: A Closer Look at the Efgartigimod PH20 SC Study, Aug. 16, 2025. Accessed at www.theglobeandmail.com/investing/markets/stocks/ARGX/pressreleases/34204435/argenxs-promising-cidp-treatment-a-closer-look-at-the-efgartigimod-ph20-sc-study.

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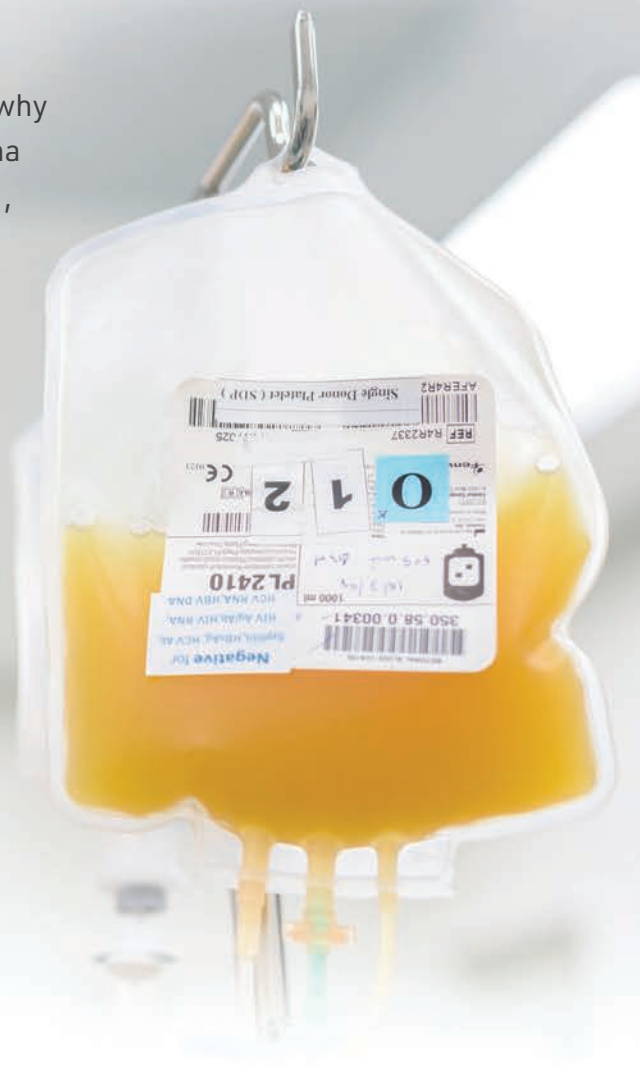

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Research

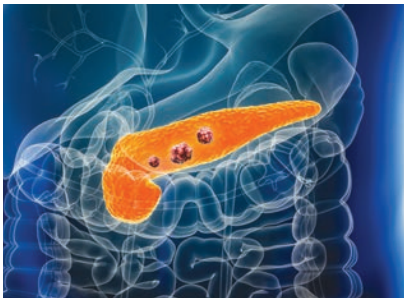
New Vaccine Shows Promise Against Pancreatic Cancer

Early clinical and preclinical results are showing that an experimental mRNA and nanoparticle vaccine produced measurable immune responses against pancreatic cancer, one of the deadliest cancers, and that in small patient groups, those immune responses correlated with delayed recurrence or prolonged survival.

Researchers at Memorial Sloan Kettering (MSK) and collaborators ran a Phase I trial in February testing a personalized mRNA vaccine called autogene cevumeran (BNT122, RO7198457) in 16 patients with operable pancreatic cancer who received surgery, chemotherapy and the vaccine. The vaccine was developed and researched through a collaboration between BioNTech and Genentech. It is not a cure for the type of cancer itself; however, signs point to improving longevity in individuals who contract the disease.

Results of the study showed half of participants mounted vaccine-induced tumor-specific T-cell responses. Also, long-term efficacy was reported as patients with a vaccine-induced immune response had a reduced risk of cancer returning at three-year follow-up appointments compared with patients whose immune systems did not respond.

"The latest data from the Phase I trial are encouraging. They suggest this investigational therapeutic mRNA vaccine can mobilize anti-tumor T cells that may recognize pancreatic cancers as foreign, potentially years after vaccination," said Vinod Balachandran, MD, a surgical oncologist at MSK, the principal investigator of the February 2025 trial and the director of the Olayan Center for Cancer Vaccines at the MSK Cancer Center. "For patients



with pancreatic cancer, our latest results continue to support the approach of using personalized mRNA vaccines to target neoantigens in each patient's tumor. If you can do this in pancreas cancer, theoretically you may be able to develop therapeutic vaccines for other cancer types." ❖

Mordowanec, N. New Vaccine Shows Promise Against One of the Deadliest Cancers. Newsweek, Aug. 11, 2025. Accessed at www.newsweek.com/cancer-vaccines-mrna-pancreatic-2111919.

How AI Is Changing the Face of Healthcare

The use of AI is growing at a brisk rate as healthcare professionals realize its potential as an indispensable partner in treating patients.

By Lee Warren

AS ARTIFICIAL INTELLIGENCE (AI) goes mainstream, it's making a big impact across the healthcare spectrum. In 2015, the U.S. Food and Drug Administration (FDA) approved just six AI devices (a glucose monitoring system, a snoring device, a retinal imaging system and a few others). In 2024, FDA approved 221 AI devices. And in just the first five months of 2025, FDA approved 147 devices for diagnostic and healthcare monitoring, ranging from improved MRI scans, cardiac amyloidosis and lymphoma.

One of the major differences in the healthcare industry regarding AI in 2025 is healthcare professionals' comfort levels in using the technology. In fact,

the risk tolerance for and confidence in AI technology has gone from low to moderate, and in some cases high (as long as safeguards are put in place).[1]

Adam Rodman, assistant professor at Harvard Medical School and a physician at Beth Israel Deaconess Medical Center, expressed his optimism in *The Harvard Gazette*. "So what excites me most about AI and medicine?" he asked. "Well, the optimist in me hopes that AI and medicine can make us doctors better versions of ourselves to better care for our patients."[2]

Alain Labrique, director for the Department of Digital Health and Innovation at the World Health Organization (WHO), offered this about the future of AI in medicine: "For us at WHO, AI is nothing short of a game-changer in public health, in clinical medicine and in maintaining our well-being as individuals."[3]

And, Ashish Sukhadeve, founder and CEO of Analytics Insight, which provides organizations with strategic insights on disruptive technologies, made this bold statement recently in a *Forbes* article: "In terms of its transformative effect, AI is doing for healthcare what electricity did for the industry."[4]

AI is indeed changing the face of healthcare in numerous ways. It is enabling personalized medicine and offering faster diagnostics and predictive analytics, as well as streamlining administrative workflow.

Enabling Personalized Medicine

AI is using the technology to tailor treatments to individuals by integrating data from genomics and wearable devices (smart watches, fitness trackers, etc.), which provide real-time data to monitor conditions such as heart disease and diabetes. AI combines behavioral and environmental factors to recommend personalized interventions that allow for customized, precise treatments to improve outcomes and reduce side effects.

A 2025 study explored how AI is transforming diabetes care by integrating real-time data from continuous glucose monitoring (CGM) devices with personalized treatment algorithms. In the study, type 2 diabetics who are not on insulin and who exhibit poor glycemic control used Dexcom CGM devices in combination with an AI platform called SugarFit Diabetes Reversal and Management Program that analyzed their glucose trends, lifestyle data and medication adherence. The 100-day study involved 1,752 patients (77.5 percent men; mean age, 50.22 years). Time in range increased from 45.74 to 49.31; time below range decreased from 7.46 to 5.34; and time above range decreased from 49.89 to 45.33. Patients also exhibited reductions in weight, HbA1c and fasting blood sugar.[5]

In a University of Southern California study, scientists used machine learning to analyze genomic and clinical data from more than 78,000 cancer patients across 20 different cancer types. Patients in the study received immunotherapies, chemotherapies and targeted therapies. The researchers discovered 95 genes significantly associated with survival in cancers such as breast, ovarian, skin and gastrointestinal cancers. Equipped with these insights, the team developed a predictive model to assess how patients with advanced lung cancer might respond to immunotherapy. The AI model helped clinicians match therapies to patients' genetic profiles, enabling them to avoid ineffective treatments. The findings were validated using real-world data from collaborators at Genentech, Roche and Stanford University. Overall, the study demonstrates how AI can analyze large-scale genomic data to personalize cancer treatment and improve clinical outcomes.[6]

AI combines behavioral and environmental factors to recommend personalized interventions that allow for customized, precise treatments to improve outcomes and reduce side effects.

Faster Diagnostics

AI-powered tools are revolutionizing diagnostics in several ways. First, they're analyzing medical imaging using deep learning (DL) models that detect anomalies in X-rays, MRIs and CT scans faster and often more accurately than human radiologists. Second, they're processing electronic health records (EHRs), quickly sifting through vast amounts of patient data to identify patterns and suggest diagnoses. And third, they're reducing diagnostic errors, providing decision support, helping healthcare workers avoid misdiagnoses and ensuring time-sensitive interventions. All these advancements are particularly impactful in areas such as oncology, cardiology and neurology, where early detection is critical.

A 2025 *European Journal of Medical Research* review examined the impact

of AI across 16 diseases using machine learning (ML) and DL technologies. The study found that AI significantly reduced diagnostic time in key areas such as medical imaging (CT, MRI, X-rays), EHR analysis and predictive modeling for early disease detection. These tools not only improved diagnostic speed but also enhanced clinical decision-making and workflow efficiency, particularly in radiology and pathology. The authors concluded that ML and DL demonstrate "remarkable accuracy and efficiency in disease prediction and diagnosis," ultimately strengthening patient outcomes.[7]

AI can analyze vast datasets, including EHRs, imaging and lab results to forecast disease progression, hospital readmissions or complications. For example, convolutional neural networks have shown high accuracy in predicting conditions like diabetic retinopathy and cancer spread, allowing clinicians to act earlier and more effectively.[9]

IBM Watson is processing vast amounts of medical journals and case studies. AstraZeneca's AI is trained on data from half a million people, which allows it to predict diseases like Alzheimer's before symptoms even appear.[3]

Predictive analytics powered by AI is helping healthcare systems anticipate patient needs, optimize resource allocation and prevent adverse events before they occur.

AI is also gaining time in administrative tasks. A 2025 study conducted at The Permanente Medical Group examined the use of ambient AI scribes across more than 2.5 million clinical interactions. Published in *NEJM Catalyst*, the study found that AI scribes saved more than 15,700 hours of documentation time in one year — the equivalent of 1,794 working days — while maintaining a neutral to positive impact on patient experience, indicating that AI did not detract from the human interaction during visits.[8]

Predictive Analytics

Predictive analytics powered by AI is helping healthcare systems anticipate patient needs, optimize resource allocation and prevent adverse events before they occur. Using advanced ML models such as DL neural networks,

An AI algorithm called NAVOY Sepsis is reported to have the potential to predict sepsis hours before its onset.[10] That means only a few hours after ICU admission, the clinical staff can receive high-performance risk assessment for sepsis in adult patients. The life-threatening condition can ordinarily be difficult to detect because many people present with nonspecific symptoms, so time is always of the essence.

A scoping review performed in 2025 analyzed 142 studies applying AI to clinical risk prediction, including chronic diseases such as diabetes. It highlighted the use of ML, DL and causal ML for predicting disease onset and treatment outcomes. Some models achieved Area Under the Receiver Operating Characteristic curve scores up to 96 percent, indicating high predictive accuracy.[11]

AI in Cancer Detection

One area in which predictive analytics is making a particularly strong impact is oncology. A new ChatGPT-style model called Clinical Histopathology Imaging Evaluation Foundation (CHIEF), designed by scientists at Harvard Medical School, trained on 15 million unlabeled images chunked into sections of interest. The tool was then trained on 60,000 whole-slide pathology images across 19 different types of cancer, including lung, breast, prostate and brain cancers. The model was trained to look at specific sections of an image, and the whole image allowed it to relate specific changes in one region to the overall context. CHIEF achieved nearly 94 percent accuracy in cancer detection.[12]

In one 2025 study involving 260,000 women, AI-assisted mammography increased breast cancer detection by 17.6 percent (95 percent confidence interval: +5.7 percent, +30.8 percent) higher than and statistically superior to the rate (5.7 per 1,000) achieved in the control group.[13] The study compared outcomes between those screened with and without AI support. Additionally, the AI group had a higher positive predictive value for recalls than the control group.[14]

Streamlining Administrative Workflows

In addition to streamlining predictive analytics, AI is also transforming the administrative side of healthcare, where it's helping to reduce paperwork, speed up processes and improve accuracy. Tools powered by AI are now automating tasks such as patient chart management, claims processing and billing and coding, allowing staff to focus more on patient care. For example, AI can automatically update EHRs, transcribe clinical notes in real time and even optimize nurse scheduling to reduce burnout and improve coverage.

A 2025 guide from Keragon, a healthcare automation platform, highlights how AI is being used to streamline operations across healthcare systems. From automating insurance workflows to analyzing data for compliance and resource planning, AI is helping healthcare organizations cut costs and improve efficiency. As these tools become more integrated into daily operations, they're expected to play a key role going forward in reducing administrative burdens and enhancing the overall patient experience.[15]

Checks and Balances

As AI becomes more integrated into clinical settings, healthcare systems are implementing a range of safeguards to protect patients and ensure ethical use. Data privacy is a top priority, with regulations such as HIPAA requiring encryption, anonymization and strict oversight of patient data. Healthcare organizations are investing in cybersecurity and conducting regular audits to prevent breaches and misuse.

To combat algorithmic bias against marginalized populations, developers are being urged to use diverse and representative datasets. Bias audits and explainability requirements are helping ensure AI tools do not perpetuate healthcare disparities or misdiagnose marginalized populations.

Additionally, many AI systems are designed with a human-in-the-loop approach, meaning clinicians retain final decision-making authority, especially in high-stakes scenarios. On the legal front, countries are adopting varied approaches: Some, like the European Union and Japan, have introduced AI-specific laws, while others, including the U.S., are adapting existing frameworks. International collaboration is growing, with organizations like WHO promoting principle-based guidelines focused on fairness, transparency and accountability.

These safeguards aim to balance innovation with patient safety, ensuring AI enhances care without compromising ethics or equity.

A Look to the Future

As AI continues to evolve, its role in healthcare is expected to expand dramatically. Emerging technologies such as multimodal AI — which integrates text, images and sensor data — promise more holistic diagnostics, while federated learning allows AI models to train on decentralized data without compromising patient privacy. Innovations such as digital twins (virtual patient models) and AI-driven drug discovery are also on the horizon, offering new ways to simulate treatment outcomes and accelerate medical breakthroughs.

At the same time, healthcare systems are implementing critical safeguards to ensure AI is used ethically and responsibly. Together, these innovations and safeguards are shaping a future in which AI not only enhances care but does so in a way that is safe, equitable and patient-centered.

An Indispensable Partner in Medicine

As AI becomes more deeply embedded in the fabric of healthcare, its potential to improve outcomes, reduce costs and empower both clinicians and patients is increasingly evident. With thoughtful safeguards and ongoing innovation, AI is poised to become an indispensable partner in medicine, enhancing the capabilities of clinicians and empowering patients like never before. ❖

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Technological Advancements in Cardiology: Improved Monitoring

With a pending shortage of cardiologists, there is a growing need for remote cardiac monitoring, and now, three FDA-cleared products are transforming how this care is provided.

By Diane L.M. Cook

ACCORDING TO THE American Heart Association's "2025 Heart Disease and Stroke Statistics Update: A Report of U.S. and Global Data from the American Heart Association," heart disease has been the leading cause of death in the U.S. for 100 years.[1] However, sadly in 2021, the Association of American Medical Colleges predicted a shortage of 120,000 cardiologists by 2030.[2]

With heart disease the leading cause of death, coupled with a projected shortage of more than 100,000 cardiologists within the next five years, innovative solutions in cardiac care are urgently needed to ensure timely and effective treatment for patients to maintain a seamless continuum of cardiac monitoring care from the hospital to home.

