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Picture by Josie Chen

EMORY UNDERGRADUATE MEDICAL REVIEW

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MISSION STATEMENT

The Emory Undergraduate Medical Review publishes student-authored research review articles on the intersection of cutting-edge medicine and the sciences. Our interdisciplinary articles span all clinical fields and are peer-reviewed by medical professionals from leading academic institutions, including Emory University, Yale University, and the Mayo Clinic.

On campus, EUMR hosts a variety of medically-related events, including frequent collaborations with Emory's School of Medicine. Our projects have been featured by Emory's News Center and have caught the attention of President Fenves.

LETTER FROM THE EDITOR

Dear Reader,

As the year draws to a close, we look back at our time as EUMR Editors-in-Chief with great nostalgia and fondness. We are sad to be leaving our positions and simultaneously thrilled for what the upcoming year promises to bring under new leadership. The spring publication was a success and we are immensely proud of the hard work and resilience of our Editorial Board.

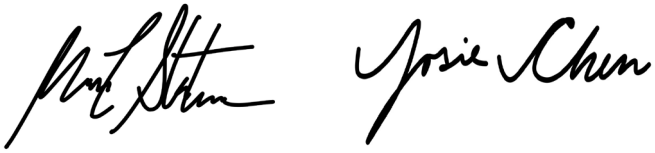
Each semester, EUMR hosts an engaging event that cuts across disciplines and fields of medicine, and this semester was no exception. On April 3rd, we successfully hosted our Emotive Arts Series event titled "Death and Dying". It was particularly gratifying to host this annual event again in-person, at the Michael C. Carlos Museum, for the first time since 2020. We are tremendously proud to have hosted a panel and art exhibit for the campus community in which doctors, palliative care experts, religious leaders, poets, and artists explored the cross-cultural meanings of death. We are deeply grateful to our events chair, Aditi Wamorkar, and the panelists and artists who contributed to the event's success.

Several new initiatives were introduced in the Spring 2023 semester. EUMR's intercollegiate podcast "MedWeb", led by Claire Zegger and Advaita Krishnan, successfully launched early in the semester after months of planning, recording, and coordination. Additionally, under the guidance of Joseph Park, Shreya Ramanathan, and Alyssa Chen, our team of writers and editors rebuilt and designed the EUMR website from scratch. The team also assisted in new publicity initiatives, ranging from increased social media presence to Wonderful Wednesday showcasing of our journals. We'd like to extend a thank you to them for their dedication to EUMR and willingness to go above and beyond.

We are incredibly excited to see the new highly motivated executive board maintain EUMR's excellence and implement new initiatives in the 2023-2024 academic year. As always, we would not have been able to publish this journal without the hard work of our Advisory Board members; their guidance and support are greatly appreciated. It is bittersweet to transition to new EUMR leadership and to say goodbye to our seniors who have continually supported and provided high-quality content for the journal and Emory community. We extend our genuine gratitude and appreciation to these graduating seniors and wish them the best of luck in their future endeavors in medicine and beyond.

Cordially,

Muriel Statman & Josie Chen
Editors-in-Chief
EUMR 2022-2023



Demystifying gonadotropin-releasing hormone analogs and their use in puberty suppression

BEN KITTLESON
Staff Writer

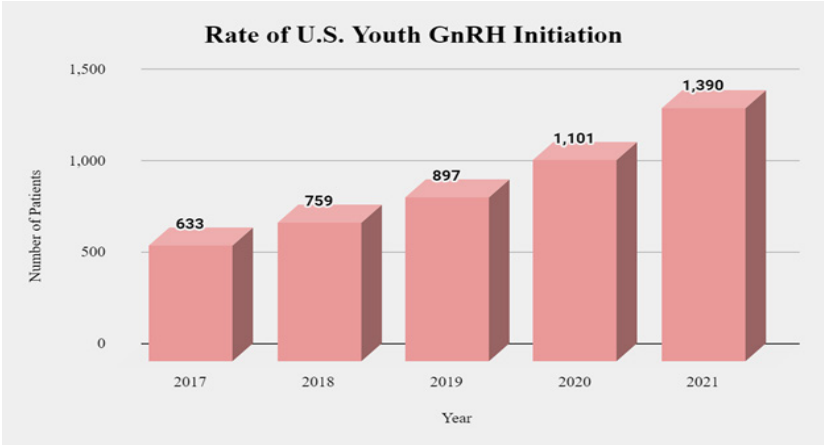


Figure 1. The number of patients aged 6-17 who initiated treatment from a previous diagnosis of gender dysphoria using puberty blockers (Terhune & Respaut, 2022).

Within the past decade, there has been a significant increase in the proportion of American youth seeking medical treatment for gender dysphoria - an incongruence between one's gender assigned at birth and one's experienced gender. The annual number of individuals under the age of 18 receiving a medical diagnosis of gender dysphoria in the United States almost tripled between 2017 and 2021 from 15,172 to 42,167 (Terhune & Respaut, 2022). As greater medical and social awareness of gender dysphoria has emerged, the dissemination of accurate information regarding the evidence-based practices that medical professionals provide to transgender youth has become increasingly important. One of these common medical practices that is often viewed as controversial is the prescription of gonadotropin-releasing hormone analogs (GnRHa), colloquially known as "puberty blockers." In 2021 and 2022, legislation was proposed in at least 25 U.S. states that would prohibit some or all gender-affirming medical care for youth (Kraschel et al., 2022). Although proponents of these laws often claim that they are designed to protect the safety of transgender youth, a great deal of evidence suggests that denying patients access to GnRHa can lead to profound negative outcomes, such as poor social life and high levels of suicidal ideation (Turban et al., 2020). While these laws typically focus on a broad range of medical therapies provided to transgender youth, this article will specifically focus on GnRHa, the current evidence-based way it is used in medical settings, and the scientific support for its continued use.

GnRHa is associated with significant, positive mental health outcomes for children with gender dysphoria.

Gonadotropin-releasing hormone (GnRH) is a decapeptide hormone produced in the hypothalamus (*Gonadotropin Releasing Hormone*, 2018). By attaching to receptors on the surface of the pituitary gland, the hormone is able to trigger the release of two hormones—luteinizing hormone (LH) and follicle-stimulating hormone (FSH)—that can stimulate the release of sex hormones. GnRHa works as an antagonist that interferes with the normal binding of GnRH to the pituitary gland and, therefore, decreases sex hormone production. GnRHa first came to prominence in medical settings as a means of treating central precocious puberty (CPP) (Eugster, 2019). CPP occurs in young children and is the result of early activation of the hypothalamic-pituitary-gonadal axis, resulting in premature sexual development in children.

GnRHa has long been used as the standard treatment for this condition, as its administration can lead to the suppression of the hypothalamic-pituitary-gonadal axis and the deactivation of GnRH receptors by desensitizing them via persistent activation, (Eugster, 2019). Starting in the 1990s, however, some physicians began prescribing GnRHa to adolescents who were experiencing significant, persistent gender dysphoria (Giordano & Holm, 2020). Shortly after this began, UK's the Royal College of Psychiatrists started recommending using GnRHa to delay puberty in young adolescents with persistent symptoms of gender dysphoria. Healthcare professional orga-

nizations have echoed these recommendations, and the World Professional Association for Transgender Health (WPATH) has since developed standards for the treatment of severe gender dysphoria in young adolescents, recommending suppression of puberty via medication, including GnRHa (Coleman et al., 2022). A vast proportion of prescribers view GnRHa as the optimal treatment because of its fully reversible effects that can be halted by the discontinuation of GnRHa administration (Eugster, 2019). The development of a specific treatment protocol, along with many social factors making transgender individuals increasingly visible, has led to a vast increase in the use of GnRHa as a means of suppressing puberty in gender dysphoric adolescents. This is reflected in data showing that the annual rate of GnRHa prescription more than doubled between 2017 and 2021 (Terhune & Respaut, 2022).

