EPPAD Bulletin

Vol 5, Number 2 September 2025

Official Biannual Publication of the Ethiopian Pharmacists and Pharmaceutical Scientists Association in the Diaspora (EPPAD)

Published in Springfield, VA - USA

Manuscripts to the Bulletin can be sent
to our email address: @ Fekadu.Fullas53@gmail.com

In This Edition

Editor's Corner

Dear readers,

The Editorial Team is pleased to publish the current issue of ***EPPAD Bulletin***, Vol 5, No.2. In the News and Highlights Section, a write-up by Dr. Ermias provides a summary of the newly constituted Horn of African Clinical Trials (HCAT) initiated by EPPAD investment wing. Accomplished scientists in various areas of specialties have joined the august team.

In the Pharmacy Pioneers Section, the exemplary academic and research career of Prof Kaleab is presented. His research and teaching profile is bound to inspire future generations of pharmacy professionals. We are also introducing Dr. Alex Akalu, one of our EPPAD Board members.

In this issue, we have included articles by Prof Bisrat Hailemeskel and Dr. Novatnack et al., respectively. Dr. Bisrat's article focusses on COVID vaccine resistance and lays out the reasons for the misconceptions about vaccines. He outlines pharmacists' role in alleviating the fears of patients. The article by Novatnack et al. discusses updates on metastatic breast cancer. It discusses the diagnosis, epidemiology and treatment aspects of breast cancer.

We hope you enjoy reading this issue.

Fekadu Fullas, PhD

Editor-in-Chief, ***EPPAD Bulletin***

EPPAD News and Highlights

Horn of African Clinical Trials (HACT) Inc.: Expanding Horizons with New Team Members, Corporate Milestones, and a New Website

(Prepared by Ermias Tilahun, MPH, PhD; EPPAD President)

The Horn of African Clinical Trials (HACT), a new initiative from EPPAD investment group, has entered an exciting new chapter in its development, marked by both institutional progress and the addition of accomplished professionals to its leadership team. Recently, HACT was officially registered as a C-Corporation in Delaware, USA, strengthening its legal and operational foundation in one of the most trusted corporate environments. In parallel, the organization has also begun the process of formal registration in Ethiopia, a step that reflects HACT's commitment to building a robust presence on the ground and advancing clinical research capacity across the region.

This dual registration not only ensures compliance with U.S. and Ethiopian regulations but also positions HACT to bridge international standards with local expertise—helping foster world-class clinical trials infrastructure in the Horn of Africa. The move represents a major milestone toward realizing HACT's vision of becoming a regional leader in clinical trials management, patient safety, and translational research.

Dr. Fissiha Antalew, PharmD,

An Associate Director of Clinical Supply at Ultragenyx Pharmaceutical Inc., Dr. Fissiha is a recognized leader in clinical supply chain operations. He brings deep experience in strategic demand and supply planning, global distribution for clinical trials, and has been honored as a 2025 BSMA *40 Under Forty Award Winner*.

Dr. Fikreab S. Admasu,

A Senior Data Scientist at MSD, Dr. Fikreab specializes in advanced statistical and machine learning approaches, including causal modeling and reinforcement learning, to drive data-informed decision-making in pharmaceutical research. His unique blend of academic and industry experience will help guide evidence-based strategies within HACT.

Dr. Biruhalem A. Bayayibign

Dr. Biruhalem currently leads pharmacovigilance at Lyomark Pharma GmbH/Bendalis GmbH, and brings rich expertise in drug safety, compliance, and clinical trials oversight. As an EU-QPPV, his insights into global pharmacovigilance standards will be invaluable for HACT's operations.

Dr. Tiruneh Hailemariam

A molecular biologist with more than 15 years of biotech industry experience, Dr. Tiruneh has spearheaded the development of multiple in vitro diagnostic devices, including the first FDA-approved molecular immunohematology assay recognized among *The Scientist* magazine's Top Ten Innovations of 2014. He currently leads clinical and medical affairs in precision medicine, focusing on co-developing targeted therapies and companion diagnostics.

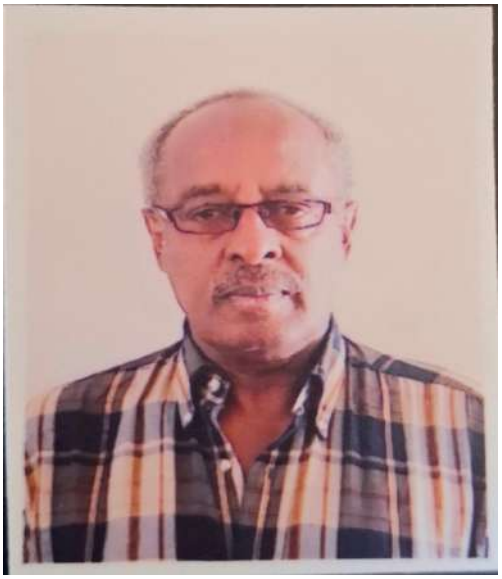
Together, these accomplished professionals embody HACT's commitment to excellence in clinical trials, regulatory compliance, data science, and translational research. Their expertise strengthens the organization's capacity to design and implement high-quality, ethical, and impactful studies that meet international standards while addressing regional health priorities.