The Importance of Remote Cardiac Monitoring

According to Anjali B. Thakkar, MD, a member of the American College of Cardiology's Health Care Innovation Council, near-continuous or continuous cardiac remote monitoring devices enable the gathering of real-world patient data and can identify life-threatening conditions and facilitate early interventions. "For patients who are suspected of having dangerous arrhythmias like complete heart block, real-time Holter monitors can be used that are being continuously monitored by ECG techs who notify the prescribing cardiologist in the event of an alarm," she explains. "Remote monitoring can also help to extend a patient's life by improving management of their chronic conditions."

"By detecting deterioration in its earliest stages, remote patient monitoring can alert patients, caregivers and providers and support early interventions to correct the course before a dangerous situation develops," says Lee Schwamm, MD, FAHA, a volunteer member of the American Heart Association's Center for Telehealth Expert Panel. "Remote patient monitoring is an increasingly important tool in modernizing healthcare delivery. It enables continuous tracking of vital signs and health metrics, allowing early detection of non-adherence to medications, need for medication

titration or lifestyle modification, or urgent medical concerns such as dangerous blood pressure elevations or cardiac arrhythmias. This leads to timely interventions and prevents complications.

"It also enhances access to care in two key ways: Firstly, patients in rural or underserved areas can receive high-quality care without frequent in-person visits, and potentially avoid visits to the emergency department or hospitalizations due to predictable and preventable deteriorations. This is especially important for those with mobility issues or chronic conditions. Secondly, this frees up access for new patient office visits or those with more serious medical conditions. These aspects empower patents to participate in their care, make care delivery more efficient [and] cost-effective and help get patients to their health goals faster."

Dr. Thakkar reiterates remote monitoring's importance: "Remote patient monitoring is important because many cardiovascular conditions, such as arrhythmias, heart failure and hypertension, progress silently before symptoms appear. In these conditions, remote patient monitoring transforms care by allowing early detection of disease progression to facilitate early intervention. Furthermore, whereas care today is mostly episodic, remote monitoring allows for continuous monitoring of certain parameters that can paint a more accurate picture of a patient's health."

Remote Cardiac Monitoring Systems

Several medical device companies have developed systems that transform how healthcare providers conduct remote patient monitoring for their cardiac patients.

AliveCor's Kardia 12L ECG system.[3] AliveCor, focused on transforming cardiovascular care for a heart-healthier future, developed the Kardia 12L ECG system, the world's first AI-powered, handheld 12-lead ECG system, featuring a single-cable design and reduced lead set. It is U.S. Food and Drug Administration (FDA)-cleared and powered by the advanced KAI 12L AI algorithm, which can detect 35 life-threatening cardiac conditions, including acute myocardial infarction and common types of ischemia.

Near-continuous or continuous cardiac remote monitoring devices enable the gathering of real-world patient data and can identify life-threatening conditions and facilitate early interventions.

What distinguishes Kardia 12L is its combination of power and portability. Weighing just 0.3 pounds and fully battery-operated, it is more compact than typical 12L ECG solutions that can weigh more than 15 pounds, making it ideal for use in remote, outpatient or space-constrained environments.

Recent clinical studies demonstrated Kardia 12L cuts ECG acquisition time and delivers accurate, actionable data comparable to traditional 12-lead ECG machines. A 2025 peer-reviewed study in the journal *Heart Rhythm O2* showed Kardia 12L cuts ECG acquisition time by 29 percent versus standard 12L ECG. A study presented in 2024 at the Heart Rhythm Society also found Kardia 12L enabled rapid acquisition of resting ECG information, with measurements and interpretations highly similar to standard 12-lead ECGs.

Another study in 2024 presented at the Computing in Cardiology conference in Germany showed that a reduced ECG lead set, as used in Kardia 12L, exhibited comparable, excellent performance in detecting major morphological cardiac abnormalities, including heart attack, as a standard 12-lead ECG.

Using only a single cable with five electrodes to acquire eight high-quality diagnostic bandwidth leads, Kardia 12L ECG combines the power of KAI 12L's AI technology and the Kardia 12L. This design makes it possible for more providers in a wider range of settings, including primary care offices, urgent care clinics, employer clinics and rural locations, to access and integrate 12-lead ECG data into cardiac care. Additionally, the device's streamlined lead set improves patient experience by reducing the need for full disrobing, making the ECG process faster, more comfortable and less invasive.

Kardia 12L delivers a clinically validated, hand-held, 12-lead ECG system that enables rapid, hospital-grade cardiac assessments anywhere. This is especially impactful in rural areas, where heart disease incidence is 40 percent higher than in urban settings and access to timely diagnostics is limited. Using Bluetooth technology, Kardia 12L wirelessly transmits ECG data to a clinician's smartphone or tablet, enabling a comprehensive view of heart activity in just minutes.

"Not only is KAI 12L the first FDA-cleared AI that can detect a heart attack on a reduced lead set, but it also returns determinations for our broadest range of

conditions yet," says Priya Abani, CEO of AliveCor. "Paired with our pocket-sized Kardia 12L ECG system, this offering is poised to disrupt traditional care pathways and represents a leap forward in cardiac care."

InfoBionic.Ai's MoMe ARC platform.[4] InfoBionic.Ai, a virtual telemetry company focused on the efficiency and economics of remote patient monitoring for cardiac patients, developed the MoMe ARC platform. Originally introduced in 2014, the most recent version was launched in May 2024.

The MoMe ARC platform is an AI-driven, cloud-based platform that combines reliable devices, actionable data and a robust analytics suite into one continuously connected ecosystem. It is an FDA-cleared platform that continuously streams six-lead ECG data in near real-time that provides hospital-grade visibility for cardiac care regardless of patient location. Unlike wearables or traditional systems that sample or compress data, MoMe ARC provides full-disclosure ECG monitoring, capturing 100 percent of every heartbeat.

The platform includes a discreet wearable six-lead sensor that provides remote cardiac telemetry that can detect 20 FDA-cleared determinations. Depending on the arrhythmia, the sensor can trigger a direct call, text or email to a clinician. Its lightweight design, at 80 grams (it fluctuates +/- 5 grams due to production), integrates seamlessly into patients' routines to ensure comfort and adherence.

The platform also includes a one-lead patch that operates independently or with an external cellular or Wi-Fi-based gateway and allows for flexibility between single and multi-lead configurations for patients' convenience and quality of data.

One wearable sensor supports Holter, Extended Holter, Event and Mobile Cardiac Telemetry modes, which is switchable without changing hardware or the need to have patients return to their provider's location. Clinicians can review every heartbeat, not just flagged events, within minutes of occurrence, enabling faster, more informed intervention.

The platform's core arrhythmia-classification engine is built on greater than 99 percent accuracy datasets, and a new collaboration with Anumana is adding FDA-cleared algorithms for low ejection fraction, pulmonary hypertension, cardiac amyloidosis and more.

MoMe Analytics gives providers powerful views of clinical, operational and financial metrics without the need to rely on third-party tools.

The MoMe ARC platform supports both multi-lead and patch-based configurations using the same rechargeable core, offering flexibility for different patient needs. Bluetooth-enabled sensors and a cellular gateway ensure uninterrupted data flow, even without Wi-Fi or phone connectivity. All data and reports are managed through a platform that integrates directly with emergency health records, reducing administrative friction. It is compact, water-resistant and intuitive to use, which improves patient comfort and compliance, leading to higher-quality, reliable data.

"We are proud to unveil a comprehensive suite of cutting-edge advancements that will equip providers with a powerful ecosystem of solutions designed to optimize every aspect of remote cardiac monitoring — from patient comfort and data quality to operational efficiency and clinical performance," says Stuart Long, CEO at InfoBionic.Ai. "By empowering providers to access, understand and utilize both practice and patient data more effectively, we look to forge ahead in our mission to advance more effective remote cardiac care."

iRhythm Technologies' Zio suite of products.[5] iRhythm Technologies, a digital healthcare company that creates solutions that detect, predict and prevent disease, developed the Zio suite of products. Zio combines wearable biosensors and cloud-based data analytics with powerful proprietary algorithms to provide remote patient monitoring services for cardiac patients. The company's comprehensive clinical evidence program encompasses more than 125 original research manuscripts, insights derived from more than two billion hours of curated heartbeat data and more than 10 million patient reports.

Zio monitor is a single-lead patch ECG device. It is breathable, using a hydrocolloid adhesive and waterproof housing, requiring no device or adhesive manipulation or battery change during the entire wear and monitoring period. The monitor is the next generation of iRhythm's Zio LTCM service, which provides continuous, uninterrupted recording for up to 14 days and provides physicians a comprehensive and actionable end-of-wear report to make a diagnosis.

iRhythm's ZEUS System, an advanced AI algorithm, supports the capture and analysis of data recorded by the monitor. The Zio monitor is 23 percent thinner, 62 percent lighter and 72 percent smaller than the previous generation. And, it demonstrates 99 percent patient compliance with prescribed wear times.

The end-to-end service includes ZioSuite for providers, which interprets reports, manages patients from any device and tracks patient monitors. And the My Zio patient app supports patients throughout their monitoring journey with digital symptom logging, educational content and reminders.

The Zio AT mobile cardiac telemetry monitoring service includes a patch

ECG device and provides continuous, uninterrupted recording for up to 14 days. It provides physicians with an actionable wear-time report, alerting them during those 14 days if an arrhythmia is detected.

iRhythm is the first company in the ambulatory cardiac monitoring category to leverage an FDA-cleared deep-learning algorithm for ECG interpretation. This AI-driven approach enhances diagnostic accuracy and efficiency by comparing collected data against a vast database of diagnosed arrhythmias, improving precision and aiding physicians in making accurate diagnoses the first time.

iRhythm's deep-learned algorithm enhances the performance of cardiologist interpretation, bringing precision to an industry where every percentage point matters. The technology's effectiveness is underscored by a 99 percent agreement rate, whereby the interpreting cardiology physician will not change the AI-guided and human expert-validated preliminary interpretation from Zio.

The Zio service can improve clinical outcomes since it is two times more likely to result in specified arrhythmia diagnoses compared to Holter monitoring services. It is also 72 percent more likely to result in specified arrhythmia diagnoses compared to event monitoring services. And it provides 2.6 times greater detection of atrial fibrillation versus routine cardiac care.

In the largest real-world evidence study of ambulatory cardiac monitoring published in the *American Heart Journal* in March 2024, the Zio LTCM service was associated with the highest clinical diagnostic yield, lower odds of retesting and lowest acute care healthcare resource utilization compared to all other monitoring services in the study.

"With wearable solutions like iRhythm's Zio service, patients can receive a medical-grade ECG monitor by mail, self-apply and activate it at home and return it — all without an in-person visit," said Mintu Turakhia, MD, MS, chief medical and scientific officer at iRhythm. "The resulting data is analyzed by FDA-cleared AI and reviewed by qualified cardiac technicians to generate a clinical report that supports physicians in making timely, informed diagnoses."

Remote Cardiac Monitoring: The Future

Remote patient monitoring assists providers with expanded access to accurate patient heart data and rapid disease detection, and addresses gaps in monitoring rural and remote patients. It also helps patients with enhanced treatment experience, reduced hospital visits and improved health outcomes.

According to Dr. Thakkar, cardiovascular care relies heavily on data to make diagnoses and guide therapeutic interventions, making remote patient monitoring essential: "In the future, I envision data from remote monitoring devices flowing directly into our existing clinical systems to facilitate easier use of this data in clinical decision-making."

She also says another major challenge with remote patient monitoring data involves data management: "When large amounts of data are collected on a daily basis, it is overwhelming for clinicians to interpret and use this data to guide decisions. I envision a future in which data analytics are used to consolidate large amounts of remote-monitoring data and present clear and accurate management recommendations on the guideline-directed next steps. In certain cases where management is driven by algorithms or guidelines, physician extenders or pharmacists can even implement these next steps, involving the physician only in edge cases. Systems like this will not only improve a cardiologist's efficiency but also enable population-based chronic disease management."

In the future, Dr. Schwamm believes wearable and implanted remote patient monitoring devices will be a commonly used method for disease management, and autonomous AI software will help monitor the data produced by these devices, freeing up doctors and nurses to attend to the patients who most need their attention: "Visits to the doctor will be data-driven, based on need and predicted outcomes, and not scheduled at arbitrary intervals like every three months or annually. Patients will be more actively engaged in measuring and monitoring their own health-related data, and will be supported by AI 'agents' that will converse with them in their own language and literacy level, and provide medical and emotional support to help them adhere to their care plans. When procedures are required, AI will help improve the diagnostic studies that are performed and better guide treatments through the use of robotics and advanced algorithms." ❖

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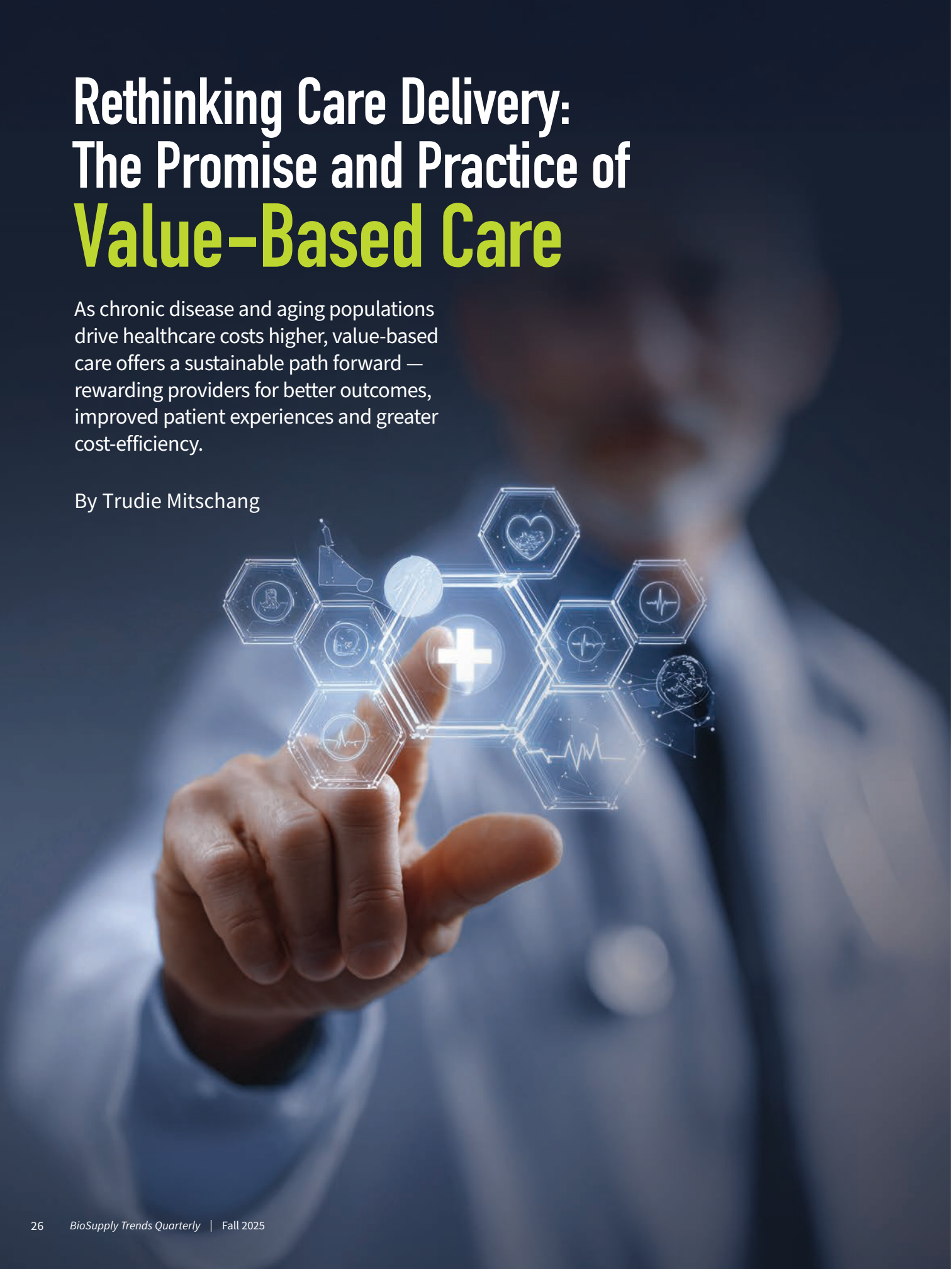
Rethinking Care Delivery: The Promise and Practice of Value-Based Care

As chronic disease and aging populations drive healthcare costs higher, value-based care offers a sustainable path forward — rewarding providers for better outcomes, improved patient experiences and greater cost-efficiency.