Although the existing body of research still largely supports GnRHa as a safe and effective treatment for gender dysphoria in youth, randomized clinical trials still need to be undertaken to further validate these recommendations.

Current evidence suggests that GnRHa is associated with significant, positive mental health outcomes for children with gender dysphoria. A review of the research surrounding puberty blockers reveals positive outcomes for individuals diagnosed with gender dysphoria. Specifically, individuals who have received this treatment report decreased suicidal ideation

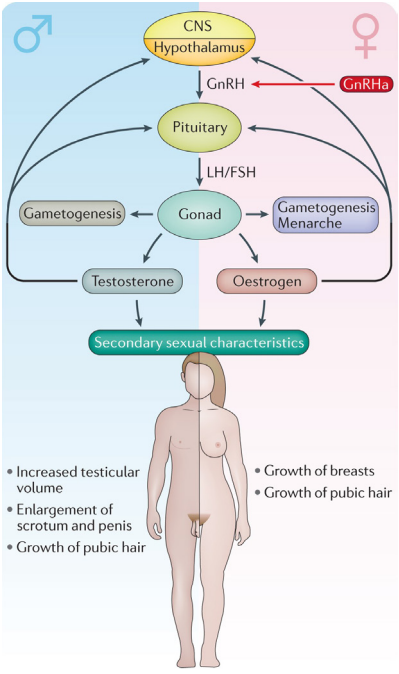


Figure 2. GnRH analogs work as puberty blockers by preventing the activation of the pituitary gland by GnRH, thereby preventing the various symptoms of puberty from ocurring (Puberty Suppression, 2016).

as an adult, improved affect, and improved social life (Rew et al., 2020). Another study investigating the impact of GnRHa treatment on suicidal ideation noted a significant reduction in lifetime suicidal ideation and attempts for patients with gender dysphoria who received puberty blockers versus those who did not (Turban et al., 2020). However, despite these positive findings, the same study reported that only 2.5% of patients who reported wanting pubertal suppression ever actually received it. This is due, in part, to the controversial nature of the drug.

Due to its use as an off-label drug and the social polarization that exists surrounding transgender healthcare, many unsupported claims about GnRHa exist in both social and medical settings. An editorial review of puberty blockers in *The Lancet* noted false claims about the safety of the medicine under the pretense of protecting children from child abuse and medical experimentation (The Lancet, 2021). Among these is the claim that GnRHa often leads to long-term fertility damage; however, a long-term study of women who were diagnosed with CPP as a child and treated with GnRHa had higher rates of unassisted pregnancy than those who weren't treated with GnRHa (Bangalore Krishna et al., 2019). Moreover, the same study found that women who received GnRHa as children showed no significant difference in reproductive function or fertility. While fewer data exist on this subject for assigned-at-birth males, analysis of semen and testosterone concentrations remained similar to that of their peers who did not receive GnRHa (Bertelloni et al., 2000). While further research should examine the long-term fertility of patients who receive GnRHa, there is little current evidence to suggest that there are fertility issues associated with the drug.

Claims of infertility in patients prescribed GnRHa are often accompanied by narratives that frame their use as medical experimentation on children. However, there is a significant history of research and documented use of GnRHa as a means of suppressing puberty. There are nearly three decades of documented use of GnRHa, and it is not any more experimental than the standard practice used by pediatricians to treat a patient for which no licensed drug exists (Giordano & Holm, 2020). In

fact, off-label medications are administered to 85% of children who are admitted to pediatric intensive care units in the US (Turban et al., 2020). Also, GnRHa was first licensed in the 1980s when regulatory rules did not mandate pediatric research, and there is little current incentive for pharmaceutical companies to conduct the specific studies needed to receive an official license for pediatric use, as it likely would have minimal effect on sales (Giordano & Holm, 2020).

With a great deal of misinformation circulating regarding the dangers of GnRHa, it becomes difficult to address the important areas of pubertal suppression that require further research.

As a result of this misframing of medical risk and experimentation, many opponents of GnRHa argue that their prescription is child abuse, as the child cannot consent to irreversible risks. However, this is incorrect for two reasons. First, the WPATH guidelines for the prescription of puberty-blocking agents detail the steps necessary for informed consent from children, including addressing any mental health issues that may interfere with the child's ability to give informed consent (Coleman et al., 2022). Even with these guidelines, parental consent is required- as is true of essentially all medical care for children (The Lancet, 2021). Also, the effects of GnRHa are reversible, as these medicines only temporarily halt testosterone and estrogen production, and normal puberty resumes after their discontinuation (Turban et al., 2020). Thus, the accusation that children are being subject to irreversible medical treatments without their or their parent's consent is incorrect.

With a great deal of misinformation circulating regarding the dangers of GnRHa, it becomes difficult to address the important areas of pubertal suppression that require further research. Specifically, concerns related to the long-term bone density of patients who receive GnRHa for pubertal suppression require further research. The timing of puberty can significantly influence bone mineral content later in life, with delayed puberty typically being associated with decreased bone density (Lee et al., 2020).

Preliminary research has demonstrated that children treated with GnRHa do not reach the same peak bone mass later in life as their peers who do not receive this treatment (Klink et al., 2015). This may put patients at risk for developing early-onset osteoporosis. However, it should be noted that transgender women have typically lower bone mineral density than cisgender men due to various other risk factors, such as high rates of vitamin D deficiencies and eating disorders in transgender women (Giacomelli & Meriggiolia, 2022).

There has also been research to demonstrate that much of the bone mass that could be lost during treatment with GnRHa can be recovered using add-back therapies concurrently with GnRHa (Sauerbrun-Cutler & Alvero, 2019). Therefore, the use of GnRHa should not begin without first assessing bone mass density and consulting a physician about the potential risks and the potential of using a concurrent add-back therapy. Continuing research is desperately needed to ensure adequate support for the bone density of adolescent patients with gender dysphoria using GnRHa. Although further research is still needed regarding bone mass density outcomes for patients on GnRHa, the current evidence supports their continued use due to the strong, positive mental health outcomes associated with their administration. Concerns about fertility, informed consent, and medical experimentation are largely unfounded and weaponized due to the social polarization rounding transgender medicine, and consequently, such narratives are making it extremely difficult for those who require pubertal suppression to receive it. ❧

AUTHOR BIO

Ben is a third year majoring in Biology and Chemistry. His interests are pharmacology, antimicrobial resistance, and novel antibacterial therapies.

Edited by Siya Malhotra, Helen Griffith, and Dr. Sarah Caston

Placed by Helen Griffith

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Moderna vs. Pfizer/BioNTech: The science of the SARS-CoV-19 vaccine lawsuit

ETHAN ESSENFELD
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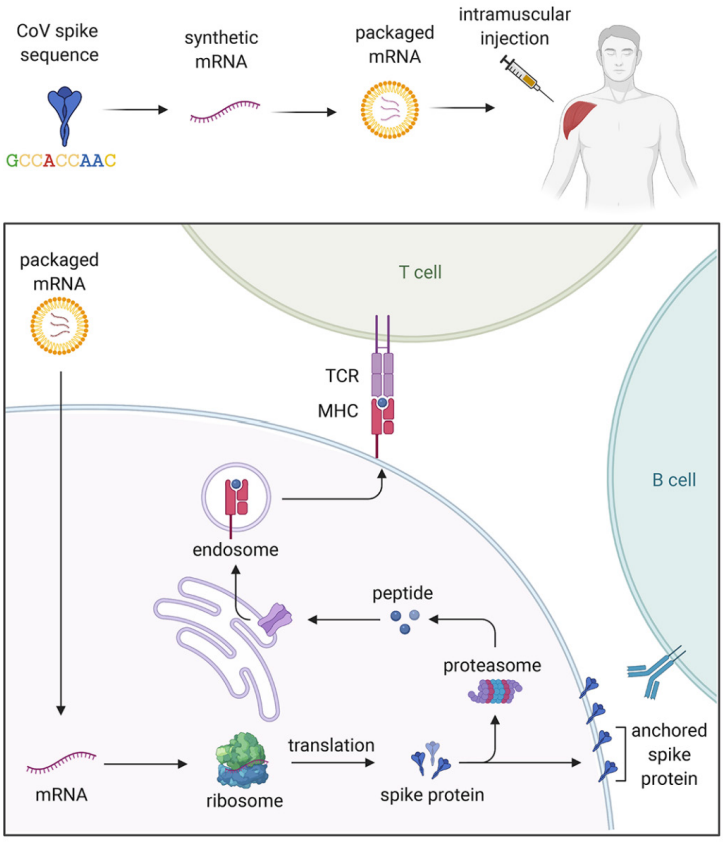

Figure 1. How mRNA COVID-19 vaccine activates the immune system in the body by directing T and B cells into attacked cells "infected" with a weakened version of the SARS-CoV-2 virus (Nance & Meier, 2021).