In addition, HACT is proud to announce the launch of its new official website: **https://gohact.org/**. The site provides an overview of HACT's mission, updates on ongoing developments, and a platform for engaging stakeholders across the globe. It is designed to be a hub for information, collaboration, and future partnerships.

With its formal incorporation as a U.S. C-Corporation, pending registration in Ethiopia, a strengthened leadership team, and now a dedicated digital presence, HACT is firmly positioned to serve as a bridge between global research and local innovation. These developments mark an important step toward HACT's mission of transforming the clinical research landscape in the Horn of Africa—laying the groundwork for groundbreaking discoveries that can improve patient outcomes and contribute to global health equity.

Pioneers of Ethiopian Pharmacy and Related Fields

The Illustrious Career of Professor Kaleab Asres
(Prepared by Fekadu Fullas, Ph.D.)



(Photograph of Professor Kaleab Asres; courtesy of *KA*)

In this issue, we are profiling the career of Dr. Kaleab Asres of the School of Pharmacy, Addis Ababa University (AAU). He received his B. Pharm. degree in 1979 with distinction and was a recipient of a Gold Medal for that year. In 1982, he obtained a British Council scholarship to study for a Ph.D. degree at the University of London School of Pharmacy under the late Dr. David Phllipson. After receiving his Ph.D. degree in pharmacognosy in 1986, he returned to Ethiopia and became an Assistant Professor. He rose through the academic ranks and became a full professor in 2017.

His productive research has been funded by the United Nations Development Program (UNDP), World Bank, Deutscher Akademischer AustauschDienst (German Academic Exchange Service) [DAAD] and AAU. His wide-ranging research projects have focused, among others, on studies on the composition, antimicrobial and antioxidant properties of essential oil-bearing Ethiopian plants; phytochemical and pharmacological investigation of plants used for the treatment of diabetes; *in vivo* anti-inflammatory and antinociceptive activities of traditionally used wound healing plants; hepatoprotective activity studies on plants used in Ethiopian traditional medicine for the treatment of liver diseases; phytochemical, antimalarial, anti-trypanosomal, antileishmanial, and anti-microbial activity studies on *Aloe* species of Ethiopia; and phytochemical and biological studies on Ethiopian medicinal plants used by traditional healers to treat cancer-like symptoms; and toxicological study of Ethiopian medicinal plants widely used in traditional medicine. His prolific research output has been recorded in over **230** scientific publications and about **50** oral/poster presentations at various conferences in Ethiopia and abroad. His research contributions have been recognized by the University community: Certificate of life-time best researcher award, 2014 (College of Health Sciences [CHS], AAU); Certificate of last 10 years best researcher award, 2014 (CHS, AAU); Certificate of dedicated long years of service, 2014 (CHS, AAU); and 2015/16 Distinguished research award for excellence in Research at AAU, 2017 (CHS, AAU). For his outstanding service to the profession of pharmacy, the Ethiopian Pharmaceutical Association (EPA) has bestowed upon him a Certificate of recognition of professional commitment and unreserved contribution to the EPA as Chairman of the Editorial Committee of ***Ethiopian Pharmaceutical Journal***, *August* 2003; The EPA Certificate of recognition and Gold Medal award for research contribution to the profession of pharmacy in Ethiopia, July 30, 2004. Professor Kaleab has also served in several journals in various capacities: Editor in Chief (***EPJ***); manuscript reviewer (***Ethiopian Medical Journal***, ***Ethiopian Journal of Health Development***, ***EPJ***, ***SINET***); editorial board member and book reviewer (***Phytotherapy Research***, UK). During his long academic career Dr. Kaleab has advised/co-advised 10 Ph.D. students and over 130 M.Sc. students. He has also been serving as an external Ph.D. Thesis adviser for students in universities in India and Germany.

Professor Kaleab's administrative roles at AAU included: Head of the Department of Pharmacognosy, School of Pharmacy (1990-1991; 1996-2015); Dean of the School of

Pharmacy (1991-1996); Chairman, Academic Commission, School of Pharmacy (1991-1996); Senate Member, AAU (1991-1996).