By Trudie Mitschang



THE CONCEPT OF value-based healthcare first gained attention in the mid-2000s, introduced by Harvard economist Michael E. Porter, a leading expert in business strategy and competitiveness. His landmark 2006 book, *Redefining Health Care: Creating Value-Based Competition on Results*, co-authored with Elizabeth O. Teisberg, was the result of a decade of research into why the U.S. healthcare system failed to reflect the competitive dynamics found in other industries.

The book argued that the American healthcare system — driven by a fee-for-service model in which providers are paid for each individual treatment — had become fragmented, inefficient and overly focused on volume rather than outcomes. This structure, the authors explained, discouraged performance and innovation, leading the U.S. to spend more on healthcare per person than any other nation without delivering superior health outcomes.[1]

Porter proposed a shift to a model centered on delivering high-quality care and maximizing value for patients. His framework called for the integration of all aspects of a patient's care, along with bundled payments to providers based on overall outcomes rather than individual services. As he put it, "Value-based healthcare's central tenet is that the overarching principle in redesigning healthcare delivery systems must be value for patients. We define value as the outcomes that matter to patients and the costs to achieve those outcomes."[1]

Since its introduction, value-based care (VBC) has sparked global interest across the healthcare spectrum — from patients and providers to payers, policymakers and suppliers. Implementation efforts have taken root in pilot programs around the world, and peer-reviewed research on the subject has grown rapidly, reflecting a broad shift toward more patient-centered, outcome-driven care.

Defining VBC's Core Principles

For physicians and healthcare organizations, understanding and embracing VBC's core principles is imperative for staying ahead in a competitive field. "Value-based care is really a care-delivery system that rewards for patient outcomes and quality of care, managing a population rather than transactional care," said Maria Ansari, MD, CEO, executive director at The Permanente Medical Group, in a January 2024 interview. "It's being rewarded for patients who live longer, healthier lives, as opposed to more siloed, transactional care that's more episodic."[2]

For physicians and healthcare organizations, understanding and embracing VBC's core principles is imperative for staying ahead in a competitive field.

At its foundation, VBC is built on a simple yet powerful equation: Value is created by health outcomes that matter to patients divided by the cost of delivering those outcomes. The aim is to improve patient health in measurable ways while making the best use of available resources. Porter emphasized that, "Value should always be defined around the customer, and in a well-functioning healthcare system, the creation of value for patients determines the rewards for all other actors in the system."[3]

A core principle of VBC is care coordination across the full continuum of a patient's needs. Rather than viewing care as isolated encounters, VBC promotes integrated care delivery — where primary care, specialty care, behavioral health and social supports work in unison to manage a patient's health. This model emphasizes the longitudinal view of care, particularly for those with chronic conditions, and incentivizes collaboration among providers. As the Centers for Medicare and Medicaid Services (CMS) notes, successful VBC programs "ensure patients receive the right care at the right time, while avoiding unnecessary duplication of services and preventing medical errors."[4]

VBC also emphasizes alignment of financial incentives with quality and outcomes, not volume. In traditional fee-for-service models, reimbursement is tied to the quantity of care delivered. VBC flips that paradigm by offering performance-based payments for achieving specific outcome metrics such as hospital readmission rates, preventive screening adherence or diabetes control. This approach not only encourages evidence-based practice but also empowers physicians to focus on what works best for their patients.

In a recent review, the American Medical Association (AMA) stated, "Value-based care models can support the goals of improving quality, reducing cost and enhancing physician autonomy — when designed with physician input and aligned with clinical realities."[5]

Addressing Common Misconceptions

Despite its growing adoption, VBC is often misunderstood — particularly among frontline physicians. One common misconception is that it is merely a cost-cutting strategy disguised as reform. While the model does aim to control healthcare costs, its primary goal is to improve health outcomes by focusing on coordinated, high-quality and preventive care. CMS says, "VBC incentivizes providers to focus on delivering the best care at the right time in the right setting, rather than maximizing service volume." In a nutshell, by rewarding outcomes over output, VBC aims to reduce unnecessary procedures — not provider income.[4]

Another misconception is that VBC is exclusively for primary care practices. While the model is often associated with primary care or chronic disease management, it is also applicable across a wide range of specialties, including surgery, mental health, skilled nursing and oncology. The principles of VBC — improving outcomes, focusing on preventive measures and reducing costs — can be applied to virtually any area of healthcare. Specialized models such as bundled payments for surgeries or value-based behavioral health programs show that VBC is more versatile than many realize.

That said, even staunch advocates of VBC have come to recognize that it cannot completely replace fee-for-service models. Rather, the two approaches will likely continue to coexist for the foreseeable future. There are certain services or specialties for which fee-for-service may still be more practical or in which a hybrid approach is most effective. The goal is not necessarily to eliminate fee-for-service entirely but to expand the use of VBC programs where it can bring the most benefit.

"Right or wrong, the fee-for-service payment structure has become the backbone of American healthcare finance," said Michael Wolford, principal at Forvis, a global consulting firm. "Abandoning the fee-for-service structure would be a decades-long and extremely disruptive undertaking. However, there must be scenarios in which the level of fee-for-service rate depression combined with the value-based care lift will discourage the former and promote the latter."[6]

Despite its growing adoption, VBC is often misunderstood — particularly among frontline physicians.

Making the Transition

Physicians can begin the transition to VBC by identifying key patient populations that drive the highest costs or suffer from the poorest outcomes — often patients with chronic conditions such as diabetes, hypertension or chronic obstructive pulmonary disease (COPD). Using electronic health record analytics and risk stratification tools, clinicians can prioritize care coordination, preventive screenings and lifestyle interventions. The Agency for Healthcare Research and Quality emphasizes that population health management is foundational to VBC, enabling providers to proactively manage care across a defined population to improve outcomes and reduce unnecessary costs.[7]

It's also important to embrace team-based, coordinated care models since VBC thrives on collaboration — not only among physicians but across care teams that include nurses, pharmacists, behavioral health specialists and social workers. By establishing workflows for care coordination and closing referral loops, physicians can ensure continuity across the care journey. AMA recommends team-based care as a core pillar of VBC, noting that practices can start small by integrating care managers or health coaches to work with high-risk patients and support shared decision-making.[8]

Physicians curious about making a shift to VBC can also consider:

- *Joining an accountable care organization (ACO).* ACOs work with healthcare professionals to enhance care coordination, expand greater healthcare access and provide coordinated high-quality care.
- *Investing in technology.* Artificial intelligence, machine learning, electronic health records, live patient data, predictive and prescriptive analytics, integrated platforms and other technologies are at the forefront of VBC transformation. Not only do these tools enhance a practice's care delivery, they offer the capabilities to design a VBC framework that mitigates risk, realigns incentives and facilitates better and more cost-effective care.
- *Implementing financial incentives.* VBC ties the amount providers earn for their services to the results they deliver for their patients, such as quality, equity and cost of care. Through financial incentives, VBC programs aim to hold providers more accountable for improving patient

outcomes while also giving them greater flexibility to deliver the right care at the right time.

• *Standardizing processes.* According to the Cleveland Clinic,[9] the goal of VBC is to standardize healthcare processes through best practices, similar to other industries. Mining data and evidence can determine which processes work and which don't. This forms a foundational care pathway to help gain the best results for patients.

• *Prioritizing continuing education.* This includes browsing the latest medical journal articles, taking continuing medical education courses or consulting fellow physicians within the ACO network. In addition, providing education and sharing VBC learnings with peers and staff can help them stay updated on developments and align with shared goals.

Envisioning a Value-Based Future

VBC is far more than a cost-containment strategy or a model limited to certain clinical settings. At its heart, VBC is a patient-centered approach that personalizes care to individual needs, spans across medical specialties and can operate alongside traditional payment models to drive broad, systemic change. Crucially, it emphasizes outcomes over volume — rewarding the quality of care delivered rather than the number of services provided.

Emerging technologies, including generative AI and predictive analytics, are accelerating this transformation. These tools help providers automate routine tasks, reduce administrative burden and manage population health more effectively — all without compromising care quality. Predictive models, in particular, can identify high-risk patients earlier and support proactive, preventive interventions. With the right technology, physicians can confidently enter risk-based contracts with payers and close care gaps in ways that were not previously possible.[10]

At its heart, VBC is a patient-centered approach that personalizes care to individual needs, spans across medical specialties and can operate alongside traditional payment models to drive broad, systemic change.

Sanjay Doddamani, MD, says that while the initial decade of VBC was heavily focused on risk adjustment, the current understanding and evolution of the model emphasize true improvements in health outcomes and quality of care, beyond just reducing total costs. He suggests that true population health initiatives now require a shift toward achieving better health for patients, driven by collaboration and leading to early positive movements in quality and outcomes. "The first decade in value-based care was really focused on risk adjustment without too much of actual true health outcomes improvement," Dr. Doddamani says. "I think we've come to a moment of reckoning that true population health has to be improving quality of care and reducing not just total cost but actually improving health outcomes. And I think that's what we've uncovered — that collaborating together, what we're seeing is very early movement in quality performance and health outcomes that will continue to evolve as we'll work together."[11]

While VBC is not a one-size-fits-all solution, it holds enormous potential when thoughtfully implemented. Real success depends on aligning systems with community needs, investing in data infrastructure and addressing social determinants of health. Physicians who embrace this shift — with a preventive mindset, collaborative spirit and commitment to continuous improvement — won't just adapt to healthcare's evolving future, they will lead it. ❖

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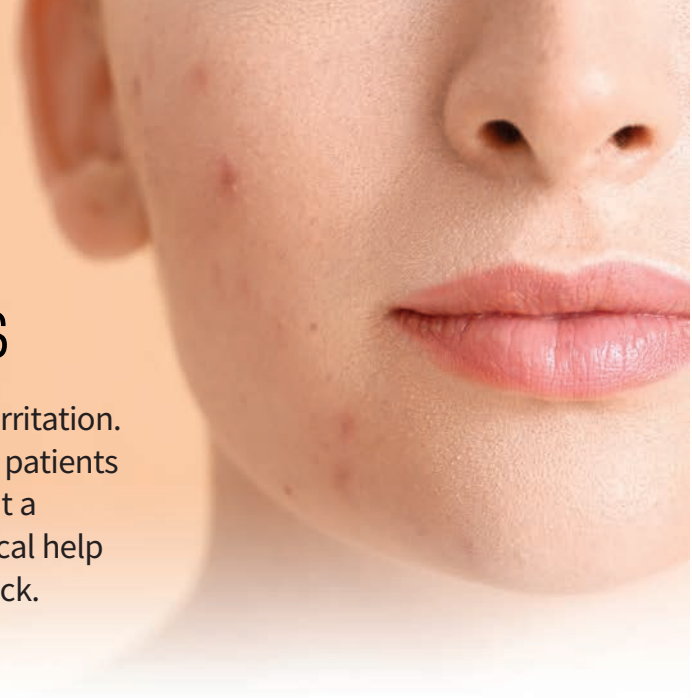

Dermatological Issues and Mental Health: Examining the Connections

Acne and rosacea can cause more than minor skin irritation. Low self-esteem, depression and anxiety can cause patients with these skin conditions to withdraw from life, but a combination of the right medicines and psychological help can ease the burden and give patients their lives back.

By Lee Warren

ACNE VULGARIS and rosacea are more than just skin conditions: They deeply affect mental health and daily life in patients who have them. Beyond physical symptoms, these conditions can lead to depression, anxiety and diminished self-esteem.

Acne vulgaris, commonly known as acne, has proven to lead to a 63 percent higher risk for depression within the first year of a diagnosis compared to individuals without the condition,[1] and around 31 percent of rosacea patients have been known to experience some level of depression.[2] Anxiety, low self-esteem and a decrease in personal quality of life are also common responses to both conditions. In fact, an alarming number of patients report suicidal thoughts (9.8 percent of those with facial dermatoses, including acne, compared to 3.2 percent in a control group; and 5.8 percent of rosacea patients, compared to 3.2 percent in a control group).

And it's not just adolescents suffering. In fact, while 85 percent of adolescents are affected by acne,[3] acne afflicts people well into adulthood, too. Acne affects 50.9 percent of women and 42.5 percent of men between the ages of 20 and 29; 35.2 percent of women and 20.1 percent of men between the ages of 30 and 39; 26.3 percent of women and 12 percent of men between the ages of 40 and 49; and 15.3 percent of women and 7.3 percent of men ages 50 and older.[4]

Rosacea affects approximately 5.46 percent of the adult population worldwide. Older populations (ages 60 to 70) report the highest prevalence at 5.7 percent. Ages 50 to 59 report a 3.5 percent prevalence; ages 40 to 49 report a two percent prevalence; and ages 16 to 39 report less than one percent prevalence.[5] While less common than acne, rosacea is no less distressing to the people who have it.

Definitions

Acne vulgaris is a chronic inflammatory skin condition affecting the pilosebaceous unit (the hair follicle and its associated sebaceous gland), typically following a prolonged course. It is commonly triggered during adolescence by Cutibacterium acnes, a bacterial species, under the influence of normal circulating levels of dehydroepiandrosterone. The condition commonly manifests with papules, pustules or nodules (also known as pimples or zits) primarily on the face but can also affect the upper arms, trunk and back. The pathogenesis of acne vulgaris involves the interaction of multiple factors that ultimately lead to the formation of its primary lesion, which is known as a "comedo."[6]

Rosacea is a chronic inflammatory disease that presents with recurrent flushing, erythema (skin redness), telangiectasia (small, widened blood vessels near the surface of the skin), and papules or pustules on the nose, chin, cheeks and forehead. There are four clinical subtypes of rosacea based on the predominant signs and symptoms: erythematotelangiectatic, papulopustular, phymatous and ocular; subtypes are not mutually exclusive. Rosacea is more common in people with fair skin. The exact cause of rosacea is unknown, but factors such as genetic predisposition, abnormal immune response and environmental triggers such as sun exposure, spicy foods, stress and alcohol can exacerbate symptoms.[7]

Case Studies

Managing these bothersome skin conditions involves a multifaceted approach that addresses both medical and psychological aspects. The following cases illustrate how these conditions can influence self-esteem, social interactions and overall mental well-being.

- After dealing with acne in high school, Natalie Elliott entered her early 20s acne-free, but then she developed cystic acne (the type of acne that causes pus-filled pimples that lodge deep in the skin). With cystic acne, scarring often occurs after the skin is

cleared. The cysts started on her cheeks and progressed to her jawline, neck and even her back. She recalled going to a party and feeling hopeless — always thinking about her acne. As it got worse, she started canceling her plans and staying home. When her breakouts were especially bad, she felt like her personality changed. She became more self-conscious and timid. After moving and seeking treatment from a board-certified dermatologist, she found relief in time to pose for her wedding pictures without worrying about breaking out.[8]

• Lex Gillies, a 30-something-year-old blogger, has rosacea. Flare-ups cause her face to turn red, and it affects her mental health. "I feel like my face is a beacon, glowing bright red and attracting stares and judgments from others. I feel self-conscious and like my body is not my own. It's often a very upsetting and disorientating experience," she said. During flare ups, people asked her if she was sunburned, drunk, blushing or dealing with an allergic reaction. Some were even rude, asking, "What's wrong with your face?" Such questions caused others to turn and stare at her face, making her feel exposed and vulnerable. Over time, she learned her triggers and how to manage them. Now she tries to educate people to raise awareness and, hopefully, discourage others from making unprompted comments.[9]

Treatment Options

While complete eradication of these conditions may not be possible, symptoms can be managed and quality of life can improve. For acne, timely and appropriate treatment can significantly reduce the severity, prevent scarring and improve overall well-being. Rosacea is not curable, but symptoms can be managed with lifestyle changes, topical treatments and medical therapies, improving both physical appearance and boosting confidence.