Much of the contrversy surrounding the COVID-19 pandemic was centered around the development and administration of vaccines. These vaccines, developed at an unprecedentedly fast rate, sparked intense debates across numerous contexts, including political, social, and even economic. Now, these vaccines are at the center of a historic legal battle between the founders of the first two approved vaccines. On August 26th, 2022, Moderna sued Pfizer and BioNTech, accusing them of using protected intellectual property in their vaccine, resulting in the loss of significant profits for Moderna (Modernatx & Moderna US, 2022). Like every other pharmaceutical company, Moderna owns patents that make it illegal for anyone else to use protected inventions in their products without a contract from the patent holders. Patents are a form of intellectual property rights that can be granted to inventors, giving them the exclusive rights to sell products associated with the science that they invented (General Information Concerning Patents | USPTO, n.d.). While this lawsuit is complex, with numerous claims of patent infringement, Moderna's claim that their intellectual property rights over N1-methylpseudouridine are being violated is one of the most critical components of the case.

To first understand how the two vaccines are similar, it is important to understand how they work. Both vaccines, due to allegedly being extremely similar, have the same mechanism of action. Both drugs utilize modified messenger ribonucleic acid, mRNA, to prevent COVID-19 from replicating in the body (Xia, 2021). Viruses are harmful, as they can interject their own genetic code into the host cells to replicate and eventually spread by being replicated utilizing the host body's replication system (Yuki et al., 2020). This replication system, known as the central dogma, consists of three primary components. The cycle typically starts with deoxyribose nucleic acid, DNA, which is converted into RNA, specifically an RNA subtype called mRNA, through a process called transcription. The mRNA undergoes translation in which it codes for the synthesis of a protein, which is then spread throughout the cell to perform its function (Crick, 1970). The host cell cannot al-

Moderna's claim that their intellectual property rights over N1-methylpseudouridine are being violated is one of the most critical components of the case.

ways differentiate between native and foreign genetic codes, resulting in the replication of any DNA or RNA present. Vaccines help the human body recognize the foreign genetic code by inserting the genetic code of a virus into the body which codes for an ineffective version of the virus. This allows for the immune system to develop a specific antibody for fighting the virus, which will be more effective for fighting the harmful version of the virus since the antibodies are already coded for (Vaccines Protect You | HHS.Gov, n.d.).

Both the Moderna and Pfizer/BioNTech vaccines utilize mRNA to code for a mutated version of the COVID-19 virus that can be easily targeted and eliminated by the immune system. This is done by the naturally occurring T and B cells, which produce specifically designed COVID-19-attacking antibodies, proteins that attack the virus directly (Nance & Meier, 2021). These vulnerable viruses cannot be coded for naturally and require the use of specially-modified mRNA, the synthesis and utility of which must be intensively researched before having a comprehensive enough understanding to learn how to apply it to medicines.

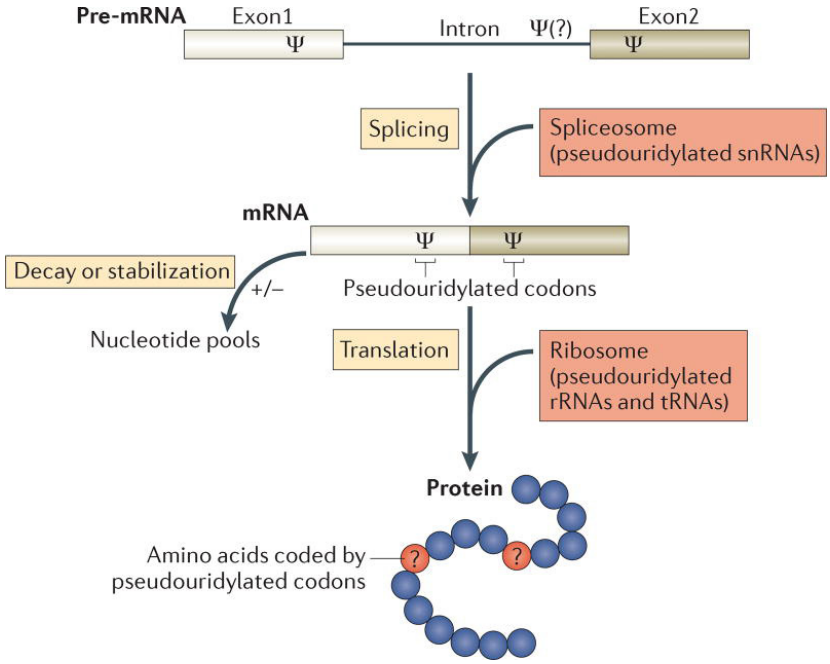

Figure 2. Effects of Pseudouridine in mRNA and protein expression (Karijolich et al., 2015).

Moderna's most prominent complaint is that Pfizer and BioNTech utilized N1-methylpseudouridine, a modified mRNA that is critical in the effectiveness of the vaccines. RNA is composed of four building blocks, also known as nucleotides, which are adenosine, cytosine, guanine, and uracil; all of them can be modified in numerous ways to have different effects on how the RNA is recognized and responded to by various proteins (Roundtree et al., 2017). These four building blocks are the nucleobase section of nucleotides, which is the entire structure of each individual component of RNA, and when combined in different orders, code for the synthesis of different proteins. The N1-methylpseudouridine modification, which alters uridine, prevents the mRNA from being degraded by the body's natural defense system. This modification also increases the mRNA's ability to translate genes (Pederson, n.d.). This modification, while not the only mRNA modification present, also increases the safety profile of the vaccine, which was crucial in both vaccines being granted approval for emergency use by the FDA (Fang et al., 2022).

The N1-methylpseudouridine modification, which alters uridine, prevents the mRNA from being degraded by the body's natural defense system.

N1-methylpseudouridine has these unique properties due to two significant chemical differences from uridine. The first change is that the nucleobase of N1-methylpseudouridine is rotated 180 degrees, allowing for the entire molecule to be more flexible as the new bond between the nucleobase and sugar ring, another component of the nucleotide, is less rigid. This increased flexibility gives the molecule the ability to bind more easily to other nucleobases and to be identified by proteins. The most noticeable change, the extra methyl group bonded to the nitrogen in the first position, creates another hydrogen bond donor that makes the N1-methylpseudouridine able to undergo