Indeed, Professor Kaleb's illustrious career serves as a role model for rising pharmacy practitioners and researchers both in Ethiopia and elsewhere. *EPPAD Bulletin* is pleased to carry his research and academic portfolio in this issue.

P.S.: -

On a personal note, during my recent visit to Addis Ababa, I stopped by the School of Pharmacy at the Black Lion Hospital campus. After several decades, I met Dr. Kaleab in his office at the SoP. We chatted for more than 30 minutes about our old academic days. We also reminisced about natural products scientists we both knew in common in various parts of the world.

Meet Our EPPAD Board Members

Dr. Alex Akalu is a pharmacist-scientist with over 15 years of experience blending science, regulation, and technology. With a foundation in physics, he specializes in regulatory science, pediatric oncology, and applied artificial intelligence (AI) in healthcare. He currently serves as a Senior Oncology Staff Fellow at the U.S. Food and Drug Administration (FDA), leading data analysis, clinical research, and AI integration for the Division of Pediatric Oncology. Dr. Akalu was instrumental in meeting FDA Reauthorization Act (FDARA) mandates by developing the Pediatric Molecular Target List, a globally utilized resource guiding pediatric cancer drug development. His contributions have shaped the review of numerous oncology drug applications (IND, NDA, BLA) and informed national regulatory strategies. His peer-reviewed research, published in JAMA Oncology, Pediatric Blood & Cancer, The Journal of Pediatric Pharmacology and Therapeutics, and The Journal of Clinical Oncology, explores pediatric extrapolation, dosage optimization, racial equity in clinical trials, and fusion oncoproteins.

Dr. Akalu advises on the ethical use of AI in regulatory science, facilitating the adoption of FDA's internal AI chatbots and analytics tools for the pediatric division. He holds an advanced certification in AI in Healthcare from prestigious institutions, underscoring his dedication to transparent, responsible AI innovation. As a board member and Regulatory team chair of the Ethiopian Pharmacists and Pharmaceutical Scientists Association in Diaspora (EPPAD), Dr. Akalu mentors emerging scientists and advocates for robust regulatory systems in low- and middle-income countries. Driven by scientific rigor, equity, and global health impact, he continues to advance regulatory science and public health worldwide.

VACCINE HESITANCY: PHARMACISTS ROLE

Bisrat Hailemeskel, Pharm.D., RPh, ABAAHP
Professor & Vice-Chair, College of Pharmacy, Howard University
bhailemeskel@howard.edu

Numerous myths about vaccines have circulated widely, especially during the COVID-19 pandemic, contributing significantly to vaccine hesitancy around the world (MacDonald et al., 2015). These misconceptions, despite being repeatedly disproven by robust scientific evidence, have gained traction through misinformation on social media, distrust in public institutions, and confusion surrounding evolving public health guidance. As a result, many individuals, particularly parents, have grown wary of vaccinating themselves and their children. This growing hesitancy has led to serious public health consequences, including the resurgence of preventable diseases such as measles, even in highly developed countries like the United States. Once considered nearly eradicated, measles outbreaks have reappeared in several states due to declining vaccination rates in certain communities. Many mothers, influenced by misinformation and fear, are delaying or avoiding childhood immunizations, placing not only their children but entire communities at risk. As a pharmacist, addressing these myths with clear, evidence-based education is critical to reversing this trend and ensuring public health safety (Dube et al., 2015; Isenor et al., 2018).

One of the most frequently cited concerns fueling vaccine hesitancy is the belief that COVID-19 vaccines were developed "too fast" to be safe. While it is true that the timeline for vaccine development was significantly shorter than usual, this acceleration was not due to shortcuts or skipped safety protocols. Instead, it was made possible by an unprecedented combination of factors: massive global funding, decades of prior scientific research—particularly on mRNA vaccine platforms—and the overlapping of clinical trial phases. For example, the U.S. federal government allocated over $18 billion through Operation Warp Speed to support vaccine development, manufacturing, and distribution, allowing pharmaceutical companies to scale production even while trials were ongoing.

Furthermore, mRNA vaccine technology had been under development for nearly two decades prior to the pandemic, with early research dating back to the early 2000s. This foundational work allowed scientists to pivot quickly once the genetic sequence of SARS-CoV-2 was published in January 2020. Within weeks, candidate vaccines were already being designed. Clinical trials for the Pfizer-BioNTech and Moderna vaccines enrolled tens of thousands of participants—with Pfizer's Phase 3 trial involving over 43,000 people—and followed rigorous protocols aligned with FDA and international regulatory standards.