Patients may find a combination of medical and psychological treatment options best address their unique situation.

For acne. Medical treatments include:

• Topical treatments

- Benzoyl peroxide is known for reducing bacteria and inflammation.

- Retinoids, such as tretinoin and adapalene, promote cell turnover to prevent clogged pores.

- Antibiotics, such as clindamycin and erythromycin, target acne-causing bacteria.

- Azelaic acid reduces inflammation and helps with post-inflammatory hyperpigmentation.

- Cabtreo is the first fixed-dose, triple-combination topical treatment for acne, combining antibiotic, retinoid and benzoyl peroxide medicines to address multiple acne-causing factors.

• Oral treatments

- Antibiotics such as doxycycline and minocycline are effective for moderate to severe acne.

- Tazarotene lotion (0.045 percent) uses polymeric emulsion technology to provide an effective, well-tolerated topical retinoid for the treatment of acne.

- Hormonal therapies, such as oral contraceptives and spironolactone, are helpful for hormonally driven acne.

- Isotretinoin is a powerful option for severe or resistant acne, but it requires monitoring due to potential side effects.

For rosacea. Medical treatment options include:

• Topical treatments

- Brimonidine gel reduces redness by constricting blood vessels.

- Metronidazole cream/gel acts as an antimicrobial and anti-inflammatory.

- Azelaic acid reduces inflammation and redness.

- Ivermectin cream targets Demodex mites and inflammation.

• Oral treatments

- Doxycycline can be used in low doses for anti-inflammatory properties.

- Isotretinoin can be used for severe rosacea in cases that are unresponsive to other treatments.

- Emrosi is a 40 mg extended-release minocycline capsule for the treatment of inflammatory lesions.

Both conditions. Patients with acne and/or rosacea may benefit from certain medical procedures including:

- Chemical peels, which can improve mild acne and reduce scars.

- Laser and light therapy, which target acne-causing bacteria and reduce oil production. Accure Laser System (which targets sebaceous glands to reduce acne lesions) was approved in 2024 by the U.S. Food and Drug Administration for the long-term treatment of mild to severe inflammatory acne vulgaris. Laser therapy such as pulsed dye laser and intense pulsed light are effective for persistent redness and visible blood vessels in rosacea patients.

- Intradermal botulinum toxin is an emerging treatment for refractory flushing for rosacea that needs further study.

Patients may also benefit from psychological treatment options:

Managing these bothersome skin conditions involves a multifaceted approach that addresses both medical and psychological aspects.

- Cognitive-behavioral therapy (CBT) is a tool for managing the psychological impacts of both acne and rosacea by helping patients recognize problematic dysfunctions in thinking and develop strategies to change thinking and behavior patterns. One study suggests CBT helps patients reframe negative perceptions of their appearance and develop coping strategies, which reduces social anxiety and depressive symptoms.[10] Another study found that patients with various dermatological conditions, including acne, who underwent CBT in addition to standard skin care demonstrated improvements in both quality of life and the severity of their skin condition.[11]

- Support groups may help patients feel less alone. Adolescents and young adults with acne can find reassurance and coping strategies in peer-led support groups, which reduce feelings of isolation. Adult patients with rosacea can benefit from connecting with others who understand the specific challenges of managing triggers and flare-ups.

- Patient advocacy organizations, such as the American Academy of Dermatology and the National Rosacea Society, offer resources for emotional and physical management.

Looking to the Future

In addition to treatments that already exist for both conditions, many others are currently in development and at various stages of clinical trials.

Acne. Nitric oxide-based treatments are being explored for their antibacterial, anti-inflammatory and sebum-reducing properties. SB204, a leading candidate, is a topical nitric oxide-releasing gel that has shown promising results in Phase III clinical trials. Microbiome therapy, such as topical probiotics or engineered bacteria, aims to restore balance to skin's microbial ecosystem.[12] B244 is undergoing Phase II trials and has demonstrated clinical efficacy. And in preclinical stages, mTOR inhibitors are showing they could restore NLA skin toward a healthier state.[13]

While complete eradication of these conditions may not be possible, symptoms can be managed and quality of life can improve.

Rosacea. JAK inhibitors such as upadacitinib and abrocitinib have been explored in case reports for the treatment of rosacea. The reports show some promising results, but the long-term safety and efficacy of both upadacitinib and abrocitinib require prospective controlled studies to assess them more comprehensively.[14] Microbiome-based rosacea topical treatments that target Demodex mites or rebalance the skin's microbiome such as OM-85 are in development to address both inflammatory and vascular symptoms. Topical VEGF (vascular endothelial growth factor) inhibitors are being investigated to reduce persistent erythema.

A Holistic Approach Offers Hope

Whether dealing with acne or rosacea, dermatological patients need to know they are not alone in their journey. With the right combination of treatments and support, it is possible to achieve significant improvements in both the physical and emotional aspects of living with these skin conditions. Continued advancements in dermatological research and treatment options provide hope for even better outcomes in the future. By working closely with healthcare providers and utilizing available resources, patients can reclaim their confidence and feel more at ease in social situations.

Integrating medical treatments with psychological support, such as CBT or support groups, can address the emotional toll that acne and rosacea often bring. Empowering patients with education about their condition and fostering open communication with dermatologists ensures they can make informed decisions tailored to their unique needs. This combined, holistic effort not only offers the hope for improved treatment outcomes but also helps give patients agency in their journey. ❖

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Myths & Facts: Prostate Cancer

Debunking the myths surrounding this second-deadliest cancer among men will help to convince them of the importance of getting screened since an early diagnosis has a 98 percent survival rate.

By Ronale Tucker Rhodes, MS

ONCE CONSIDERED rare, prostate cancer (PC) is now the most common cancer in men. Approximately 12.9 percent of men will be diagnosed with PC at some point during their lifetime, based on 2018 through 2021 data, excluding 2020 due to the COVID pandemic. In 2022, there were an estimated 3,518,978 men living with PC in the United States. Based on age-adjusted 2018 through 2022 cases and 2019 through 2023 deaths, the rate of new cases of PC was 120.2 per 100,000 men per year, and the death rate was 19.2 per 100,000 men per year (Figure). Between 2015 and 2021, the five-year survival rate was 97.9 percent. And, estimates for PC in the United States for 2025 are about 313,780 new cases and about 35,770 deaths.[1]

The history of PC spans nearly 200 years. George Langstaff reported the first surgical case of PC in 1817. And, John Adams subsequently described the first histologically confirmed case of PC in the London Hospital in 1853, noting the condition as "a disease of very rare occurrence."[2] Later advancements in PC occurred in the 20th and 21st centuries, mostly in terms of treatments such as hormonal therapies, surgical techniques, radiation and chemotherapy.[3] Today, researchers continue to refine treatment approaches and improve outcomes for men diagnosed with PC.

However, while overall, the treatment of PC has taken huge leaps forward, there are still many myths surrounding the disease. And, since PC is lethal without treatment, it's crucial that these myths be cleared up.

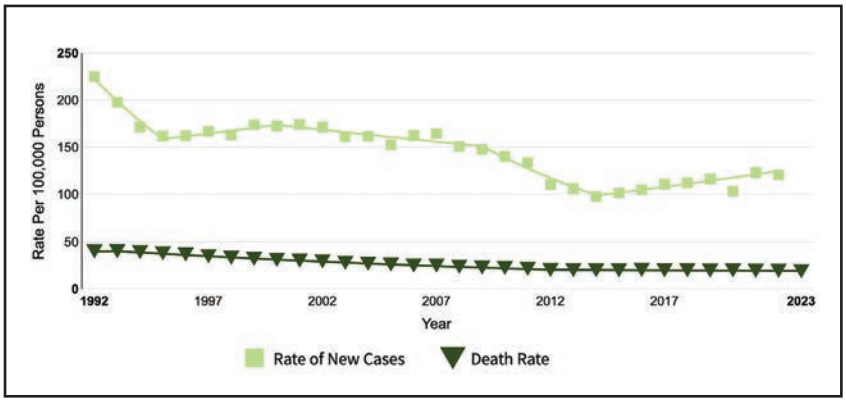
Separating Myth from Fact

Myth: All PCs are the same.

Fact: Actually, research shows there are at least 29 types of PC, which can be indolent, harmless or aggressive. And, there are four different stages of the disease, five different grade risk groups and more than 10 different combinations of Gleason score (a grading system for PC based on how abnormal the cancer cells appear under a microscope) ranging from 6 (low-grade cancer) to 10 (high-grade cancer).[4,5]

According to the American Cancer Society, a staging system is a standard way for the cancer care team to describe how far a cancer has spread. The American Joint Committee on Cancer's TNM system is the most widely used staging system for PC, the most recent update of which occurred in 2018. The TNM system for PC is based on five key pieces of information:[6]

Figure. Rates of New Cases of and Deaths from Prostate Cancer: 1992-2023[1]



• The extent of the main (primary) tumor (T category)

• Whether the cancer has spread to nearby lymph nodes (N category)

• Whether the cancer has spread (metastasized) to other parts of the body (M category)

• The PSA level at the time of diagnosis

• The grade group (based on the Gleason score), which is a measure of how likely the cancer is to grow and spread quickly determined by the results of the prostate biopsy (or surgery).

The main stages of PC range from I through IV. Some stages are split further (IIA, IIB, IIC, etc.). As a rule, the lower the number, the less the cancer has spread, and the higher the number, such as stage IV, means cancer has spread more. Within a stage, an earlier letter means a lower stage (Table).[6]

Myth: Only elderly men get PC.

Fact: The majority of men diagnosed with PC *are* older, but it does occur in younger men, with approximately 50 percent of all cases occurring in men younger than 65. "It's not uncommon at all for men in their 50s and some in their 40s to have prostate cancer," says Oliver Sartor, MD, a professor of medicine and urology at the Tulane University School of Medicine in New Orleans. It's rare in men younger than 40, however.[7]

According to the MD Anderson Cancer Center guidelines, men at average risk of cancer should start talking with their doctor about the benefits and limitations of prostate screening beginning at age 50. It is recommended that men with a family history of PC start PSA screening earlier, at age 40 or 45.[7] For African Americans or those who have a family history (father, brother, son) of PC, screening should include a digital rectal exam and PSA test every year starting at age 45. At age 50 to 75, it is recommended that all men get a digital rectal exam and PSA test every year to check for PC. At 75 to 85 years, a doctor can help men decide if they should continue screening. MD Anderson does not recommend cancer screening for men age 85 and older.

Myth: Men usually get PC if there is a family history of it.[8]

Fact: Men who have a brother or father with PC are two times as likely to develop the disease.[9] Two family members with prostate cancer hikes the risk fivefold.[7] However, most PCs occur in men *without* a family history of it. Other important risk factors include age, race, physical health and lifestyle.[9]

Myth: There is no relationship between PC and other cancers.

Fact: Research shows that hereditary (or familial) PC is not only associated with prostate cancer in first-degree relatives but also breast cancer, ovarian cancer and pancreatic cancer. According to Edward M. Schaeffer, MD, PhD, urologic oncologist and chair of the Department of Urology at Northwestern Medicine, "Individuals with a strong history of breast cancer, ovarian cancer and occasionally pancreatic cancer can have genes that increase their risk for developing prostate cancer."[9]

Myth: A man doesn't have PC if he shows no symptoms.

Fact: Actually, PC doesn't always present with noticeable symptoms, and in its early stages, PC often has no symptoms at all.[4]

Most PCs are found at an early stage, and early-stage PC often doesn't cause symptoms. However, if there are symptoms at the early stage, they can include blood in the urine, which might make the urine look pink, red or cola-colored; blood in the semen; needing to urinate more often; trouble getting started when trying to urinate; and waking up to urinate more often at night.

If the PC spreads to other parts of the body, which is called metastatic PC, stage IV prostate cancer or advanced prostate cancer, signs and symptoms can include accidental leaking of urine, back pain, bone pain, difficulty getting an erection (erectile dysfunction), feeling very tired, losing weight without trying and weakness in the arms or legs.[10]

Myth: Screening tests for PC aren't beneficial.

Fact: Since symptoms do not often occur with early-stage PC, it is important for men to discuss their risk factors and whether they should be screened with their healthcare provider. And, while medical organizations have different recommendations regarding screening for PC, all agree the most important aspect of screening is to have a conversation with a healthcare provider about the benefits and risks of screening tests. The most common screening tests include:[11]

• *Prostate-specific antigen (PSA) blood test.* PSA is a substance that can be found in blood. Elevated PSA levels are often found in men with PC; however, noncancerous conditions such as prostatitis (inflammation of the prostate) and benign prostatic hyperplasia (enlarged prostate) can also cause PSA levels to increase.

• *Digital rectal exam.* With this test, the doctor feels for hard areas or lumps in the prostate by inserting a gloved, lubricated finger into the rectum.

If the results from either of these tests come back abnormal, further testing is often required.[11]

One myth about PC is that PSA screening reduces prostate cancer mortality only by about one in 1,000. But, according to Andrew Vickers, PhD, of Memorial Sloan Kettering Cancer Center, PSA screenings have reduced deaths significantly more than that. "This number is frequently cited, and it makes it look like the benefits are small, but

Table. Stages of Prostate Cancer [6]

AJCC Stage	Stage Grouping	Stage Description
I	cT1, N0, M0 Grade Group 1 (Gleason score 6 or less) PSA less than 10	The doctor can't feel the tumor or see it with an imaging test such as transrectal ultrasound. (It was either found during a transurethral resection of the prostate (TURP) or was diagnosed by needle biopsy done for a high PSA [cT1].) The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1, and the PSA level is less than 10.
	OR	
	cT2a, N0, M0 Grade Group 1 (Gleason score 6 or less) PSA less than 10	The tumor can be felt by digital rectal exam or seen with imaging, such as transrectal ultrasound, and is in one half or less of only one side (left or right) of the prostate [cT2a]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1, and the PSA level is less than 10.
	OR	
	pT2, N0, M0 Grade Group 1 (Gleason score 6 or less) PSA less than 10	The prostate has been removed with surgery, and the tumor was still only in the prostate [pT2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1, and the PSA level is less than 10.
IIA	cT1, N0, M0 Grade Group 1 (Gleason score 6 or less) PSA at least 10 but less than 20	The doctor can't feel the tumor or see it with imaging such as transrectal ultrasound. (It was either found during a transurethral resection of the prostate (TURP) or was diagnosed by needle biopsy done for a high PSA level [cT1].) The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1. The PSA level is at least 10 but less than 20.
	OR	
	cT2a or pT2, N0, M0 Grade Group 1 (Gleason score 6 or less) PSA at least 10 but less than 20	The tumor can be felt by digital rectal exam or seen with imaging such as transrectal ultrasound and is in one half or less of only one side (left or right) of the prostate [cT2a]. OR the prostate has been removed with surgery, and the tumor was still only in the prostate [pT2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1. The PSA level is at least 10 but less than 20.
	OR	
	cT2b or cT2c, N0, M0 Grade Group 1 (Gleason score 6 or less) PSA less than 20	The tumor can be felt by digital rectal exam or seen with imaging such as transrectal ultrasound. It is in more than half of one side of the prostate [cT2b] or it is in both sides of the prostate [cT2c]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1. The PSA level is less than 20.
IIB	T1 or T2, N0, M0 Grade Group 2 (Gleason score 3+4=7) PSA less than 20	The cancer has not yet spread outside the prostate. It might (or might not) be felt by digital rectal exam or seen with imaging such as transrectal ultrasound [T1 or T2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 2. The PSA level is less than 20.
IIC	T1 or T2, N0, M0 Grade Group 3 or 4 (Gleason score 4+3=7 or 8) PSA less than 20	The cancer has not yet spread outside the prostate. It might (or might not) be felt by digital rectal exam or seen with imaging such as transrectal ultrasound [T1 or T2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 3 or 4. The PSA level is less than 20.
IIIA	T1 or T2, N0, M0 Grade Group 1 to 4 (Gleason score 8 or less) PSA at least 20	The cancer has not yet spread outside the prostate. It might (or might not) be felt by digital rectal exam or seen with imaging such as transrectal ultrasound [T1 or T2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1 to 4. The PSA level is at least 20.
IIIB	T3 or T4, N0, M0 Grade Group 1 to 4 (Gleason score 8 or less) Any PSA	The cancer has grown outside the prostate and might have spread to the seminal vesicles [T3], or it has spread into other tissues next to the prostate, such as the urethral sphincter (muscle that helps control urination), rectum, bladder and/or the wall of the pelvis [T4]. It has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 1 to 4, and the PSA can be any value.
IIIC	Any T, N0, M0 Grade Group 5 (Gleason score 9 or 10) Any PSA	The cancer might or might not be growing outside the prostate and into nearby tissues [any T]. It has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Grade Group is 5. The PSA can be any value.
IVA	Any T, N1, M0 Any Grade Group Any PSA	The tumor might or might not be growing into tissues near the prostate [any T]. The cancer has spread to nearby lymph nodes [N1] but has not spread elsewhere in the body [M0]. The Grade Group can be any value, and the PSA can be any value.
IVB	Any T, any N, M1 Any Grade Group Any PSA	The cancer might or might not be growing into tissues near the prostate [any T] and might or might not have spread to nearby lymph nodes [any N]. It has spread to other parts of the body, such as distant lymph nodes, bones or other organs [M1]. The Grade Group can be any value, and the PSA can be any value.