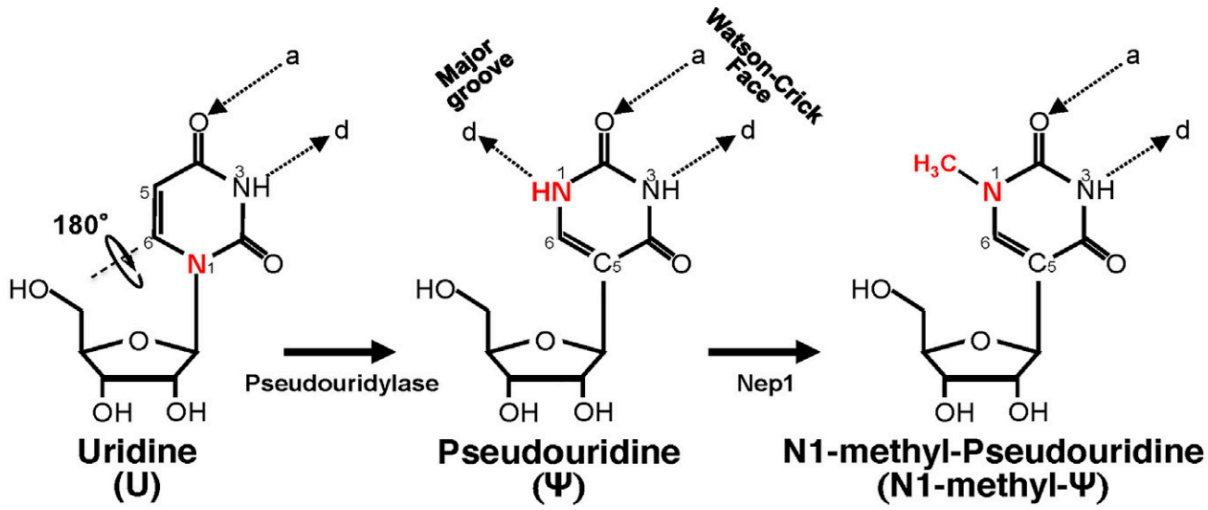

Figure 3. N1-methylpseudouridine, one of the RNA modifications in Moderna's patents that is also present in Pfizer's/BioNTech's COVID-19 vaccines. The differences between N1-methylpseudouridine are highlighted, specifically the rotation of the nucleobase and addition of the methyl group on the N1 (Morais et al., 2021).

more base pairing as well as improving other attributes that result in a more stable mRNA molecule (Morais et al., 2021). These two changes allow the vaccine to be more active than if the modification wasn't present. This modification also improves the vaccine mRNA translation by causing the mRNA itself to live longer in the cell. The longer the COVID-19 vaccine mRNA is present, the more it can be translated, creating a stronger immune response. N1-methylpseudouridine also decreases the rate at which mRNA is translated, which is ideal when considering that this mRNA is more stable within the body. These impacts from N1-methylpseudouridine prevent the immune system from reacting too much to the vaccine, which helps patients avoid severe allergic reactions and even anaphylactic shock. It should be noted that N1-methylpseudouridine is not always a productive modification with regards to other mRNAs (Nance & Meier, 2021).

It is important to note that neither company originally discovered pseudouridine, which was discovered in 1957, or N1-methylpseudouridine, which was discovered to be present in a variety of types of RNA in 2014 (Carlile et al., 2014; Cohn & Volkin, 1951). Since N1-methylpseudouridine and its uses were already old discoveries by the time Moderna was given intellectual property rights over it for the use of COVID-19 vaccines, the lawyers representing Moderna will have to prove that they were the first to use this modification in this way as well as proving that Pfizer and BioNTech intentionally copied this technology. Meanwhile, the lawyers representing Pfizer and BioNTech will have to persuade the judge that they did not copy Moderna's protected technology and that Moderna should not legally be given the intellectual property right over N1-methylpseudouridine.

But if Moderna's patents are not upheld in this case, then any biotechnology or pharmaceutical company can utilize the positive effects of N1-methylpseudouridine.

Since all of this research will require a significant amount of time and money, companies that have made novel discoveries are eager to gain and retain the intellectual property rights to their discoveries. This ensures that they do not lose any profits to companies that may copy their work. While no specific part of the general vaccine process can be protected under a patent, the composition of the vaccines can be protected, forcing other companies to invent their own unique vaccine formulas. Overall, regardless of the outcome of the case, these scientific developments will inspire other companies to pursue different modifications in their vaccines. This is a positive outcome, regardless of whether or not Moderna's patents are upheld in full. Ultimately, more vaccines will likely be made by other companies containing different mRNA modifications because Moderna has

proven that mRNA modifications are an effective vaccine design. If the courts rule in favor of Moderna, other companies will be forced to pursue utilizing different mRNA modification, but if Moderna's patents are not upheld in this case, then any biotechnology or pharmaceutical company can utilize the positive effects of N1-methylpseudouridine.

N1-methylpseudouridine is explicitly stated as an essential component of one of the three primary patents in this lawsuit, as every uridine nucleotide present in the vaccine is replaced by N1-methylpseudouridine (ModernaTX, 2021). However, this is only a fraction of the scrutinized science behind the vaccines that the lawsuit covers. This case will result in a final judgment on whether or not Pfizer and BioNTech copied Moderna's effective vaccine, especially with both vaccines containing N1-methylpseudouridine as an element, as well as whether Moderna really deserves to have the intellectual property rights over N1-methylpseudouridine and the other components of the vaccine. This will undoubtedly have massive ramifications on the pharmaceutical and scientific world as a whole since all mRNA modifications have a wide range of uses, which could potentially be limited depending on how the judge rules. Depending on the outcome, this lawsuit could result in the revisitation on the ethics of patenting and if it really contributes to the development of new therapeutics. ❧

AUTHOR BIO

Ethan is a senior majoring in Chemistry. His interests lie in bringing medicine to the market, specifically the drug development process vand intellectual property components.

Edited by Siya Malhotra, Helen Griffith, and Dr. Johnathan Crane

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Beyond the metaverse: The future of virtual reality in surgery

CLAIRE ZEGGER
Staff Writer

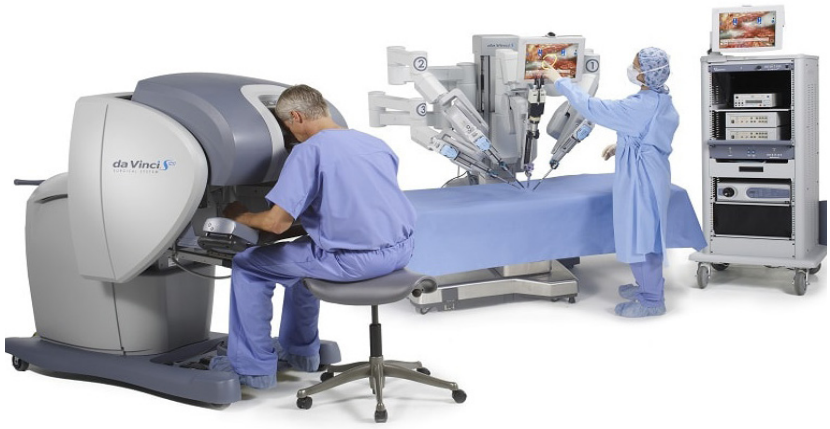

Figure 1. The Da Vinci robotic surgical system, which includes a surgical arm (right) and a separate surgeon console (left).

As the capabilities of modern technology soar to new heights, it is no surprise that virtual reality is revolutionizing the surgical field. Simulation is becoming increasingly common in surgical training as a safe and effective method for novice surgeons to learn how to use robotic surgical equipment. The implementation of virtual reality to plan and practice complex surgeries is also making headlines. In 2022, a team of surgeons in Brazil successfully separated three-year-old conjoined twins with the help of virtual reality (McCallum, 2022). In this case, virtual reality enabled surgeons from all over the world to tune into the same operating room to assist in the procedure. Not only is virtual reality training improving surgical outcomes, but it is also extending the boundaries of what is possible in the realm of surgery.

Since the 20th century, equipment in the operating room has become increasingly sophisticated. Laparoscopic surgery, a technique that involves creating small incisions through which a surgeon operates with the help of a camera and other appendages, is widely used because it is minimally invasive and accelerates recovery time (NHS, 2018). Robotic-assisted surgical systems combine the concepts of laparoscopic surgery with machinery capable of extremely delicate movements that extend a surgeon's capabilities without compromising patient safety. To this end, robotic-assisted surgical systems have made great strides in the surgical field; they allow surgeons to perform difficult procedures without increasing operation risks or recovery time.