In December 2020, both Pfizer-BioNTech and Moderna vaccines received Emergency Use Authorization (EUA) from the FDA after demonstrating over 94% efficacy in preventing symptomatic COVID-19 and strong safety profiles. Importantly, the FDA emphasized that no trial phases were skipped; instead, phases were conducted in parallel to save time without compromising data integrity (FDA, 2021). Subsequent full approvals and ongoing safety monitoring have continued to support the safety and effectiveness of these vaccines. Thus, while the timeline was unprecedented, it was built on years of research and extraordinary global collaboration—not on reduced scientific rigor.

Another common concern among vaccine-hesitant individuals is the belief that receiving multiple vaccines at once can "overwhelm" or weaken the immune system, particularly in infants and young children. However, this claim is not supported by immunological science. In reality, the human immune system is remarkably robust and well-equipped to handle a vast number of antigens daily. From birth, the body is exposed to countless bacteria, viruses, and other microbes in the environment, each presenting far more antigenic challenges than those introduced by vaccines. In fact, it is estimated that a child's immune system could theoretically respond to 10,000 vaccines at once without being compromised (Offit et al., 2002).

Vaccines contain only a tiny fraction of the antigens that the immune system encounters naturally. For instance, the entire U.S. childhood immunization schedule contains fewer than 200 antigens, a significant reduction compared to the over 3,000 antigens found in vaccines administered in the 1980s. This reduction is due to advances in vaccine technology, which have made vaccines more targeted and safer than ever before. Multiple clinical studies have

confirmed that receiving several vaccines at once—such as during routine well-child visits—does not impair immune function, increase the risk of infection, or lead to adverse health outcomes.

The Centers for Disease Control and Prevention (CDC), the American Academy of Pediatrics (AAP), and the World Health Organization (WHO) all recommend combination vaccinations and co-administration of vaccines as safe and effective practices. These recommendations are based on decades of data showing no negative impact on immune health from administering multiple vaccines simultaneously. Dispelling this myth is essential to maintaining high vaccination coverage and protecting children from serious, preventable diseases.

Among the most persistent and damaging myths is the belief that vaccines cause autism. This concern originated from a now-discredited 1998 study by Andrew Wakefield, which falsely claimed a link between the MMR (measles, mumps, and rubella) vaccine and autism in children. The study received widespread media coverage and sparked fear among parents, leading to decreased vaccination rates in some countries. However, the study was later retracted by *The Lancet* due to ethical violations and fraudulent data, and Wakefield lost his medical license. Despite this, the myth continues to influence vaccine hesitancy even today.

Extensive research over the past two decades has repeatedly shown that there is no connection between vaccines and autism. Large-scale epidemiological studies involving hundreds of thousands of children have failed to find any link. Leading health authorities—including the Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), and the Institute of Medicine (IOM)—have all concluded that vaccines are safe and do not cause autism (IOM, 2004; CDC, 2023). Autism is now better understood as a neurodevelopmental condition influenced by genetic and early developmental factors, not by immunizations. Perpetuating this myth not only undermines public trust in vaccines but also distracts from meaningful research into the actual causes of autism.

Another misconception is that diseases like COVID-19 are "not serious for young people." While younger individuals are typically at lower risk for severe illness, they are not immune to complications and can still spread the virus to more vulnerable populations (Lee et al., 2022; CDC, 2023). The belief that "natural immunity is better" than vaccination is also misleading. Although infection can generate immune protection, evidence shows that hybrid immunity—a combination of prior infection and vaccination—offers the most durable and effective defense against future illness (Bobrovitz et al., 2023).

Concerns that vaccines alter a person's DNA are also scientifically unfounded. mRNA vaccines, such as those used for COVID-19, do not enter the cell's nucleus where DNA is housed and cannot integrate or interfere with genetic material (NIH, 2021).

Finally, while there have been claims that people died from the vaccine, thorough investigations by public health agencies have shown that the vast majority of these cases were unrelated to the vaccination itself (CDC, 2023).

These myths continue to circulate widely but lack credible scientific support. Addressing them with clear, evidence-based information is essential for protecting public health and reinforcing trust in vaccines as one of the most powerful tools in modern medicine.

What We Hear—and How to Respond

Let's face it—we've all heard these concerns from patients. These are real statements people make, and it's important that we respond with empathy, respect, and accurate information.