it is based on a misunderstanding of a well-known trial," Dr. Vickers explains. "Experts disagree about the best estimate, but one study published in *The New England Journal of Medicine* gave a number closer to 10 in 1,000."[12]

In another study that sought to determine whether PSA screening decreases PC mortality for up to 16 years and to assess results following adjustment for nonparticipation and the number of screening rounds attended, researchers found that PSA screening significantly reduces PC mortality, showing larger absolute benefit with longer follow-up and a reduction in excess incidence.

The multicenter population-based randomized screening trial was conducted in eight European countries and included 182,160 men, followed up until 2014 (maximum of 16 years), with a predefined core age group of 162,389 men (55 to 69 years), selected from a population registry. The rate ratio of PC mortality was 0.80 (95 percent confidence interval [CI] 0.72-0.89, p<0.001) at 16 years. The difference in absolute PC mortality increased from 0.14 percent at 13 years to 0.18 percent at 16 years. The number of men needed to be invited for screening to prevent one PC death was 570 at 16 years compared with 742 at 13 years. The number needed to diagnose was reduced to 18 from 26 at 13 years. Men with PC detected during the first round had a higher prevalence of PSA >20ng/ml (9.9 percent compared with 4.1 percent in the second round, p<0.001) and higher PC mortality (hazard ratio=1.86, p<0.001) than those detected subsequently. The researchers concluded that repeated screening may be important to reduce PC mortality on a population level.[13]

"Almost all men will get prostate cancer if they live long enough," explains Dr. Vickers. "So we aren't at all interested in prostate cancer as an endpoint. What we want to know is whether PSA can predict who gets the sort of prostate cancer that can cause symptoms and threaten a patient's life. It turns out that PSA is very good at doing that."[12]

Myth: If a man has a high PSA score it means he has PC.

Fact: While the most common cause of elevated PSA is PC, PSA levels increase with age and can reflect different conditions that affect the prostate.[14] Because the PSA test is very sensitive, if a man's PSA is low, he can be reassured that he is at low risk of having an aggressive PC. However, because the test is not specific, a higher PSA level doesn't necessarily mean a man will get PC since there can be many other reasons it is elevated.[12]

Other conditions or factors that may raise a PSA level include:[14]

- Enlarged prostate (benign prostatic hyperplasia)
- Prostate inflammation (prostatitis)
- Urinary tract infections
- Urinary catheter
- Certain medications, including betamethasone and testosterone replacement therapy

Generally speaking, PSA levels for men who are age 60 or older should be at or below 4.0 mg/mL, and men who are age 59 or younger should be at or below 2.5 mg/mL. The average PSA for men in the younger group is <1.0 mg/mL.[15] The likelihood of PC increases along with blood PSA levels. If a man has a relatively high PSA level (approximately 4.0 mg/mL or above), most physicians recommend repeat testing supplemented by other noninvasive tests, such as an MRI scan,[16] to determine whether a biopsy is needed, and if so, what kind.

A prostate biopsy is the removal of tiny samples of prostate tissue to examine it for signs of PC. There are three ways to perform a prostate biopsy:[17]

- *Transrectal — through the rectum.* This is the most common method that inserts a lubricated ultrasound probe into the rectum to guide the biopsy needle inserted into the prostate to take a sample.
- *Transperineal — through the perineum (the skin between the anus and the scrotum).* This is being used more frequently and involves inserting an ultrasound probe into the rectum to image the prostate while a needle is inserted into the perineum to collect prostate tissue.
- *Transurethral — through the urethra.* This is not used very often. It involves inserting a flexible tube with a camera on the end (cystoscope) through the opening of the urethra at the tip of the penis.

Myth: A prostate biopsy can cause PC to spread.

Fact: While a prostate biopsy *can* theoretically cause cancer to spread, it is extremely rare. When it does happen, it's called "tumor seeding," a process that occurs when the needle inserted into a tumor during the biopsy dislodges and spreads cancer cells. Tumor seeding may also be referred to as "needle tract seeding" because the cancer cells grow along the needle's track.

Several studies have been performed that confirm how rare tumor seeding is. A study of more than 2,000 patients by researchers at Mayo Clinic's campus in Jacksonville, Fla., dispelled the myth that cancer biopsies cause cancer to spread. The study showed that patients who received a biopsy had a better outcome and longer survival than patients who did not have a biopsy. According to the study's senior investigator and gastroenterologist Michael Wallace, MD, MPH, professor of medicine, while the researchers studied pancreatic cancer, the findings likely apply to other cancers because diagnostic technique used in this

study — fine needle aspiration — is commonly used across tumor types.

"This study shows that physicians and patients should feel reassured that a biopsy is very safe," Dr. Wallace says. "We do millions of biopsies of cancer a year in the U.S., but one or two case studies have led to this common myth that biopsies spread cancer." Rather, he says, biopsies offer "very valuable information that allow us to tailor treatment. In some cases, we can offer chemotherapy and radiation before surgery for a better outcome, and in other cases, we can avoid surgery and other therapy altogether."[18]

PC doesn't always present with noticeable symptoms, and in its early stages, PC often has no symptoms at all.

Myth: Treatment for PC must be started right away after a diagnosis.

Fact: This is not always the case. Some men with early-stage, slow-growing prostate cancer may not need treatment right away. In fact, the stage of cancer is one of the most important factors in choosing the best way to treat it. For prostate cancers that haven't spread (stages I to III), doctors also use risk groups (based on how far the prostate tumor has grown, PSA level, grade and prostate biopsy results) and sometimes special lab tests to help guide treatment options. If it is determined the cancer is in the very-low-risk stage, it is very unlikely to grow and spread, even if it isn't treated. Instead, active surveillance is typically recommended. For men who have medical problems that might shorten their lifespan, surveillance might be an option as well because the tumors are unlikely to cause any harm, whereas treatments such as radiation and surgery can have side effects that can affect quality of life. Even men in the low-risk stage may be offered active surveillance, since very few of low-risk-stage cancers will spread to distant parts of the body. If the cancer starts to show signs of growing at some point, treatment can then be considered.[19]

Some common treatments for PC are:[20]

- Prostatectomy: an operation in which doctors remove the prostate. Radical prostatectomy removes the prostate, as well as the seminal vesicles (glands that produce the fluids that will turn into semen)
- Radiation therapy (photon and proton): a procedure that uses high-energy rays (similar to X-rays) to kill the cancer. There are two types of radiation therapy:

1) External radiation therapy in which a machine outside the body directs radiation at the cancer cells

Traditional photon radiation therapy uses photons in the form of X-ray beams that release radiation along the entire length of the beam, which means they continue to penetrate into the body after passing through the tumor. This "exit dose" can potentially damage healthy tissues and organs near the prostate, including the bowel, bladder, penile bulb, testicles, rectum, urethra and bones in the pelvis and the hip joint, which can increase the risk of long-term complications and of developing new cancers in the future.

In contrast to photon radiation, proton therapy is a newer therapy that more precisely targets the tumor, limiting exposure to other organs and tissues and lowering the risk of future cancers in radiated areas. Proton therapy uses proton particles that can be set to travel a certain distance into the tumor and stop. This allows radiation oncologists to deliver the right dose of radiation to different parts of the tumor to effectively kill PC. Proton therapy can be used in most stages of PC, including early-stage, mid-stage, late-stage (locally advanced), PC that has spread to adjacent organs or tissues, PC that has spread to the lymph nodes (lymph-node positive PC) and PC that has returned after surgical removal and is detected through the PSA test, indicating biochemical recurrence.[21]

2) Internal radiation therapy (brachy-therapy) in which radioactive seeds or pellets are surgically placed into or near the cancer to destroy the cancer cells

Depending on whether the PC has spread, there are other treatment options:[20]

- Cryotherapy: placing a special probe inside or near the PC to freeze and kill the cancer cells (this is a less common treatment)
- Chemotherapy: using special drugs to shrink or kill the cancer after it has spread to other parts of the body (the drugs can be pills or medicines given through the veins or, sometimes, both)
- Biological therapy: works with the body's immune system to help it fight cancer or to control side effects from other cancer treatments
- High-intensity focused ultrasound: directs high-energy sound waves (ultrasound) at the cancer to kill cancer cells (this is a less common treatment)
- Hormone therapy: blocks cancer cells from getting the hormones they need to grow (also called androgen deprivation therapy)
- Targeted therapy: uses drugs that attack cancer cells while minimizing

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damage to healthy cells (used to treat PC that has spread to other parts of the body and is no longer responding to hormone therapy)

Myth: PC treatment always causes impotence or incontinence.

Fact: Most men, but not all, experience erectile dysfunction immediately after surgery or radiation. But nearly all men with intact nerves report a significant improvement after one year. The risk of these side effects depends on the type of prostate cancer treatment, overall health, the extent of the cancer and the skill of the surgeon. And, if there are side effects, urologists and therapists can help men manage them, and most will see an improvement within one year. According to Dr. Sartor, one year after surgery, approximately 25 percent of patients will say their sexual function is fine, 25 percent will have mild dysfunction, 25 percent will have moderate dysfunction and 25 percent will say they have severe dysfunction.[7,9]

If incontinence (bladder problems) occurs, it's more likely minor leakage than major accidents, and in most men, the situation is temporary or treatable. "The majority of people do not have significant urinary problems," Dr. Sartor says. For the best outcome after surgery, Dr. Sartor recommends looking for a surgeon who has performed the procedure many times — surgeons who are on their 900th procedure, for example, not their 41st.[7]

Studies have suggested that proton therapy may cause fewer side effects, such as impotence and incontinence, than traditional radiation, since doctors can better control where the proton beams deliver their energy. Studies have also shown that proton therapy does not significantly affect testosterone levels, while photon radiation treatments *can* lower testosterone. However, proton therapy is much more expensive than photon radiation therapy and is available only in specialized proton therapy centers.[21]

Myth: If PC reoccurs, it can't be treated again.

Fact: Biochemical recurrence, or biochemical relapse, can range from 40 percent to 70 percent in patients whose PC is found in the seminal vesicles or other tissues on the edges of the surgical site. But, just because PC comes back, it doesn't mean it can't be treated again and that remission can't be reached again.

New research from the University of Florida (UF) Health Proton Therapy Institute suggests proton therapy can be highly effective in treating recurrent PC following prostatectomy. In the study of 102 men who were enrolled on an outcome tracking protocol between 2006 and 2017 at the UF Health Proton Therapy Institute and treated with proton therapy after prostatectomy, the five-year biochemical relapse-free and distant metastases-free survival rates were, respectively, 57 percent and 97 percent overall, and compared favorably with other conventional radiation therapies.[22]

Myth: PC is always fatal.

Fact: While PC is a serious disease, most men who are diagnosed with this disease do not die from it. In fact, the five-year survival rate is about 98 percent, which is why catching prostate cancer early is important because doing so significantly improves survival rates.[11]

Dispelling the Myths Now

PC is a major health challenge in the U.S., and the second leading cause of cancer deaths among men.[23] Unfortunately, men's fear of PC often caused by the myths surrounding it leads many to avoid screenings, experience anxiety and depression at diagnosis, and leads to fear and avoidance of treatment because of side effects. But PC is slow-growing, and most cases are caught early. And, with the advances in treatment, most men live full lives without major side effects. ❖

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Update on Premenstrual Dysphoric Disorder (PMDD)

This severe form of PMS is characterized by significant mood and physical symptoms, and is now recognized and listed as a mental disorder that can be treated and even cured.

By Jim Trageser

THE MONTHLY CYCLES associated with women's reproductive systems have been a source of scientific curiosity for millennia. As far back as 3,800 years ago, the Kahun Gynaecological Papyrus described the experiences associated with menstruation — including back pain, migraines and heavy bleeding.[1] And about 2,000 years after that, Hippocrates further described these symptoms.

In 1931, Robert T. Frank, MD, proposed that when these monthly symptoms are so severe as to intrude into a patient's day-to-day life, it should be recognized as a condition he termed premenstrual tension. In 1953, the current term of premenstrual syndrome (PMS) was adopted.

While 90 percent of women will have at least some discomfort associated with their menstrual cycle — typically cramping, headaches and/or bloating[2] — about three-quarters of all women will endure PMS at some point in their life, according to the Mayo Clinic.[3]

And while PMS is itself disruptive enough that there are numerous treatments available, for a smaller subset of women, their mental health symptoms surrounding their menstrual cycle are so severe that they make meeting the demands of daily life extremely challenging. This condition is known as premenstrual dysphoric disorder (PMDD). While first included in the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* in 1994,[4] the condition remains poorly understood, is likely underdiagnosed and is almost certainly poorly treated in too many cases.[5]

What Is PMDD?

PMDD, alongside PMS, is grouped as a premenstrual disorder. It is considered a more severe form of PMS and affects between three and eight percent of women.[6]

In the current fifth edition of *Diagnostic and Statistical Manual of Mental Disorders (DSM-V)*, published in 2013, PMDD is categorized as a depressive disorder. The World Health Association's International Statistical Classification of Diseases (11th edition) lists PMDD with other genitourinary diseases, although it is also cross-listed with depressive conditions.

While premenstrual disorders have been known to medical science for many centuries, even with advances in scientific rigor in the field during the 20th century,

they were not afforded the same attention as other conditions. Diagnostic standards were haphazard and treatment uneven. Too often, patients were told it was "all in their head" or it was dismissed as female emotionalism.[1] In response, in 2008, the International Society for Premenstrual Disorders was founded to bring consistency to the treatment of these conditions, including PMDD.[5]

One of the recurring debates regarding premenstrual disorders revolves around whether it makes sense to view these symptoms as a disorder, when many researchers and clinicians believe it is simply a natural variation in how women experience their menstrual cycles.[5] This view holds that the pharmaceutical companies have a vested (and outsized) interest in expanding the definitions of "disorder" to increase diagnoses and, thus, prescribing of their products. (This roughly mirrors similar debates regarding both autism spectrum and attention deficit/hyperactivity disorder in which a significant number of clinicians feel normal, healthy individuals are being unnecessarily classified as having a disorder.)