Currently, there are three main types of robotic surgical systems that function with varying levels of independence. Systems such as the PROBOT contain pre-programmed procedures that can be conducted with substantial independence, requiring only oversight from a human operator. Other systems involve a combination of pre-programmed procedures and physical guidance by a surgeon. Finally, robotic systems such as the da Vinci lack any pre-programmed procedures but act as a sophisticated appendage controlled by the surgeon (Lane, 2018). The predecessor of the da Vinci platform was initially invented to allow surgeons to remotely treat wounded soldiers on the battlefield (Lane, 2018). The da Vinci system consists of an arm and a camera, controlled by the hand movements of the surgeon through a console. While operating, the surgeon does not look directly at the operating site, but rather at a digital representation on the console based on the images obtained by the endoscopic camera and anatomical markers superimposed by the system (Azizian et al., 2020). The system offers the benefit of a more precise and less invasive surgical procedure. It not only allows the surgeon to operate through a much smaller incision, but it also "can modify the signals, so as to filter out the surgeon's normal physiological tremor, or to scale down their motions for enhanced precision" (Azizian et al., 2020). This characteristic is tremendously helpful because of the intense level of precision that many surgical procedures require. Although the da Vinci system is classified as a robotic surgical system, augmented real-

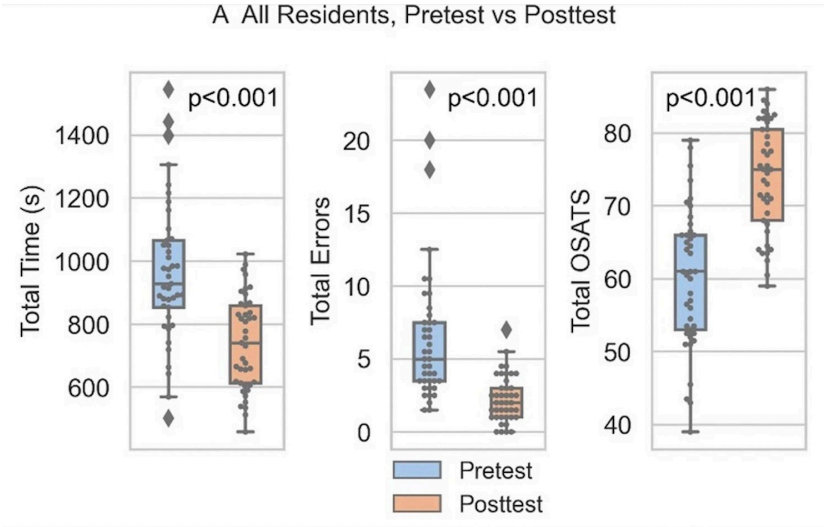

Figure 2. Evaluating performance of surgical residents before and after undergoing VR training (Radi et al., 2022).

ity enhances the robotic features to optimize surgical success.

With the growing prevalence of robotic-assisted surgery, surgical residents need a safe and effective way to practice the complex techniques of robotic surgery outside of the operating room. This demand for more sophisticated training platforms was met by the development of virtual reality simulation training. Intuitive, the same company that owns da Vinci, developed SimNow, a virtual reality curriculum for surgical trainees to master the techniques required to use robotic surgical equipment (Radi et al., 2022). In a two-year retrospective study by the University of Texas Southwestern Medical Center, the outcomes of 41 surgical residents trained using the SimNow VR robotic simulator yielded promising results. According to the researchers, "after performing VR training, residents showed major improvements in total time, total errors, and total OSATS [Objective Structured Assessment of Technical Skills] on the inanimate drills," indicating that skills they learned using virtual reality were transferable to a physical environment (Radi et al., 2022). These results are encouraging for many reasons. First, virtual reality is a cost-effective method to practice surgery outside of the operating room. Second, it minimizes the risk of potentially damaging equipment and prioritizes patient safety. Most importantly, virtual training provides skills that translate effectively into the surgical environment, ensuring that residents are well-equipped for the demands of human surgery.

The power of virtual reality is that it can reconstruct a personalized model of the patient prior to their surgery.

Even more innovative than the advancements of virtual reality in surgical training are the strides it has made in the operating room. From orthopedics to gynecology, virtual reality techniques are being implemented across many surgical disciplines. The power of virtual reality is that it can reconstruct a personalized model of the patient prior to their surgery. Generally, the model is constructed from scans and imaging and is used to plan and practice the surgical procedure to maximize success (Guerriero et al., 2018). This preoperative practice round enables surgeons to detect abnormalities and plan accordingly to avoid potential complications. With the help of virtual reality, pioneers in the surgical field are taking a stab (with their scalpel) at ambitious surgeries—and succeeding. In 2022, a team of surgeons successfully separated 3-year-old craniopagus twins, fused at the skull since birth. In a groundbreaking feat of international collaboration, surgeons from across the globe tuned into a virtual operating room to assist in this unprecedented surgery, which took nearly 27 hours to complete (BBC News, 2022). Prior to the surgery, the surgeons spent hours studying the anatomy of the twins and practicing surgical techniques on a virtual model of the twins consisting of CT and MRI scans. In this case, virtual reality technology not only allowed the surgeons to plan in advance for any complications, but also enabled widespread collaboration, resulting in surgical success.

With the help of virtual reality, pioneers in the surgical field are taking a stab (with their scalpel) at ambitious surgeries—and succeeding.

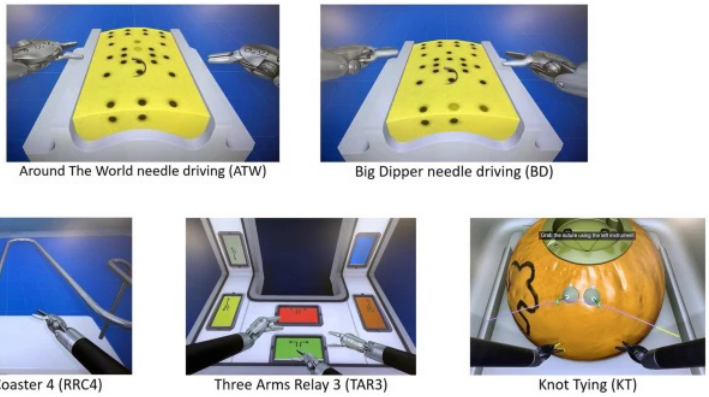

Figure 3. Examples of SimNow virtual reality training exercises to help surgeons practice maneuvering robotic equipment (Radi et al., 2022)

On a case-by-case basis, virtual reality appears to have a huge impact on surgical outcomes. The implementation of virtual reality as a training technique and in the operating room has been low risk and has been shown to maximize patient safety. However, most studies on the effect of having virtual reality as an additional resource in the operating room examine only a few cases, making it difficult to draw statistically significant conclusions. With respect to virtual reality simulation training, literature on whether this method improves surgical technique more so than traditional training methods is limited, making it difficult to understand the full extent of its benefits. Therefore, while virtual reality will likely not replace traditional training methods in their entirety, it offers significant benefits as a training supplement. From enabling wide-scale collaboration to sophisticated procedures, the capabilities of virtual reality in the operating room offer only a glimpse into the possibilities it holds for the future. ❧

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The power of the pill, considered: The past, present, and future of oral contraception

GRACE WARD
Staff Writer

In 1960, Enovid, a combination pill containing synthetic versions of the sex hormones estrogen and progestin, was approved by the US Food and Drug Administration (FDA) as an oral contraceptive (OC) that prevented ovulation (Enovid: The First Hormonal Birth Control Pill | The Embryo Project Encyclopedia, n.d.). Though it was initially only prescribed to married women, the novel contraception transformed the lives of women across the world. In the years since Enovid's introduction, much has changed regarding OCs, including pharmacological formulations, reasons for prescription, the pill's societal role, and clinical understanding of its side effects. OC's rise in popularity was as contentious as it was revolutionary, and this contention exists even now, over 60 years after Enovid was introduced. Furthermore, the role of contraception varies greatly between sociocultural groups, both within the US and globally. Regardless of criticism, OC's impact on women's health and gender equality is undeniable. Understanding how the pill's social and biological impacts have changed over time provides fascinating insight into the intersection between medicine and social trends, and, more importantly, is essential to future scientific and social progress regarding OC and reproductive health.