When a patient says, "These vaccines were made too fast. I don't trust them," you might respond:

"That's a fair concern. What many people don't realize is that scientists had already been studying this vaccine technology—especially mRNA—for years. The speed was due to unprecedented funding, global collaboration, and urgency, but none of the safety steps were skipped. In fact, the FDA thoroughly reviewed all safety and efficacy data before authorizing the vaccines." (FDA, 2021)

If a patient says, "What about long-term side effects?", you can reassure them by saying:

"That's a common question. The most reported side effects—like fatigue, headache, or a sore arm—usually go away within a day or two. Serious side effects are extremely rare. Historically, vaccine-related side effects show up within the first two months after vaccination, not years later." (Shimabukuro et al., 2021; Plotkin et al., 2018)

When someone says, "I heard vaccines cause autism," you can clarify with:

"That theory has been thoroughly studied and disproven. Multiple large-scale studies found no connection between vaccines and autism. The original paper that made that claim was proven fraudulent and retracted. Both the CDC and Institute of Medicine have confirmed that vaccines are safe in that regard." (IOM, 2004; CDC, 2023)

If a patient says, "I already had COVID. I'm immune now," you can say:

"You're right that recovering from COVID gives you some protection. But research shows that getting vaccinated after infection provides even stronger, longer-lasting protection. That's called hybrid immunity, and it's currently the best defense we have." (Bobrovitz et al., 2023)

Finally, if someone says, "It's my body, my choice," it's important to affirm their autonomy while gently broadening the perspective:

"Absolutely—your choices matter, and your autonomy is respected. At the same time, it's important to consider how your decision affects others, like elderly family members, neighbors, or coworkers with weakened immune systems. Vaccines not only protect you but help safeguard your entire community." (Omer et al., 2009)

What We Can Do as Pharmacists

As pharmacists, we have a unique opportunity to meet patients where they are, especially when it comes to sensitive topics like vaccines. Asking open-ended questions such as, "What are your thoughts on this vaccine?" can open the door to honest conversation. It's important to avoid judgment, validate their concerns, and gently offer science-backed information in a way that feels respectful and personal. Having printed materials available can be helpful, but sometimes, simply offering to talk more at another time can be just as meaningful. Most importantly, remind patients that your role goes beyond filling prescriptions—you are there to support them, guide them, and walk alongside them in their health journey. In many cases, a calm, reassuring conversation can have more impact than any handout or poster.

Conclusion:

Pharmacists are not just vaccine providers—we're trusted guides in a confusing time. When we listen, inform, and reassure with care and science, we help patients make empowered decisions. Let's lead those conversations with confidence, because every heart changed could mean a life saved.

References

Bobrovitz, N., Ware, H., Ma, X., et al. (2023). Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: A systematic review and meta-regression. The Lancet Infectious Diseases, 23(4), 408–419.

Centers for Disease Control and Prevention (CDC). (2023). Vaccines and Immunizations.

Dube, E., Gagnon, D., MacDonald, N.E. (2015). Strategies intended to address vaccine hesitancy: Review of published reviews. Vaccine, 33(34), 4191–4203.

Food and Drug Administration (FDA). (2021). Emergency Use Authorization for Vaccines Explained.

Institute of Medicine (IOM). (2004). Immunization Safety Review: Vaccines and Autism. Washington, DC: The National Academies Press.

Isenor, J.E., & Bowles, S.K. (2018). Opportunities for pharmacists to increase immunization coverage through vaccine administration services. Canadian Pharmacists Journal, 151(5), 279–282.

Lee, S., Watson, K.E., & Apollonio, D.E. (2022). Community pharmacists and communication in the time of COVID-19: Applying the health belief model. Research in Social and Administrative Pharmacy, 18(1), 2425–2430.

MacDonald, N.E., & SAGE Working Group on Vaccine Hesitancy. (2015). Vaccine hesitancy: Definition, scope, and determinants. Vaccine, 33(34), 4161–4164.

National Institutes of Health (NIH). (2021). Understanding mRNA COVID-19 vaccines.

Offit, P.A., Quarles, J., Gerber, M.A., et al. (2002). Addressing parents' concerns: Do multiple vaccines overwhelm or weaken the infant's immune system? Pediatrics, 109(1), 124–129.

Omer, S.B., Salmon, D.A., Orenstein, W.A., deHart, M.P., & Halsey, N. (2009). Vaccine refusal, mandatory immunization, and the risks of vaccine-preventable diseases. New England Journal of Medicine, 360, 1981–1988.

Plotkin, S.A., Orenstein, W.A., & Offit, P.A. (2018). Vaccines (7th ed.). Elsevier.

Shimabukuro, T.T., Cole, M., & Su, J.R. (2021). Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the US—December 14, 2020–January 18, 2021. JAMA, 325(11), 1101–1102.

World Health Organization (WHO). (2019). Ten threats to global health in 2019.