Countering this view is the fact that women with PMDD are statistically more prone to suicide, making prompt diagnosis and treatment all the more important.[7]

What Causes PMDD?

As with PMS, the specific causes of the symptoms of PMDD are not yet well understood. Researchers have noted that many patients with PMDD have lower than normal levels of serotonin, which may be tied to how an individual's body reacts to the natural hormonal changes associated with the menstrual cycle.[8] This ties in with studies that have found women with PMS and PMDD have normal hormone levels — it is their body's reaction to the hormones that causes the symptoms, not maladjusted hormone levels.[9]

In 2007, researchers at the National Institute of Mental Health performed genetic testing and analyses on women with PMDD and healthy control subjects and found variants in the estrogen receptor alpha gene are associated with PMDD. They discovered that this association is seen only in women with a variant form of another gene, catechol–o–methyltransferase, which is involved in regulating the function of the prefrontal cortex.[10] (See the Physician Profile on p.47 for more information about research findings surrounding genetics and PMDD.)

Diagnosing PMDD

If a patient presents with symptoms consistent with PMDD, referral to a mental health clinician may be warranted. The clinician will likely have the patient fill out the Premenstrual Symptoms Screening Tool, a 19-question form that allows the patient to quickly record how severe her symptoms are.[11] Other similar tools include the Calendar of Premenstrual Experiences,[12] the Daily Record of Severity of Problems[13] and the Patient Reported Outcomes Measurement Information System.[14]

Making a diagnosis of PMDD is a four-step process under DSM-V:

1) Patient experiences five of the following 11 criteria:

- Feelings of depression or hopelessness
- Feeling tense or anxious
- Significant mood swings
- Persistent anger or irritability
- Lowered interest in normal activities
- Difficulty concentrating
- Fatigue or lethargy
- Change in appetite
- Change in sleep patterns
- Feeling overwhelmed or out of control
- Physical symptoms consistent with PMS: sensitive breasts, bloating, weight gain, joint pain, etc.

2) The symptoms are severe enough to interfere with school, work or personal life.

3) The symptoms are directly tied to the menstrual cycle — i.e., beginning around ovulation, and easing after menstruation begins.

4) This pattern is consistent for at least two consecutive menstrual cycles (if there is an inconsistency, then include a third cycle).

In addition, other possible explanations for the symptoms, including major depressive disorder, should be ruled out before making a diagnosis of PMDD. And even if symptoms are shown to be tied to the menstrual cycle, a separate diagnosis of depression can co-exist with PMDD.[6]

Treating PMDD

Because PMDD is tied to normal, natural cycles, the only cure for PMDD is menopause. And as the specific triggers that cause some women to have PMDD remain unknown, there is also no prevention for the condition.

Treatment of PMDD is aimed at reducing the severity of symptoms. Because PMDD is a chronic condition, treatment will likely last until the patient reaches menopause. And because PMDD involves both physical and psychological elements, primary care physicians should work with psychiatrists or psychologists in a team approach.

Treatment typically consists of a combination of lifestyle changes, medications and counseling.

The most effective lifestyle changes involve diet and exercise. Eating better, and perhaps increasing intake of complex carbs between ovulation and

menstruation, is thought to play a role in increasing levels of serotonin.[5] While the mainstream press has numerous articles touting various vitamin and mineral supplements as effective at treating PMDD, the scientific literature indicates the evidence is actually not clear on their effectiveness.

Moderate aerobic exercise has been shown to help improve mood, and helps increase overall health as well.[15] However, these lifestyle changes take time to show results.

The typical first-line treatment for PMDD is anti-depressants. The class of anti-depressants used to treat PMDD are known as selective serotonin reuptake inhibitors (SSRIs), which can increase levels of serotonin in the brain. They include:

- Fluoxetine (Prozac, Sarafem)
- Paroxetine (Paxil, Pexeva, Aropax, Seroxat, Brisdelle)
- Sertraline (Zoloft)
- Escitalopram (Lexapro)
- Citalopram (Celexa)

The U.S. Food and Drug Administration (FDA) has approved the first three specifically to treat PMDD; the other two are widely used off-label. Other types of anti-depressants have not shown to be as effective as SSRIs.[16]

While some studies had indicated SSRIs could be effective if taken at the onset of symptoms, subsequent research indicates they are most effective for most patients when taken continuously, although dosages can be lower than for treating other conditions.[17] Side effects

PMS vs. PMDD: Understanding the Difference

PMDD is an extreme form of PMS with emotional and physical symptoms much more intense and that last longer. Some of the characteristics of PMS and PMDD are similar; however, there are distinct differences between the two.

PMS	PMDD
Triggered by hormonal changes, particularly the drop in estrogen and progesterone during the luteal phase of the menstrual cycle (7-14 days leading up to a woman's period). Hormonal shifts are normal, but how the brain and nervous system respond to those shifts is abnormal in PMS and PMDD.	Triggered by hormonal changes, particularly the drop in estrogen and progesterone during the luteal phase of the menstrual cycle (7-14 days leading up to a woman's period). Hormonal shifts are normal, but how the brain and nervous system respond to those shifts is abnormal in PMS and PMDD.
Symptoms are cyclical, meaning they tend to show up around the same time each month and dissipate completely at other times of the month.	Symptoms are cyclical, meaning they tend to show up around the same time each month and dissipate completely at other times of the month.
Affects up to 75 percent of women	Affects 3 to 8 percent of women
Symptoms are typically milder, yet significant, but for most, are manageable. Women might feel tired, moody or bloated, but the symptoms don't usually disrupt day-to-day life in a major way.	Emotional symptoms are significantly more intense. Women often experience extreme mood swings, severe depression or anxiety, feelings of hopelessness or even thoughts of self-harm. These symptoms can be so overwhelming that they interfere with their ability to function, whether it's at work, in relationships or in their daily routine.
Physical symptoms include: • Cramping • Bloating • Acne • Anxiety • Breast tenderness • Sugar cravings • Mood swings • Depression • Sleep disturbance • Irritability • Symptoms typically disappear once a woman's period starts or shortly thereafter	Physical symptoms include: • Cramps • Bloating • Anxiety • Breast tenderness • Mood swings • Depression • Irritability • Headaches • Joint pain • Muscle pain • Hot flashes • Insomnia • Extreme fatigue • Appetite changes • Difficulty concentrating • Feelings of helplessness • Suicidal thoughts • Bouts of rage • Bouts of extreme sadness • Decreased interest in usual activities • Symptoms typically disappear once a woman's period starts or shortly thereafter

can be intense (nausea, insomnia, fatigue, loss of sexual desire), and only half of patients prescribed SSRIs continue with them for more than six months.[5]

Other types of drugs used to relieve symptoms of PMDD are those that suppress ovulation. Both hormonal therapies and birth control pills will prevent monthly ovulation by altering the hormonal cycles, and they can be effective in preventing onset of PMDD. However, there is growing evidence that newer synthetic hormonal treatments are not as effective as earlier formulae.[5]

Since PMDD is classified as a form of depression, lifestyle changes, anti-depressants and ovulation prevention will often be combined with ongoing therapy — particularly cognitive behavioral therapy (CBT). With this form of psychotherapy, a therapist leads the patient through a series of exercises to help her better control negative thoughts and worries.

While relatively few studies specifically look at CBT's success in relieving PMDD symptoms, its well-documented success in treating other forms of depression and anxiety suggests further study is warranted and that patients are likely to benefit from it.[18] And of the studies that have been conducted, results show an efficacy about equal to that of anti-depressants.[19]

Further, for those patients who find the side effects of the pharmacological treatments unbearable, CBT offers another option that can help them better deal with symptoms, including irritability, depression and anxiety. While CBT is known to provide relief for insomnia in other cases, its effectiveness for treating PMDD-related insomnia is less clear.[20]

Finally, for patients with severe PMDD that does not respond to any of the above treatments, and if future children are not desired, surgical intervention to remove the ovaries may be considered. Before proceeding, it is generally recommended that drugs that suppress ovarian function be tried first to ensure it helps with the PMDD. While removal of the ovaries will bring about immediate menopause, hormone replacement therapy is often required after surgery to alleviate potential side effects.[5]

Looking Ahead

As with the entirety of the animal kingdom — all of life, in fact — the human body was designed to reproduce the species. PMDD is likely an accidental byproduct of natural selection, and thus physicians will likely be treating it for the foreseeable future.

However, our understanding of PMDD has increased dramatically over the past few decades. It is now known to be a real condition some women experience — not something imagined. That alone is a huge step forward that is allowing researchers to focus on more effective treatments to better balance symptom relief against potentially unpleasant side effects.

FDA's clinicaltrials.gov database lists only a few dozen research projects into PMDD. But there are some novel approaches being explored. One study at the Tübingen University Hospital in Germany will compare inflammation and brain imaging in women with major depressive disorder and PMDD patients to see what differences (and commonalities) there are.[21] Another is investigating the effect of acceptance and commitment therapy on PMDD.[22] And a third, in Sweden, is exploring whether Internet-based online CBT can be effective at helping women gain effective control of emotional symptoms of PMDD.[23]

As these and other studies come to fruition, physicians and therapists should have more effective treatments to help their patients tackle the symptoms of PMDD in years to come. ❖

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PMDD: *A Patient's Perspective*

By Trudie Mitschang

FOR SIX long years, beginning in her late 20s, Sarah Gillespie lived under the shadow of a condition that few people had even heard of: premenstrual dysphoric disorder, or PMDD. Unlike premenstrual syndrome (PMS), which might cause mood swings or irritability, PMDD plunged Sarah into a state of physical and mental collapse every month. "Due to a genetic quirk," she explains, "I have a brain sensitivity that makes my body intolerant to its own hormonal changes."

This intolerance didn't just affect her mood — it overtook her personality. During the latter half of each menstrual cycle, Sarah would become virtually unrecognizable to herself: "I became catatonic and racked with pain. Dysphoria bloomed in my brain, making me depressed and paranoid. I binged on carbohydrates, needing 3,000 calories a day just to function."

Each episode lasted between seven and 14 days. Then, like clockwork, the fog would lift — but with clarity came devastation. "There were relationships to repair, overdue bills to pay and excess pounds to lose," she recalled. "It was the life of Sisyphus: Every month, I roll the boulder up the mountain, only for it to roll down again."

According to data from the World Health Organization (WHO), PMDD affects 5.5 percent of women of childbearing age. Alarmingly, more than a third of those diagnosed have attempted suicide. In 2022, WHO classified PMDD as a recognized gynecological disease, distinguished from PMS by the severity of its symptoms and their impact on functioning.[1] In addition, a recent study led by Thomas Reilly, BSc (Med Sci), MBChB, MRCPsych, at the University of Oxford's Department of Psychiatry estimates that approximately 31 million women and girls suffer from PMDD globally.[2]

The findings do little to ease Sarah's memories of her own frustrating journey through the healthcare maze. After years of suffering, Sarah finally received a diagnosis and began a series of progressive interventions. From supplements like chasteberry and magnesium to contraceptives, antidepressants and, eventually, hormone replacement therapy, nothing provided lasting relief. As her body aged and her hormones grew even more erratic, her condition actually worsened.

Having exhausted other treatment options, Sarah made the difficult decision to request a bilateral salpingo-oophorectomy — surgical removal of her ovaries and fallopian tubes. It was a drastic choice, but one with a 96 percent satisfaction rate among those with severe PMDD.[3] "I was advised that following surgery, all hormone fluctuations would stop," she said. "I would enter menopause and need hormone replacement therapy until my 50s. It would also make me infertile."

For Sarah, even this last-resort treatment wasn't easy to access. First, she endured a trial period of chemical menopause via monthly injections. Rather than providing relief, the injections triggered a continuous 11-month PMDD episode. "I languished in bed and gulped down painkillers and sleeping pills like candy," she explained. Her physical and mental health also crumbled, and her trust in the medical system was deeply shaken. One physician dismissed her condition entirely, saying, "If it hasn't worked, that suggests it's not PMDD… I should probably refer you to a psychiatrist."

After months of begging, she was finally referred to a surgeon — but the assumption that the condition was all in her head lingered, and her procedure was denied. Undeterred, she says the Internet became her lifeline — not for support groups, but for science. She dug through medical journals to validate her desire for surgery, and her research led her to a European clinic that offered bilateral salpingo-oophorectomy. Sarah contacted the Nordclinic in Kaunas, Lithuania, forwarded them her medical records and was relieved when the staff surgeon agreed to operate. For Sarah, the postsurgical transformation was almost immediate: "I still can't believe how well I feel. My future unfurls before me without interruption. I have so much time now: time to write, to see friends and family, to travel, go on dates, paint and sing and read and run. Time to cook, as I can now handle knives without fear of self-harm."

Today, Sarah is no longer at war with her own body. And for the first time in years, she is looking forward without dread: "I don't need to keep starting again and again and again every month. Life without PMDD is so, so wonderful."

Still, Sarah remained deeply affected by the years she lost to PMDD. "I still need to reckon with all the time taken from me over the past six years," she says. "My trust in our healthcare system is broken and will probably never be restored." ❖

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PMDD: *A Physician's Perspective*

DAVID R. RUBINOW, MD, is a distinguished professor and chair of psychiatry at the University of North Carolina (UNC) School of Medicine, and founding director of the UNC Center for Women's Mood Disorders. With more than 25 years of research into the neurobehavioral effects of gonadal steroids, Dr. Rubinow has focused extensively on conditions like premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD).

BSTQ: Why is the timing of symptoms crucial to understanding and accurately diagnosing PMDD?

Dr. Rubinow: PMDD is a time-oriented not symptom-oriented diagnosis: Symptoms must consistently occur during the luteal phase of the menstrual cycle, after ovulation, and resolve during the follicular phase, after menstruation begins. This cyclical pattern is what defines PMDD more so than any specific symptoms. That said, typical symptoms include depression, sadness or hopelessness; mood swings; concentration problems; fatigue and lethargy; and feelings of being out of control. Breast swelling or tenderness, headaches, joint or muscle aches, weight gain and bloating may also occur.

BSTQ: How did you help define the criteria for PMDD?

Dr. Rubinow: In the mid-1980s, two key developments in PMDD occurred. First, a national conference aimed to standardize diagnostic procedures for PMS. Around the same time, I organized a National Institute of Mental Health (NIMH) workshop to establish formal criteria for PMS that could be used across studies. These efforts led to the development of what was initially termed late luteal phase dysphoric disorder, which included the same symptoms now recognized as PMDD.

BSTQ: You also led a study identifying genetic variants linked to PMDD. What did you discover?

Dr. Rubinow: We used gene-based haplotyping to study five genes, focusing in particular on estrogen receptors alpha and beta. We analyzed single nucleotide polymorphisms (SNPs) variations in the DNA sequence, selecting representative ones to cover large regions of each gene, which uncovered four SNPs in the fourth intron of the estrogen receptor alpha (ERα) gene that were significantly associated with PMDD. When combined into what's called a haplotype, the association became even stronger. Interestingly, this genetic link was evident only in women who also carried a specific variant of another gene: catechol-O-methyltransferase (COMT).

BSTQ: Why is the COMT gene so significant in this context?

Dr. Rubinow: COMT helps metabolize estrogen and breaks down dopamine in the prefrontal cortex. Estrogen influences prefrontal blood flow during cognitive tasks, and other research has confirmed the prefrontal cortex's importance in mood. The COMT variant we studied is known as Val/Val at position 158 (Valine/Valine). This form breaks down dopamine more rapidly, which may deplete dopamine in the prefrontal cortex. When combined with the identified ERα haplotype, this dopamine depletion could help explain why some women are more vulnerable to hormone-triggered mood disorders like PMDD. In short, we found a receptor for a hormone (estrogen) known to impact mood, and a gene variant (COMT) that alters how the brain processes that hormone and its downstream neurotransmitters.

BSTQ: Do these genetic insights change how PMDD should be diagnosed or treated?