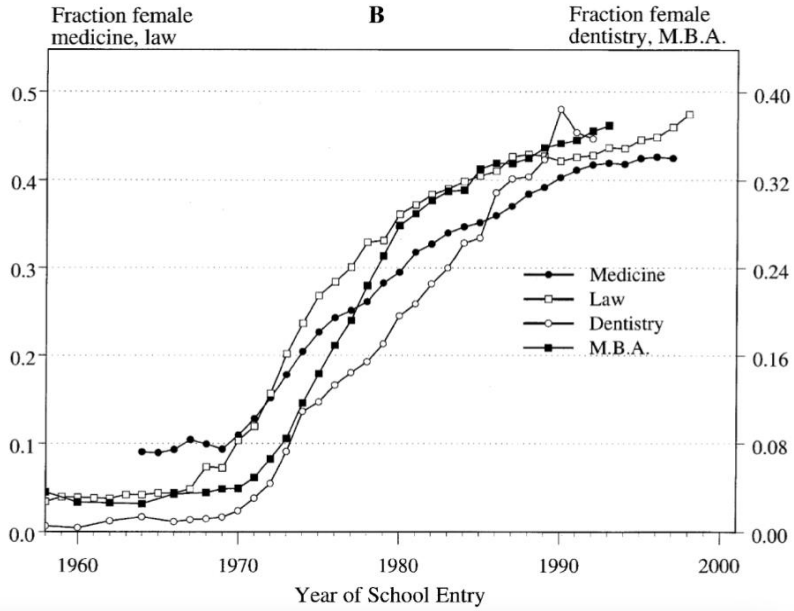

Figure 1. Number of first year female professional students as a fraction of total professional enrollment (Goldin, Katz 2002).

The introduction of the pill granted women more agency over family planning and reduced the risk of unplanned pregnancies, thus women's presence in the professional world increased dramatically. Before OC, women bore the uncertainty of pregnancy risk or abstained entirely if they wanted to pursue long-term career goals. As Figure 1 demonstrates, the fraction of female students in professional degree programs increased in the years following Enovid's approval (Goldin & Katz, 2002). As activist Grace Atkinson remarks in the article that conceptualized 'second-wave feminism,' "it's just not honest to talk about freedom for women unless you get the child-rearing off their backs" (Lear, 1968).

The fact that the onset of second-wave feminism—a movement focusing on workplace equality and reproductive rights—coincides so closely with OC's rise to popularity is no coincidence, either.

Until the 1980s, OC was advertised exclusively as contraception, but in more recent years pharmaceutical companies' advertisement of the pill has shifted to focus on its non-contraceptive effects (Watkins, 2012). This rebranding of OC as a 'lifestyle drug'—a medication "designed to improve a person's quality of life by treating less serious conditions"—focuses on its use as a treatment for heavy periods, dysmenorrhea (painful menstruation), acne, and premenstrual syndrome (PMS) (Dhont, 2011; Watkins, 2012).

Enovid was initially marketed as a treatment for gynecologi-

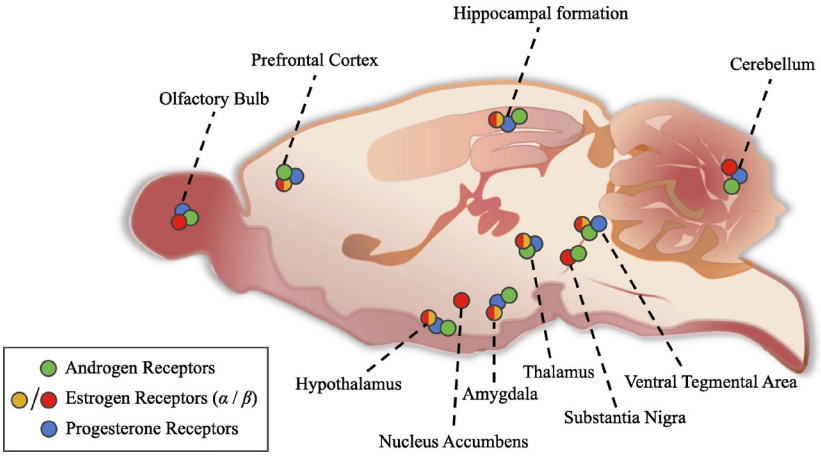

Figure 2. Distribution of cells containing androgen, estrogen, and progesterone receptor mRNA in an adult female rat brain (sagittal view) (Hilz, 2022).

cal conditions prior to its approval as birth control, but after 1960 it became primarily known for its contraceptive properties until the 'lifestyle drug' marketing shift (Enovid: The First Hormonal Birth Control Pill | The Embryo Project Encyclopedia, n.d.). The social deterrents in the 1980s (the AIDS crisis and abortion debates) along with the fact that pharmaceutical companies were granted permission to advertise to consumers around that time, largely explain why the pharmaceutical industry began to focus its attention on the pill's new 'brand' as a lifestyle drug in the 1990s (Watkins, 2012). It is fascinating to note that, through the rhetoric of female empowerment used in the advertisement of OC as a lifestyle drug, the modern woman's use of OC as a way to maintain control of her body mirrors the female agency that it originally fostered in the 20th century (Kissling, 2013). The source of empowerment garnered from OC has changed extensively over time (control over contraception to control over bodily function), and this example of the sociological trends of women's health demonstrates how modern medicine and society greatly inform one another.

Although the use of OC as a non-contraceptive treatment has improved the quality of life of countless individuals, it can be dangerous to treat the pill as a panacea without seriously considering the effects of its use. One example of possible concern regarding the use of OC as a lifestyle drug is its use in adolescents. Many of the non-contraceptive conditions for which OC is prescribed, such as dysmenorrhea and acne, are especially prevalent during adolescence. Since the rebranding of the 1990s OCs have frequently been prescribed to teenagers to treat these issues despite the fact that research is lacking on the long-term effects of adolescent OC use (Davis & Westhoff, 2001; Hooff et al., 1998). The availability of contraception to adolescents is undeniably an important development in reproductive health, but it is important to consider the implications of under-researched adolescent OC use. For instance, studies have found that adolescent OC use is correlated with short- and long-term susceptibility to depression (Anderl et al., 2020). OCs alter estrogen and progestin (the synthetic analog of progesterone) levels in the body. Because the brain, which extensively develops during adolescence, contains many estrogen and progesterone receptors, it makes sense that using the pill during such a critical period of development may have substantial long-term neurological or physiological effects (Figure 2). Availability of OCs to adolescents certainly has many benefits, but this finding emphasizes the clinical importance of considering a patient's physiological nuances in prescribing treatment, as the body and brain of an adolescent girl are an entirely different pharmacological playing field than those of an adult woman.

Our use and understanding of OC have proven to be inextricably linked to medical advancements, social movements, and political climates.

For many individuals, decreased quality of life due to side effects is a fairly common reason for discontinuation of the pill (Westhoff et al., 2007). Commonly reported side effects nausea, weight gain, abnormal menstruation/bleeding, mood disturbances, and acne. Studies have also found more serious potential side effects of OCs, such as thrombosis and breast cancer, but these are not commonly cited as reasons for discontinuation (Frye, 2006). Despite the fact that so much anecdotal evidence

for these minor side effects exists, many of them are backed up by little scientific evidence, leading to frequent dismissal of patient concerns and experiences in clinical settings as 'myths' (Stevens, 2018). This is particularly precarious because it is important for clinicians to provide patients with adequate and accurate information about OCs, but complete dismissal of patient experiences can foster feelings of distrust and disconnect between patients and providers.