Updates in Metastatic Breast Cancer: A Reason for Hope

Michael Novatnack, PharmD, MBA, US Medical Affairs Fellow[1], Aimee Faso, PharmD, BCOP, CPP[2], Benyam Muluneh, PharmD, BCOP, FHOPA, Assistant Professor[1]

[1] Division of Pharmacotherapy & Experimental Therapeutics University of North Carolina Eshelman School of Pharmacy
[2] University of North Carolina Medical Center

Introduction

Breast cancer is one of the leading causes of cancer worldwide, accounting for nearly 25% of all cancers in women (Onger et al., 2023). In 2025, there is an estimated 375,000 newly diagnosed, invasive or noninvasive, breast cancer cases with an approximation of less than 45,000 deaths in the United States (Shockney, 2025). To put this in perspective, one in every eight women, in the United States, will develop breast cancer in their lifetime (CDC, 2024). In Ethiopia, breast cancer accounts for nearly a fifth of all cancer cases in the country, showing similar incidence to the United States (Dandena et al., 2024). Early diagnosis of the disease is crucial, as this leads to a better prognosis. If not detected and treated early, the cancer may spread to other parts of the body leading to stage IV or metastatic breast cancer (MBC).

Epidemiology & Diagnosis

Organizations like the American Cancer Society (ACS), have the 5-year survival rate in patients with either localized or metastatic breast cancer to be around 99% and 30%, respectively (Shockney, 2024). Similarly, researchers in Ethiopia analyzed the 5-year survival rate in patients with Stage IV breast cancer to be around 25% (Tiruneh et al., 2021). Despite the 5-year survival rates of stage IV breast cancer being relatively comparable in both countries, the timing of diagnosis differs per country. In the US, many patients, around 66%, are diagnosed in the early-stage disease (stages I/II), while in Ethiopia, nearly 65% are diagnosed in the advanced stage (stage III/IV) (National Breast Cancer Foundation, 2024 & Bekele et al., 2024).

There are several diagnostic tools that can be used to determine the presence and severity of a breast cancer diagnosis. These tools include routine breast exams, ultrasounds, mammograms, digital breast tomosynthesis (DBT), and breast magnetic resonance imaging (MRI). Additionally, one other approach that has been effective and is universally recommended is genetic testing. Genetic testing is used to identify possible gene mutations that can contribute to the development of cancers (DePolo, 2025). Prominent genes associated with breast cancer risk include breast cancer gene 1 (BRCA1) and breast cancer gene 2 (BRCA2), which are tumor suppression genes that play a crucial role in cell regulation by producing proteins that repair damaged DNA (Casaubon et al., 2023). Furthermore, there is evidence supporting approximately 60% of women who carry a mutated BRCA 1 or 2 gene will develop breast cancer over the course of their life (NCI, 2024). Other common gene mutations within breast cancer are ATM, CDH1, PTEN, TP53, and STK11 (Shiovitz, 2015). Countries like the United States have implemented genetic testing into practice, as this is widely available. In contrast, routine genetic testing for breast cancer remains limited in Ethiopia due to various financial and logistical obstacles in both rural and urban settings (Yoshiko et al., 2023).

Another important measure that plays a pivotal role in selecting the most effective treatment for patients is the assessment of cancer tumor markers. In breast cancer, there are three prevalent tumor markers: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2). These biomarkers can then be further utilized in categorizing the breast cancer diagnoses based on the specific subtype for the proper selection of treatment. They are as follows: hormone receptor positive (ER and/or PR positive), human epidermal growth factor (HER2 positive) and triple negative (ER/PR and HER2 negative). Interestingly, the United States and Ethiopia have differing rates in the prevalence of tumor marker status. In the US, roughly 70% of breast cancer patients express ER/PR, close to 15% express HER-2, 10% are triple negative, and 5 to 7% unknown. (American Cancer Society, 2024). Conversely, in Ethiopia, approximately 48-53% of breast cancer cases express ER/PR, approximately 14% express HER-2, and 33% are triple negative (Belachew, 2023).

Treatment

Metastatic cancer remains one of the most common causes of death in patients with breast or other solid tumor malignancies (Mani et al., 2024). A European registry study found nearly 67% of solid tumor deaths resulted from metastasis of cancer (Dillekås et al., 2019). The process of metastasis begins with cancer cells diffusing from the localized area and invading other sites of the

body such as the lungs, brain, lymph nodes, liver, and bone. Interestingly, there is scientific evidence showing varying locations of metastasis based on the unique molecular subtype of the tumor. Notably, tumors that are hormone receptor (HR) positive will likely metastasize to bone, and tumors that are HR negative but positive for human epidermal growth factor 2 (HER2) will proliferate to either the brain or liver (Wu, 2017). These scientific findings support the need for molecular tumor testing as it can serve as a guide for both treatment selection and the predictive location of metastasis.