Dr. Rubinow: These findings could eventually lead to new molecular targets for treatment and deepen our understanding of how mood is regulated — not just in hormone-related disorders but in mood disorders more broadly. Unlike most forms of depression, PMDD has a clear physiologic trigger: hormonal changes during the menstrual cycle. That gives us a unique opportunity to study mood regulation and potentially apply what we learn to broader psychiatric conditions.

BSTQ: What approach have you used in your clinical practice to treat PMDD?

Dr. Rubinow: Selective serotonin reuptake inhibitors are very effective for some of these disorders. Another form of treatment is ovarian suppression. (It's not a first-line treatment, but it is a way of determining whether there is a hormonal etiology of the disorder.)

BSTQ: What do you hope healthcare providers take away from your research?

Dr. Rubinow: Always ask women of reproductive age about mood symptoms. These issues are often dismissed or misunderstood — by both patients and clinicians. Yet effective treatments do exist. The key to successful treatment is accurate diagnosis. Recognizing PMDD and other menstrual cycle-related mood disorders should be standard practice for gynecologists, psychiatrists and primary care providers alike. ❖

TRUDIE MITSCHANG is a contributing writer for *BioSupply Trends Quarterly* magazine.

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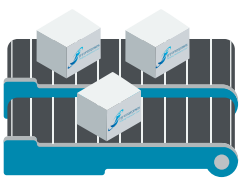

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Therapeutic Plasma Exchange: A Promising New Treatment for Sepsis and Septic Shock

By Keith Berman, MPH, MBA

EACH YEAR, the pharmaceutical industry introduces new therapeutics to add to the vast armamentarium that clinicians already rely upon to treat human disease. Nearly all are single molecular entities that either target underlying disease pathology or counter its secondary effects. Many are lifesaving: Think of thrombolytics for myocardial infarction and acute ischemic stroke; insulins for type 1 diabetes; immunotherapies, hormone therapies and antimetabolites to treat various cancers.

Then there is sepsis, which isn't a disease but a syndrome caused by a dysregulated inflammatory response to infection. Sepsis is the catch-all term for a spectrum of conditions that may include multiple organ dysfunction, hypotensive shock, systemic coagulopathy and immune suppression (Figure 1).[1] For any given individual, its course is shaped by the type of pathogen, site of infection, genetic determinants, age, pre-existing comorbidities and overall health

Figure 1. Multiple Organ System Derangements That Can Accompany Sepsis[1]

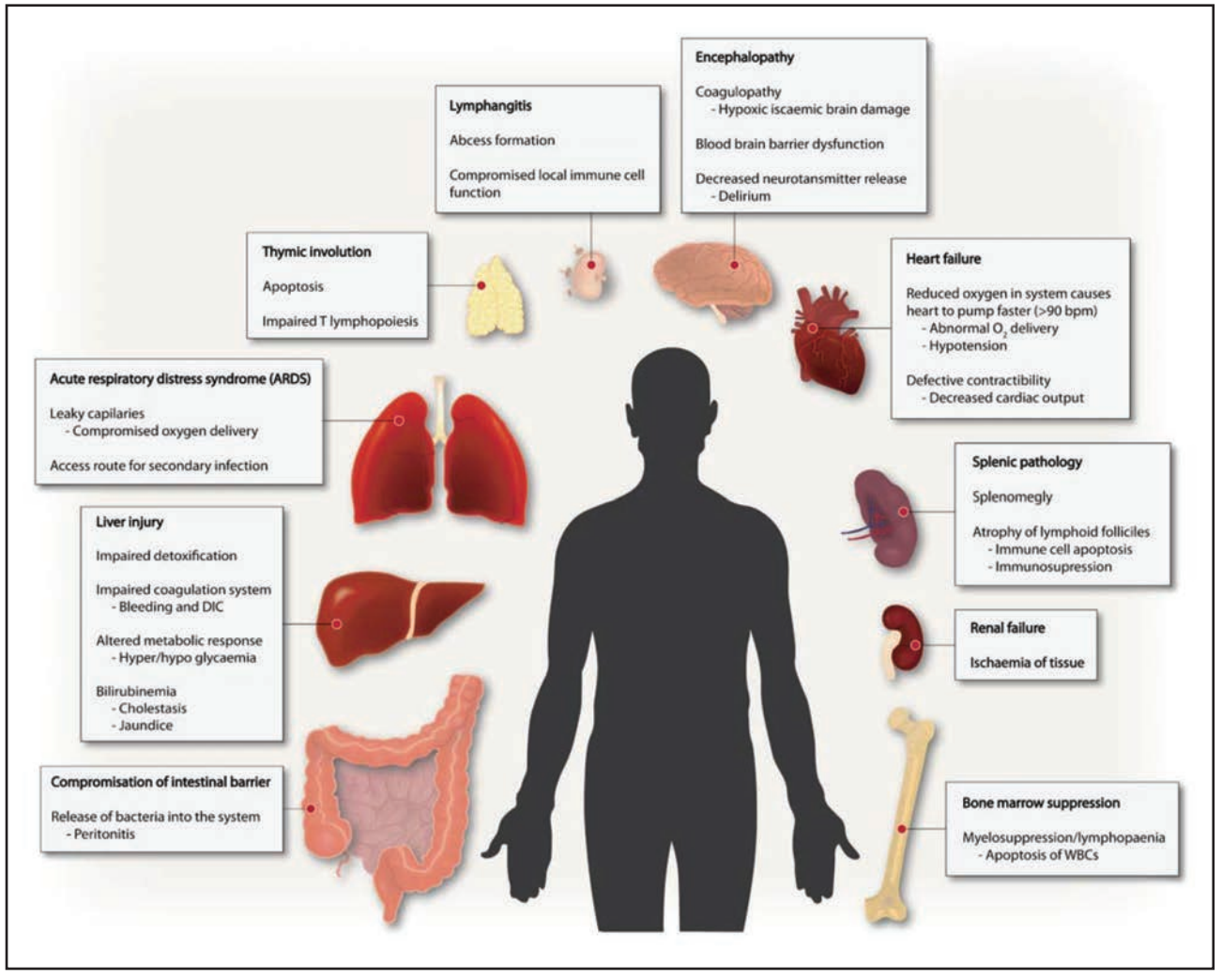
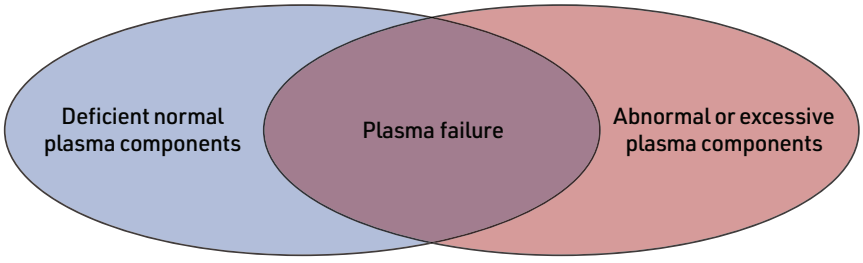


Figure 2. Plasma Failure: Deficiencies and Excess of Essential Circulating Factors[7]



status.[2] In the unfortunate subpopulation of patients who progress to septic shock, 30-day mortality well exceeds 30 percent.[3] Today, sepsis accounts for more than one-third of all hospital deaths. Some 350,000 of the 1.7 million adults who develop sepsis each year will die during or shortly after their hospitalization.[4,5]

Yet notwithstanding antibiotics, vasopressors and other drugs used in standard ICU treatment, there are no available therapies to treat sepsis itself. Well over 100 randomized clinical trials (RCTs) evaluating numerous drug candidates in hopes they could modulate the septic response and improve survival have all failed.[6] The explanation for this dismal record lies in the complex pathophysiology of sepsis itself, much of which remains incompletely understood.

In a state of health, a balance between pro- and anti-inflammatory mediators and their interactions with local cellular stimuli govern the normal adaptive inflammatory process that helps promote leukocyte migration, complement-mediated lysis and other immune responses to the invasive pathogen. To cite just one example, the anti-inflammatory cytokine TGF-ß suppresses production of inflammatory cytokines, downregulates endothelial adhesion and inhibits synthesis of nitric oxide to limit its potent vasodilatory activity.

But in a state of sepsis, this balanced interplay of numerous cellular and circulating elements becomes deranged. There is overproduction of specific pro-inflammatory mediators such as IL-1ß, TNF, C3a and C5a, while plasma levels of anti-inflammatory factors (e.g. TGF-ß, IL-10 and complement factor H) that normally regulate the inflammatory response can become exhausted. This hyperinflammatory, dysregulated state can result in widespread tissue damage and multiple organ dysfunction syndrome (MODS). In turn, injury to organ microvasculature in MODS can result in widespread formation of microthrombi, depleting circulating anticoagulant proteins such as antithrombin III (AT-III), protein C and tissue factor pathway inhibitor. In patients with severe sepsis and septic shock, profound dysregulation of coagulation function can progress to disseminated intravascular coagulation (DIC), with a mortality rate as high as 50 percent.

"Plasma Failure" and Therapeutic Plasma Exchange

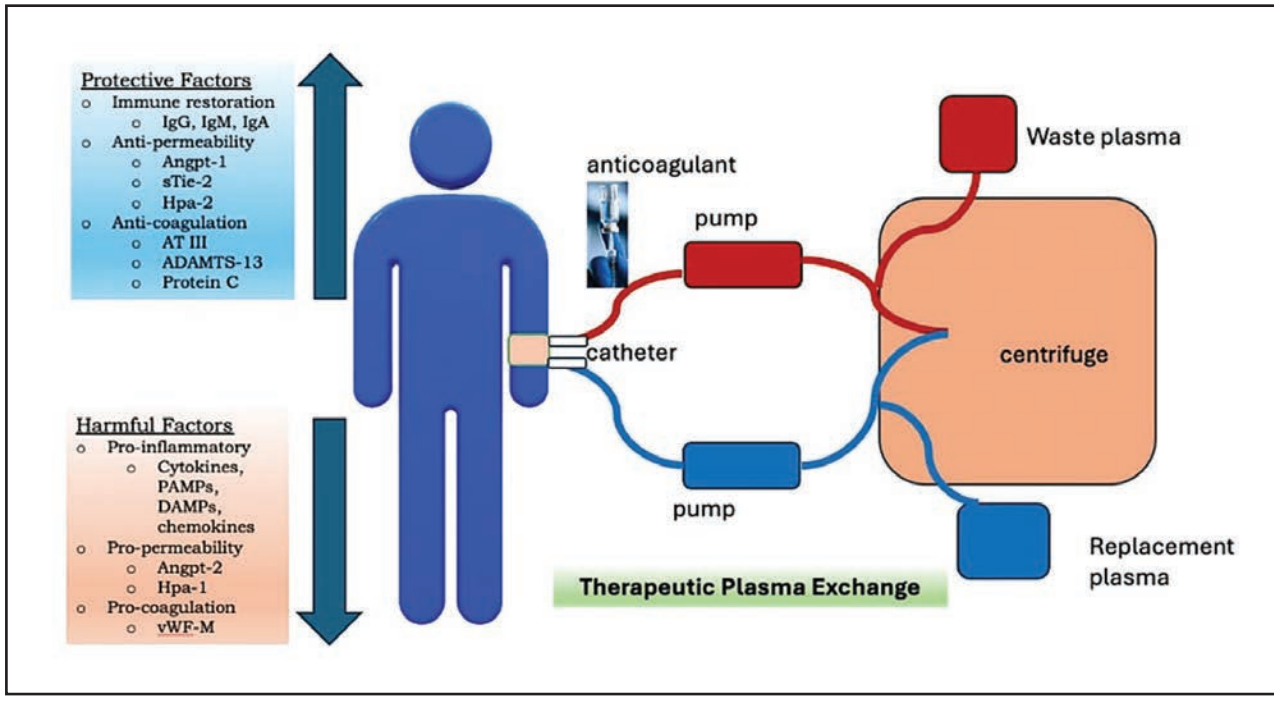
It is widely agreed that the hyperinflammation and microvascular thrombosis observed in sepsis result from simultaneous excessive levels of circulating proinflammatory and procoagulant plasma elements, coupled with depleted levels of other circulating plasma elements that normally act to limit these responses to an invasive pathogen.

Diseases arising from deficiency of a single plasma protein, such as hemophilia A from a deficiency of factor VIII, can be effectively treated with replacement of the missing factor. But the pathophysiology of sepsis-induced organ dysfunction involves numerous dysregulated plasma components and pathways. So it's not at all surprising that no one has found a "magic bullet" that can help restore homeostasis in these patients.

A recent review by critical care and apheresis medicine specialists has applied the term "plasma failure" in relation to sepsis in its various manifestations — the collective failure of numerous circulating plasma elements to control the hyperinflammatory and coagulopathic response to an invasive pathogen. Plasma failure is not unique to sepsis patients with MODS; it occurs as well in patients with trauma-induced coagulopathy, acute liver failure and severe COVID-19 (Figure 2).[7]

In patients with severe sepsis and septic shock, profound dysregulation of coagulation function can progress to disseminated intravascular coagulation, with a mortality rate as high as 50 percent.

Figure 3. Treatment Effects of Plasma Exchange in Patients with Sepsis[13]



When understood in this context, a potential adjunctive treatment for worsening sepsis stands out: therapeutic plasma exchange (TPE) with fresh frozen plasma (FFP) to remove and replace the patient's "failed" plasma with fresh donor plasma that contains balanced, physiologic levels of critical plasma elements needed to restore homeostasis. Repeated TPE can both reduce harmful supraphysiologic circulating levels of proinflammatory and procoagulant proteins and restore depleted levels of proteins whose function is to keep systemic inflammation and coagulation activity in check (Figure 3).

A number of small RCTs and case-control studies dating back more than two decades have been conducted in attempts to assess the potential effects of TPE on various clinical and laboratory outcome parameters.[8,9,10] Most document 30 percent to 60 percent reductions in short-term (e.g., 28-day or in-hospital) mortality with the use of TPE compared to standard care. While mortality is the primary endpoint of interest in nearly all of these trials, other measured outcomes have included Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation (APACHE II) score, plasma levels of both inflammatory cytokines and other injury-mediating factors, and protective factors such as AT-III, protein C and ADAMTS-13.

A number of small RCTs and case-control studies dating back more than two decades have been conducted in attempts to assess the potential effects of TPE on various clinical and laboratory outcome parameters.

Unfortunately, the validity of these individual studies is limited both by their very small enrollment sizes and a host of known confounders. Nevertheless, results from a number of very recent meta-analyses, including three published in 2023 and 2024, consistently find that TPE therapy meaningfully improved survival in patients with severe sepsis and septic shock:

• Lee et al (*J Intensive Care Med* 2023): This meta-analysis of small RCTs

and observational studies totaling 280 adult patients with severe sepsis found patients supported with TPE using FFP replacement had lower mortality (relative risk ratio [RR], 0.64; 95% confidence interval [CI], 0.49, 0.84) compared to those who did not.[11] Interestingly, an analysis of studies in children with severe sepsis found TPE was associated with increased mortality.

• Kuklin et al (*Crit Care* 2024): Five small RCTs were selected for this meta-analysis, which included 331 septic patients of whom 166 received TPE. Patients treated with adjunctive TPE had a lower mortality rate (RR: 0.62; 95% CI: 0.46, 0.83) compared to those who received standard therapy alone.[12] Separate analyses of six retrospective and nine prospective matched cohort studies respectively found patients who received TPE had significantly (RR: 0.33; 95% CI: 0.14, 0.76) and non-significantly (RR: 0.83; 95% CI: 0.44, 1.58) reduced risk of short-term mortality.