The lack of pharmaceutical innovation of OC in the past 40 years seems to indicate that the pill is already perfected. However, women still commonly discontinue OC use due to adverse effects, and studies show that nearly half of unplanned pregnancies occur due to incorrect contraception use (Tanne, 2008; Westhoff et al., 2007). Clearly, the pill is not 'good enough': empirical evidence continually suggests that its side effects are relevant, and information about proper OC use is not effectively disseminated. Despite this, the momentum of research and development for contraception in the United States has largely been at a standstill for years. The 1980s brought about lower dosages and new formulations, and over time various new drug delivery methods, such as intrauterine devices and implants, have been introduced, but broadly speaking the innovation of OC does not seem to live up to the magnitude of its societal impacts (Liao & Dollin, 2012). By 1987, less than 20 years after Enovid's 1960 FDA approval, only four drug firms in the world (and only one in the US) were carrying out birth control R&D (Watkins, 2012). There are many reasons that OCs development is not largely pursued by pharmaceutical giants: they are already profitable as is and function well enough, aging population trends imply that investment in young 'healthy' demographics is not advantageous, and the commitment to studying the long term effects of OC is not deemed worthwhile. Nevertheless, it is clear that we still have much to learn about the complexities of OC's mechanism and function, and there are many improvements to be made when it comes to pharmaceutical development and consumer education about OC.

Regardless of these challenges, it is difficult to imagine a corner of American society that isn't touched by the power of the pill.

The creation of OC in 1960 undoubtedly transformed the world; its place in our society is so central that it is able to claim the title, the pill. As such, its effect on society, and society's effect on it, is ever-changing. Despite this mutability, research and development have fallen behind due to assumptions that OC is already 'good enough.' However, we have a long way to go. The effects of long-term use, use in unprecedented populations, discrepancies between patient experience and scientific literature regarding side effects, and countless other aspects are far from being fully understood. As Carl Djesseri puts it, "the pill is a stone thrown into water that has produced ripples and waves way beyond any reasonable expectation" (Djerassi, 2007). The pill has always found a way to make waves, regardless of social context, clinical challenges, or political constraints. Doubtless, the pill has the potential to spark social movements, transform lives, and inspire change for generations to come. To lay the foundations for the reproductive health of future generations, it is the scientific community's responsibility to promote research, development, and education about OC, fostering further innovation and discovery. ❧

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Grace Ward is a third-year majoring in Biology and Anthropology with Human Biology. She is interested in biomedical research with a focus on physiology and pharmacology.

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Positions on the poop pill: Stigma surrounding fecal microbiota transplantation

JUSTIN HAHM
Staff Writer

It is estimated that approximately 48,000 people in the United States receive Fecal Microbiota Transplantation (FMT) annually. FMT is the administration of a solution of fecal matter into the intestinal tract of a recipient in order to directly change the recipient's microbial composition (Gupta, 2016). Despite public presumptions of pseudoscience, the transplantation of stool as a legitimate medical treatment has been dated back to 4th century China (De Groot, 2017). In modern medicine, FMT is ubiquitous for the treatment of recurrent and lethal infections. Recent scientific studies have continued to corroborate the medical efficacy of this treatment option in the case of antibiotic failure for severe GI bacterial infections. However, the range of applications for FMT continues to expand. While the US Food and Drug Administration (FDA) has begun to authorize the first commercial FMT products on American shelves, medical professionals continue to grapple with effectively debunking the unsanitary and pseudoscience stigmas held by the general public when recommending FMTs.

FMTs provide a successful alternative to the excessive antibiotic prescriptions associated with modern medicine as shown by novel GI research. FMT has largely remained as a later line treatment to antibiotics because of social aversion and cost reasons. However, in 2017, the Centers for Disease Control (CDC) reported a $1 billion price tag for the treatment of CDI with an emphasis on the high prices of excessively prescribed antibiotics. The most apt and prevalent usage of FMT is for recurrent bacterial infections caused by Clostridioides difficile (CD), a gram-positive spore-forming bacterium. The infection normally reappears following a first-line treatment of antibiotics such as vancomycin. CD infections are a part of the encroaching and concerning wave of antibiotic-resistant microbe infections. The uncertainty regarding the usage of FMT results from inconsistent standard protocol in addition to lacking literature on the long-term health outcomes of its usage. Systematic reviews of the treatment have revealed that FMT can have upwards of 90% success rate for the treatment of CDI which is significant compared to the variable 49% to 100% range of efficacy for vancomycin (Quraishi, 2017).

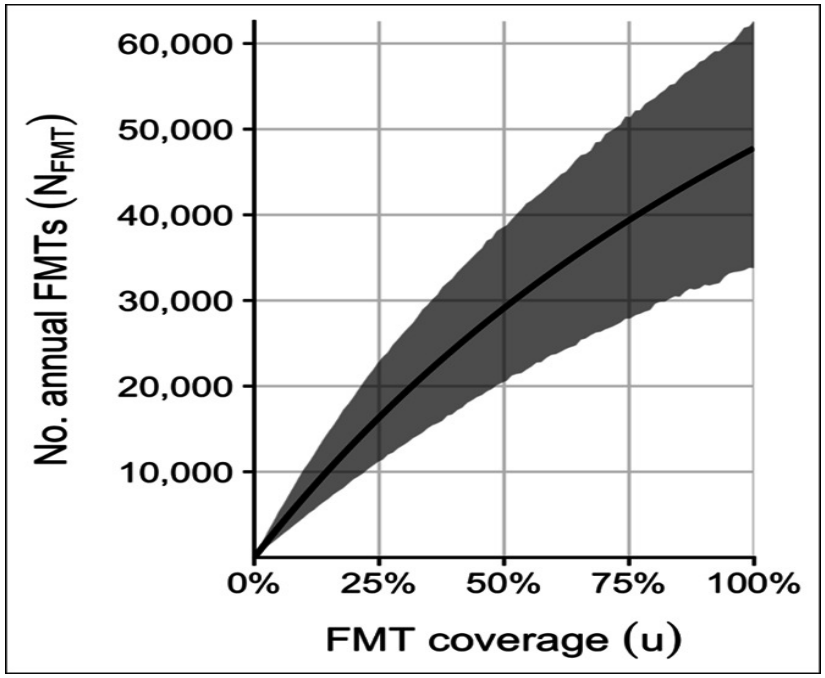

Figure 1. FMT coverage of CDI is strongly correlated with the number of annual FMT used in the US.

However, in 2017, the CDC reported a $1 billion price tag for the treatment of CDI with an emphasis on the high prices of excessively prescribed antibiotics.

Findings on the efficacy of FMTs for CDI have resulted in the expansion of its application for numerous bowel diseases, such as ulcerative colitis. Ulcerative colitis, an inflammatory bowel disease (IBD) can also respond to FMT. Dr. Randy Longman, director of the Jill Roberts Center for Inflammatory Bowel Disease at Weill Cornell Medicine, stated, "Fecal microbiota

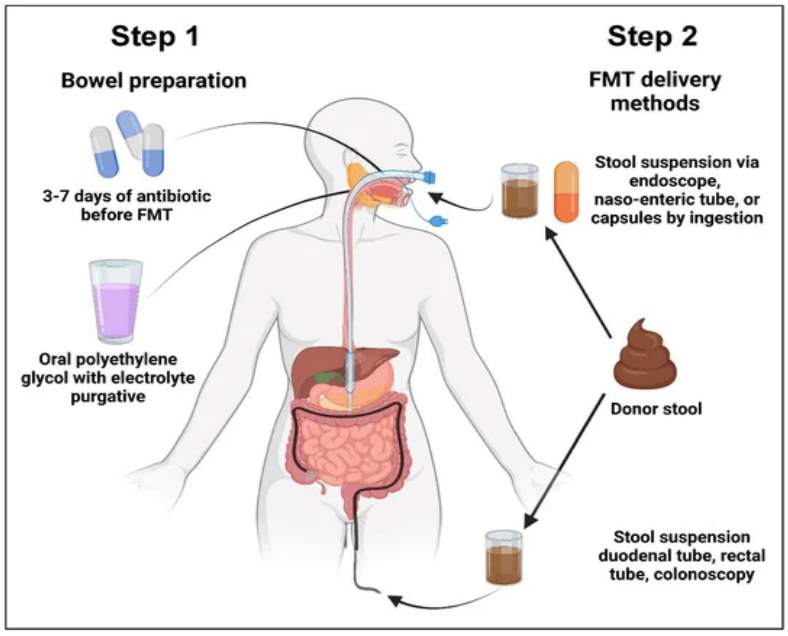

Figure 2. There are multiple methods of preparation and administration of FMT in patients.

transplant has been shown to be effective in several clinical trials, but ultimately we need to identify the specific microbial factors that make it work and focus on delivering those" (Researchers, 2023). In 2022, researchers were able to isolate the exact bacterial species, Odoribacter splanchnicus, in the stool responsible for effective treatment, demonstrating the potential of this medication in resolving gut issues (Lima, 2022). Growing evidence even suggests that FMT may relieve other diseases such as Parkinson's (Xue, 2020).