Treatment for MBC can be quite complex given the heterogeneity of the patient population. The National Comprehensive Cancer Network's (NCCN) Harmonized guidelines, which has been adopted by the Ethiopian Federal Ministry of Health, highlights treatment options based on patient-specific components such as patient preference, patient comorbidities, and tumor marker status. In postmenopausal patients with breast cancer subtypes of HR+ and HER-, the recommended first-line therapy consists of an aromatase inhibitor (AI), including anastrozole, exemestane, or letrozole, in combination with a cyclin-dependent kinase (CDK) 4/6 inhibitor containing either palbociclib, ribociclib or abemaciclib (NCCN, 2024). If unavailable, a fulvestrant injection with or without a CDK 4/6 inhibitor also serves as part of the first line therapy. Similarly, premenopausal patients follow the same medication regimens in addition to receiving ovarian suppression/ablation therapy (NCCN, 2024).

In patients being treated for HR- and HER2+ subtype, the suggested treatment incorporates HER-2 directed therapy (combination of trastuzumab and pertuzumab) with docetaxel as the preferred recommendation (NCCN, 2024). For those who may not respond to this frontline approach, the latter treatment involves a tyrosine kinase inhibitor, neratinib, with capecitabine, an antineoplastic agent (NCCN, 2024).

In patients who are being treated for HR+ and HER2+ subtype, a few possible medication regimens may be incorporated, depending on the patients' treatment history and preferences. The guideline recommendation for first line therapy is a combination of HER2-targeted medications, trastuzumab or pertuzumab with chemotherapy, which is a similar approach to treatment of patients with HR- and HER2+ disease, or endocrine therapy alone or in combination with HER2-targeted medication (NCCN, 2024).

The guidelines suggest the first line therapy to consist of a combination of a HER2-targeted medication, trastuzumab or pertuzumab, with chemotherapy or endocrine therapy alone or in combination with a HER2-targted medication (NCCN, 2024). This is a similar approach to treatment with patients with HR- and HER2+. However, due to toxicity concerns associated with chemotherapy in the first line option, patients may opt to select an HER2-targeted medication, trastuzumab, with an endocrine medication, such as anastrozole or letrozole (NCCN, 2024).

Finally, for patients with triple negative tumor subtype, the advised treatment consists of systemic chemotherapy including platinum agents such as cisplatin and carboplatin (NCCN, 2024). Despite the NCCN's Harmonized guidelines serving as a beneficial tool for clinicians in Ethiopia, systemic treatment options, as recommended, for patients with stage IV breast cancer are limited. In fact, from 2014 to 2019, only a third of patients received hormonal medications for treatment (Wondimagegnehu et al., 2022). Despite the lack of accessibility for some patients, Ethiopia has made substantial efforts in recent years in enhancing their healthcare infrastructure.

Worldwide Collaboration

Recently, the Federal Ministry of Health (FMOH) in Ethiopia has collaborated with the American Cancer Society (ACS), the Norwegian Cancer Society (NCS), and the Clinton Health Access Initiative (CHAI) to improve cancer care delivery. These collaborations resulted in the enhancement of diagnostic and pathologic measures and educational training sessions for oncology professionals (Tilahun et al., 2019). Correspondingly, the partnership also resulted in higher quality oncology medications, increased chemoradiation treatment facilities, and incorporated treatment-related accessibility to patients in both rural and urban settings of Ethiopia. (Tilahun et al., 2019)

Conclusion

Breast cancer is the leading cause of cancer affecting women worldwide (Bray et al, 2023). If not treated promptly, the disease can evolve into an aggressive form of breast cancer resulting in poor prognosis for patients. Nevertheless, breakthroughs in novel diagnostic techniques, such as tumor molecular biomarkers, and genetic testing can significantly guide personalized treatment regimens impacting patient outcomes. Despite the limitations in diagnostic and treatment access, the Ethiopia's FMOH has made meaningful progress in

improving treatment and accessibility for patients through public-private partnerships and cross-country collaborations. This teamwork has positively affected both the rural and urban populations of Ethiopia by providing more access to treatment facilities, more chemotherapies, and well-trained healthcare professionals. Ultimately, these positive initiatives can improve patient outcomes resulting in a reason to hope for all breast cancer patients.

References:

American Cancer Society. *Breast Cancer Facts & Figures 2024-2025*. Atlanta: American Cancer Society, Inc. 2024.

Bekele, K., Nugusu, F., Beressa, G. *et al.* Proportion of early-stage breast cancer at diagnosis in Ethiopia: a systematic review and meta-analysis. *BMC Cancer* 24, 1017 (2024). https://doi.org/10.1186/s12885-024-12768-8.