• Hernandez et al (*Cureus* 2024): A weighted analysis of three small RCTs and one cohort study comparing TPE to standard care in patients with septic shock again showed TPE is associated with a significantly reduced risk of mortality (RR: 0.43; 95% CI: 0.26, 0.72).[13]

Other studies have shown TPE improved hemodynamics in patients who had progressed to septic shock. A German group, for example, reported that the norepinephrine requirement to maintain systolic pressure in septic shock patients who received a single exchange of 12 units of FFP was significantly reduced relative to those who received standard care. In parallel, the mean lactate concentration showed a significant decline in the TPE group, while no decline was observed in the standard care group.[14]

Needed: Definitive Clinical Trials

While none of the sepsis/TPE trials reported to date have enrolled enough patients to overcome potential bias and random effects, collectively their results strongly suggest adjunctive TPE can meaningfully improve survival in adults across a range of sepsis presentations.

Needed now are carefully designed and adequately powered clinical trials that address different sepsis subsets, including in particular sepsis with MODS and severe sepsis or septic shock with laboratory-confirmed DIC. In addition to defining enrollment inclusion and exclusion criteria, study investigators will need to reach consensus on a number of key parameters that include:

• Timing of initiation of TPE therapy (ideally within 24 hours of diagnosis/qualification)

• Volume of plasma exchanged with FFP

• Number of plasma exchanges

• Time interval between plasma exchanges

Then, of course, there is the elephant in the room: how to pay for these large, complex trials. The primary disposable supply item used to perform a single centrifuge- or membrane-based TPE procedure generates just a few hundred dollars for its manufacturers, at least an order of magnitude less than the per-treatment revenue a successful new drug can potentially generate for a drugmaker to justify a multi-million-dollar R&D investment. The money to support costly clinical trials to evaluate use of TPE in sepsis will have to come from elsewhere.

Without an industry sponsor, it will be especially challenging for proponents of TPE/sepsis research to secure the funding required for clinical trials able to definitively answer whether TPE can provide important survival benefit for patients diagnosed with sepsis or septic shock with multi-organ failure.

Hopefully that funding will materialize sooner than later for critical care specialists who see the lifesaving potential of TPE and are prepared to organize and conduct these trials. There may be no better opportunity to reduce the numbers of hospital deaths in all of medicine. ❖

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AI Assistants Offset Nursing Workload

THE ONGOING national nursing shortage continues to strain hospitals and healthcare facilities. While the United States saw a one percent increase in supply of registered nurses (RNs) between 2022 and 2025, demand has nevertheless outpaced supply. In fact, the need for RNs increased by three percent over the course of those same three years.[1] Baby boomers continue to age, increasing their need for healthcare interventions; burnout drives nurses away; and nursing schools are struggling to keep up with the demand for educating new nurses. According to Health Workforce Analysis, federal authorities project a shortage of 78,610 full-time RNs in 2025 and a shortage of 63,720 RNs by 2030.[2] The gap between care needed and care available is getting wider. There's no question: Nurses need help.

Enter artificial intelligence (AI). AI is taking the healthcare industry by storm, creating new opportunities for offsetting the nursing squeeze and improving patient care at the same time. Designed to work with RNs, these AI-powered robots support clinical work by completing essential non-patient-facing tasks that so often get in the way of providing patient-focused care. According to a recent study, at least 10 percent of a nurse's shift is spent on delegable and non-nursing activities such as gathering medical supplies, delivering lab samples, retrieving medications, etc.[3] Increasingly, AI-powered robots are able to lighten RN workload. Here are two stand-out examples of what these innovative clinical helpers can do.

Moxi Robot Assistant

Diligent Robotics is changing the way robotic assistants interact with and provide assistance to human healthcare workers. Moxi works in hospitals, helping clinical staff do more work in less time. Routine activities such as transporting patient supplies, delivering lab samples, fetching items from central supply locations, distributing personal protective equipment and delivering medications are completed 24/7 with automation and ease. Moxi responds to human calls, autonomously executes point-to-point deliveries and can navigate entire buildings, not just one department floor. As a semi-humanoid robot with expressive eyes and a robotic arm, it is a friendly and functional addition to the clinical team. It can operate elevators and open doors; won't bump into people or objects in hallways; can grab, pull and open and guide objects on its own. Moxi detects people and navigates around them and other obstacles. As it works, it learns: The more a staff uses Moxi, the more Moxi learns about and adapts to a facility's environment and processes. According to the company, Moxi gives time back to employees, supports current nursing staff and helps lower nurse turnover rate. The best part? Implementation takes weeks, not months. For more information, or to book a demo, visit *www.diligentrobots.com/moxi*.

Aethon Hospital Robots

From medicine and meals to linens and labs — there's always something on the move in hospitals. Transporting things from one place to another takes time and energy away from clinicians whose time is better spent on patient care. Enter Aethon, a robotics company with a vision to integrate autonomous robots into healthcare settings. Aethon hospital robots are mobile delivery solutions that transform the way hospital work is done. Automated routine logistics and delivery tasks empower the clinical team and support staff, giving them more time to spend on patient care. Robots support laboratory and pharmacy deliveries; help manage waste removal; provide cost-effective options for meal delivery; and deliver linens and supplies when and where they are needed. And, robots interact with doors and elevators on their own. With robust 24/7 technical support, project management and repair and maintenance services, Aethon hospital robots are more than a technological solution: They are an integral part of the healthcare team. For more information, visit *aethon.com/hospital-robots-healthcare*.

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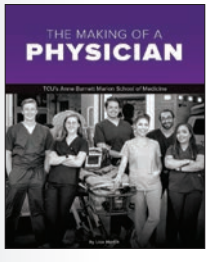
The Making of a Physician: TCU's Anne Burnett School of Medicine Teaches Empathy Alongside Scholarship

Author: Lisa Martin

To better understand the medical school and its innovative vision for patient care, *TCU Magazine* followed six of the inaugural students at the Anne Burnett School of Medicine at Texas Christian University through their four-year journeys. Writer Lisa Martin spent hundreds of hours conducting interviews and observing all six both in the classroom and in clinical settings as they not only faced the typical challenges of medical school, but also unique ones born out of the COVID-19 pandemic that struck during the students' first year.



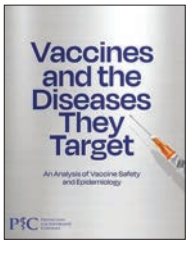
www.amazon.com/Making-Physician-Medicine-Alongside-Scholarship/dp/087565892X

Vaccines and the Diseases They Target: An Analysis of Vaccine Safety and Epidemiology

Author: Physicians for Informed Consent

Vaccines and the Diseases They Target — also known as the Silver Booklet — is a clear, concise resource for parents, healthcare providers and policymakers seeking balanced, evidence-based information on childhood vaccines and the diseases they aim to prevent. Created by Physicians for Informed Consent, this book presents side-by-side comparisons of disease symptoms, treatments and long-term risks with the side effects and effectiveness of corresponding vaccines. Each section includes graphs and visuals to help readers understand the data at a glance.

www.amazon.com/Vaccines-Diseases-They-Target-Epidemiology/dp/B0FK4262N3

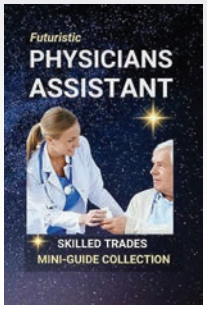


IACI Provider Manual

Author: Center for Recovery from Complex Chronic Illness

Created by the Cohen Center for Recovery from Complex Chronic Illness at the Icahn School of Medicine at Mount Sinai, this manual provides evidence-based guidance for clinicians working with patients affected by infection-associated chronic illnesses (IACIs), including long COVID, myalgic encephalomyelitis/chronic fatigue syndrome, and chronic tick- and vector-borne illnesses such as post-treatment Lyme disease syndrome.

icahn.mssm.edu/research/cohen/resources?pk_vid=3f3f55dd1cda1f6b17570163192c1276



Physician Assistant: Healthcare's Right Hand — Delivering Compassionate Care

Author: Kenneth Edlin

Physician assistants (PAs) play a critical role in patient care, working closely with doctors to diagnose and treat illnesses. A career as a PA offers variety, responsibility and growing demand. This guide explores education pathways, clinical skills and emerging AI tools enhancing healthcare delivery. PAs can discover scholarships and community foundations to support their career journey.

www.amazon.com/Physician-Assistant-Healthcares-Delivering-Compassionate/dp/B0FG3G2G93

Medicare Immune Globulin Reimbursement Rates

Rates are effective Oct. 1, 2025, through Dec. 31, 2025

	Product	Manufacturer	J Codes	ASP + 6% (before sequestration)	ASP + 4.3% (after sequestration)
IVIG	ALYGLO	GC Biopharma	J1552	$260.47	$256.29
	ASCENIV	ADMA Biologics	J1554	$993.48	$977.54
	BIVIGAM	ADMA Biologics	J1556	$154.78	$152.30
	GAMMAGARD SD	Takeda	J1566	$157.59	$155.06
	GAMMAPLEX	BPL	J1557	$127.37	$125.32
	OCTAGAM	Octapharma	J1568	$95.05	$93.53
	PANZYGA	Octapharma/Pfizer	J1576	$145.99	$143.65
	PRIVIGEN	CSL Behring	J1459	$101.47	$99.85
	YIMMUGO	Kedrion	C9399**	*	*
IVIG/SCIG	GAMMAGARD LIQUID	Takeda	J1569	$90.63	$89.17
	GAMMAKED	Kedrion	J1561	$97.93	$96.36
	GAMUNEX-C	Grifols	J1561	$97.93	$96.36
SCIG	CUTAQUIG	Octapharma	J1551	$142.32	$140.04
	CUVITRU	Takeda	J1555	$168.42	$165.72
	HIZENTRA	CSL Behring	J1559	$143.37	$141.07
	HYQVIA	Takeda	J1575	$181.51	$178.60
	XEMBIFY	Grifols	J1558	$148.45	$146.07

* ASP-based Medicare payment rate not yet available; payment rate assigned by your Medicare Administrative Contractor.

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Immune Globulin Reference Table

	Product	Manufacturer	Indication	Size
IVIG	ALYGLO	GC Biopharma	PI	5 g, 10 g, 20 g
	ASCENIV LIQUID, 10%	ADMA Biologics	PI	5 g
	BIVIGAM LIQUID, 10%	ADMA Biologics	PI	5 g, 10 g
	GAMMAGARD S/D Lyophilized, 5% (Low IgA)	Takeda	PI, ITP, B-cell CLL, KD	5 g, 10 g
	GAMMAPLEX Liquid, 5%	BPL	PI, ITP	5 g, 10 g, 20 g
	GAMMAPLEX Liquid, 10%	BPL	PI, ITP	5 g, 10 g, 20 g
	OCTAGAM Liquid, 5%	Octapharma	PI	1 g, 2.5 g, 5 g, 10 g, 25 g
	OCTAGAM Liquid, 10%	Octapharma	ITP, DM	2 g, 5 g, 10 g, 20 g, 30 g
	PANZYGA Liquid, 10%	Octapharma/Pfizer	PI, ITP, CIDP	1 g, 2.5 g, 5 g, 10 g, 20 g, 30 g
	PRIVIGEN Liquid, 10%	CSL Behring	PI, ITP, CIDP	5 g, 10 g, 20 g, 40 g
	YIMMUGO, 10%	Kedrion	PI	5 g, 10 g, 20 g
IVIG/SCIG	GAMMAGARD Liquid, 10%	Takeda	IVIG: PI, MMN, CIDP	1 g, 2.5 g, 5 g, 10 g, 20 g, 30 g
			SCIG: PI	
	GAMMAKED Liquid, 10%	Kedrion	IVIG: PI, ITP, CIDP	1 g, 2.5 g, 5 g, 10 g, 20 g
			SCIG: PI	
	GAMUNEX-C Liquid, 10%	Grifols	IVIG: PI, ITP, CIDP	1 g, 2.5 g, 5 g, 10 g, 20 g, 40 g
			SCIG: PI	
SCIG	CUTAQUIG Liquid, 16.5%	Octapharma	PI	1 g, 1.65 g, 2 g, 3.3 g, 4 g, 8 g
	CUVITRU Liquid, 20%	Takeda	PI	1 g, 2 g, 4 g, 8 g, 10 g
	HIZENTRA Liquid, 20%	CSL Behring	PI, CIDP	1 g PFS, 2 g PFS, 4 g PFS, 10 g PFS
	HYQVIA Liquid, 10%	Takeda	PI, CIDP	2.5 g, 5 g, 10 g, 20 g, 30 g
	XEMBIFY Liquid, 20%	Grifols	PI	1 g, 2 g, 4 g, 10 g

CIDP Chronic inflammatory demyelinating polyneuropathy
CLL Chronic lymphocytic leukemia
DM Dermatomyositis
ITP Immune thrombocytopenic purpura
KD Kawasaki disease
MMN Multifocal motor neuropathy
PI Primary immune deficiency disease
PFS Prefilled syringes

2025-2026 Influenza Vaccines

Administration Codes: G0008 (Medicare plans)
Diagnosis Code: V04.81

Product	Manufacturer	Presentation	Age Group	Code
Trivalent				
AFLURIA (IIV4)	CSL Seqirus	0.5 mL PFS 10-bx	3 years and older	90685
FLUAD (IIV4)	CSL Seqirus	0.5 mL PFS 10-bx	65 years and older	90694
FLUARIX (IIV4)	GSK	0.5 mL PFS 10-bx	6 months and older	90686
FLUBLOK (ccIIV4)	Sanofi	0.5 mL PFS 10-bx	18 years and older	90682
FLUCELVAX (ccIIV4)	CSL Seqirus	0.5 mL PFS 10-bx	6 months and older	90674
FLULAVAL (IIV4)	GSK	0.5 mL PFS 10-bx	6 months and older	90686
FLUMIST (LAIV4)	Astrazeneca	0.2 mL nasal spray 10-bx	2-49 years	90672
FLUZONE (IIV4)	Sanofi	0.5 mL PFS 10-bx	6 months and older	90686
FLUZONE (IIV4)	Sanofi	5 mL MDV	6 months and older	90658
FLUZONE HIGH-DOSE (IIV4)	Sanofi	0.7 mL PFS 10-bx	65 years and older	90662

ccIIV4 Cell culture-based trivalent inactivated injectable
IIV4 Egg-based trivalent inactivated injectable
LAIV4 Egg-based live attenuated trivalent nasal spray

* Providers should check with their respective payers to verify which code they are recognizing for Flucelvax Trivalent 5 mL MDV product reimbursement for this season.

2025-2026 COVID-19 Vaccines

Product	Manufacturer	Presentation	Age Group	Code
SPIKEVAX COVID-19 Vaccine, mRNA	Moderna	0.5 mL SDV 10-pk	12 years and older	91321
mNEXSPIKE COVID-19 Vaccine, mRNA	Moderna	0.2 mL SD PFS 10-ctn	65 years and older 12-64 years with one underlying high-risk condition	TBD
MODERNA COVID-19 Vaccine, mRNA	Moderna	0.25 mL SDV 10-pk	6 months to 11 years	91322
NOVAVAX COVID-19 Vaccine, Adjuvanted	Novavax	0.5 mL SDV 10-pk	12 years and older	91304
COMIRNATY COVID-19 Vaccine, mRNA	Pfizer-BioNTech	0.3 mL PFS 10-bx	12 years and older	91320

2025-2026 Respiratory Syncytical Virus (RSV) Products

Product	Manufacturer	Presentation	Age Group	Code
ABRYSVO	Pfizer	0.5 mL Kit 1-ctn	60 years and older	90678
ABRYSVO	Pfizer	0.5 mL Kit 5-ctn	60 years and older	90678
ABRYSVO	Pfizer	0.5 mL PFS and Act-O vials 10-ctn	60 years and older and pregnant individuals 32-34 weeks gestation	90678
AREXVY	Pfizer	0.5 mL SDV 10-bx	60 years and older	90679
BEYFORTUS	Sanofi	0.5 mL PFS 5-bx	children up to 24 months	90380
BEYFORTUS	Sanofi	1 mL PFS 5-bx	children up to 24 months	90380
ENFLONSIA	Merck	0.7 mL PFS 10-pk	neonates and infants born during or entering their first RSV season	90382
mRESVIA	Moderna	0.5 mL PFS 10-bx	60 years and older	90683

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