Belachew EB, Desta AF, Gebremariam TY, et al. Immunohistochemistry-derived subtypes of breast cancer distribution in four regions of Ethiopia. *Front Endocrinol (Lausanne)*. 2023;14:1250189. Published 2023 Nov 9. doi:10.3389/fendo.2023.1250189.

Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024; 74(3): 229-263. doi:10.3322/caac.21834.

Casaubon JT, Kashyap S, Regan JP. BRCA1 and BRCA2 Mutations. [Updated 2023 Jul 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470239/.

CDC. (2024). *U.S. Cancer Statistics Breast Cancer Stat Bite*. Centers for Disease Control and Prevention. https://www.cdc.gov/united-states-cancer-statistics/publications/breast-cancer-stat-bite.html.

Dandena, F.G., Teklewold, B.T., Darebo, T.D. *et al.* Epidemiology and clinical characteristics of breast cancer in Ethiopia: a systematic review. *BMC Cancer* 24, 1102 (2024). https://doi.org/10.1186/s12885-024-12822-5.

DePolo, J. (2025, March 29). *Genetic testing for Breast Cancer*. Breast Cancer.org. https://www.breastcancer.org/genetic-testing.

Dillekås H, Rogers MS, Straume O. Are 90% of deaths from cancer caused by metastases?. *Cancer Med*. 2019;8(12):5574-5576. doi:10.1002/cam4.2474.

Mani, K., Deng, D., Lin, C. *et al.* Causes of death among people living with metastatic cancer. *Nat Commun* 15, 1519 (2024). https://doi.org/10.1038/s41467-024-45307-x.

National Breast Cancer Foundation. (2024). *Breast Cancer Facts & Stats 2024 – Incidence, age, survival, & more*. https://www.nationalbreastcancer.org/breast-cancer-facts/.

National Cancer Institute. (2024, July 19). *BRCA gene changes: Cancer risk and genetic testing fact sheet*. Fact Sheet - NCI. https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet.

Onger, T., Barot, S., Lebda Turk, P., Vassil, A., Abraham, J., & Kruse, M. (2023). Breast Cancer. In *Bethesda Handbook of Clinical Oncology* (pp. 162–162). essay, Lippincott Williams & Wilkins.

Referenced with permission from the NCCN Clinical Practice Guidlines in Oncology (NCCN Guidelines©) for Harmonized Guidelines for Sub-Saharan Africa: *Breast Cancer.* V.3.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed September 29, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org.

Shiovitz S, Korde LA. Genetics of breast cancer: a topic in evolution. *Ann Oncol*. 2015;26(7):1291-1299. doi:10.1093/annonc/mdv022.

Shockney, L. D. (2024). *Stage 4 (IV) breast cancer: Survival rates, treatment & prognosis*. National Breast Cancer Foundation. https://www.nationalbreastcancer.org/breast-cancer-stage-4/.

Shockney, L. (2025, August 22). *Breast cancer facts & stats* . National Breast Cancer Foundation. https://www.nationalbreastcancer.org/breast-cancer-facts/#facts-stats.

Tilahun, Y., Ahmed, F., Grosz, J., & de Chazal, S. (2019). *Ethiopia expands breast cancer care nationally, helping women access the treatment they need*. Clinton Health Access Initiative. https://www.clintonhealthaccess.org/blog/ethiopia-expands-breast-cancer-care-nationally-helping-women-access-the-treatment-they-need/.

Tiruneh, M., Tesfaw, A., & Tesfa, D. (2021). Survival and Predictors of Mortality among Breast Cancer Patients in Northwest Ethiopia: A Retrospective Cohort Study. *Cancer Management and Research*, *13*, 9225–9234. https://doi.org/10.2147/CMAR.S339988.

Wondimagegnehu A, Negash Bereded F, Assefa M, Teferra S, Zebrack B, Addissie A, Kantelhardt EJ. Burden of Cancer and Utilization of Local Surgical Treatment Services in Rural Hospitals of Ethiopia: A Retrospective Assessment from 2014 to 2019. Oncologist. 2022 Nov 3;27(11):e889-e898. doi: 10.1093/oncolo/oyac127. PMID: 35791963; PMCID: PMC9632304.

Wu, Qi et al. "Breast cancer subtypes predict the preferential site of distant metastases: a SEER based study." *Oncotarget* 8 (2017): 27990 - 27996.

Yoshiko, Iwai et al., Breast Cancer Germline Genetic Counseling and Testing for Populations of African Heritage Globally: A Scoping Review on Research, Practice, and Bioethical Considerations. *JCO Glob Oncol* 9, e2300154(2023). DOI:10.1200/GO.23.00154.