There are barriers to implementing FMT that the FDA has previously reinforced. In 2013, the FDA demanded an investigational new drug application for FMT usage, meaning physicians would have to submit an additional application each time they requested the treatment (CRITICAL, 2014). This point of contention was later relieved with the approval by the FDA to allow for FMTs in the case of recurrent and refractory CDI. However, there might have been precedent for having these barriers in place. For instance, during the screening of stool donors life-threatening situations have been uncovered. In 2019, the FDA reported instances of two immunocompromised adults receiving E. coli. Additionally at the height of the pandemic, the FDA released a report that stool could transmit SARS-Cov-2 which limited the accessibility of stool banks.

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Mistrust of the treatment ultimately lies in social stigmas that healthcare professionals and patients subconsciously hold. Dr. Judy Stone, an infectious disease physician, calls this the "'ick' factor". She states, "Thus far, resistance to transplants I have recommended has not come from patients or their families, who are desperate for relief. It has come from other health care workers, especially physicians, who seem to find the idea particularly distasteful." In an experiment performed on a focus group of 15 adult patients and 7 parents of children with colitis from the University of Chicago Medical Center, many felt initial distaste and the "yuck factor," which is quite similar to Dr. Stone's perspective of an "ick factor" (Kahn, 2011). However, the study found that participants eventually understood the perceived benefits and feasibility outweighed the risks. This gives insight that better communication from educated healthcare professionals can allow for more acceptance and willingness to receive FMTs.

The first wave of FMT products, if given FDA approval, could lead to more cost-efficient and effective medical treatment. On November 30th, 2022, the FDA began this trend with the approval of Rebyota, the first FMT that has been in compliance with their regulations. Peter Marks, M.D., Ph.D. Director of the FDA's Center for Biologics Evaluation and Research has stated,"Recurrent CDI impacts an individual's quality of life and can also potentially be life-threatening. As the first FDA-approved fecal microbiota product, today's action represents an important milestone, as it provides an additional approved option to prevent recurrent CDI (Commissioner, 2023)." Rebyota is administered rectally; however, many patients

are, understandably, not eager to employ this method of administration. New trials exist now for a "poop pill" which would provide an alternative to the traditional administration of FMT. This pill called SER-109, produced by Seres Therapeutics and derived from human feces, has filed for FDA approval and could completely alter the stool bank system that has been foundational to this treatment (Servick, 2022).

Medical professionals must collaborate on making this information accessible to and more cowmfortable for the general public and each other. Our evolving knowledge of FMTs has made it clear that it is not just pseudoscience but a just as legitimate treatment as a blood transfusion. It is the responsibility of the healthcare community to spread accurate and legitimate information on its usage. In the foreseeable future, FMTs and other microbiome treatments may become more relevant decisions for a variety of diseases. Furthermore, as more research and more effective products continue to be released, the social stigmas that have surrounded FMTs must be recognized so they can more appropriately be addressed. ❧

AUTHOR BIO

Justin is a second year double majoring in Economics and Biology. His interests are in autoimmune conditions, controversial big pharma policies, and economic issues pertaining to healthcare equity.

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The role of purinergic signals in biological processes and as a catalyst for disease

UMA OBALAPURAM
Staff Writer

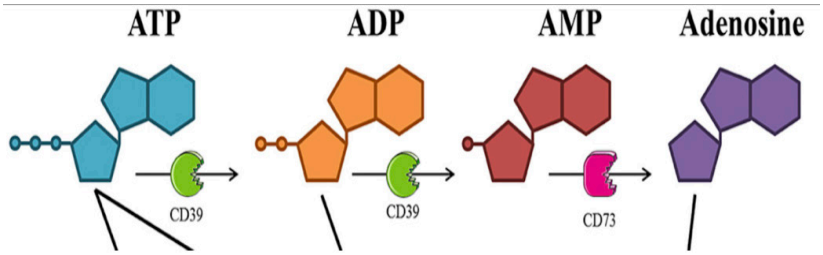

Figure 1. This shows the structure of purinergic signals. All the molecules have a ribose sugar and a nitrogenous base; some have phosphate group(s) added depending on their level of phosphorylation. (Thompson, 2021)

Purinergic signals are some of the oldest signaling molecules known to life forms on earth. These small molecules provide a wide variety of functions in the cell cycle, development, metabolism, and immune function. Purinergic signaling molecules come from DNA nucleotides that take part in many biological and metabolic pathways, making them very useful to the body, but also very dangerous. One malfunction or mutation in a purinergic signal can cause a multitude of diseases ranging from gout to cancers. Purinergic signals have many different functions that are necessary for life; however, they can also lead to a host of illnesses if mutated or disturbed.

Purinergic signals are a class of extracellular signaling molecules derived from adenine and guanine DNA nucleotides. These molecules have a deoxyribose sugar attached to either a guanine or adenine base; this can include adenosine/guanosine, adenosine/guanosine monophosphate (AMP/GMP), adenosine/guanosine diphosphate (ADP/GDP), or adenosine/guanosine triphosphate (ATP/GTP).

Purinergic signals can leave the nucleus and their originating neuronal or neuroendocrinal cell using exocytosis (Burnstock, 2009). After purinergic signals leave the cell, cell-surface enzymes, known as ectonucleotidases, hydrolyze these molecules to remove phosphate groups. Once the appropriate number of phosphate groups has been removed, the molecule moves to the target cell or receptor (Beldi 2008). In the target cells, there are three main types of receptors for Purinergic signals: P1, P2X, and P2Y. P1 receives adenosine signals and is a G protein-coupled receptor. P2X receives ATP signals and is a ligand-gated ion channel. P2Y is a G protein-coupled receptor and can be activated by ATP or ADP (Eltzschig, 2012). Although both guanine and adenine-derived molecules are considered purinergic signals, not much research has been done on the receptors used for guanine nucleotides or on the pathways it affects, so this article will focus mainly on adenine-purine signals.

Purinergic signals have many different functions that are necessary for life; however, they can also lead to a host of illnesses if mutated or disturbed.

Although purinergic signals may seem simple on the surface, they are integral to a host of biological functions. These signaling molecules are essential in cell proliferation, differentiation, motility, and death. They are also integral to regeneration, wound healing, epithelial cell turnover, and DNA methylation (Burnstock, 2009; Linden, 2019). They play a central role in the circulatory system, controlling heart rate, contractility, and coronary flow. The heart even has multiple types of purinergic signal receptors with different functions (McIntosh, 2012). Another system in which these signaling molecules play a large role is the immune system. Purinergic signals are important immune activation checkpoints. They can serve either as immunostimulatory or immunosuppressive depending on the signal type and the receptors present on the target cell (Junger, 2011). In addition to these major functions, purinergic signals are also present in the digestive, endocrine, renal, respiratory, and skeletal systems, where they play minor roles. These molecules exert powerful forces in the human body as they serve such versatile functions; however, this also creates much room for error.

Since purinergic signals participate in so many different biological and physiologi-

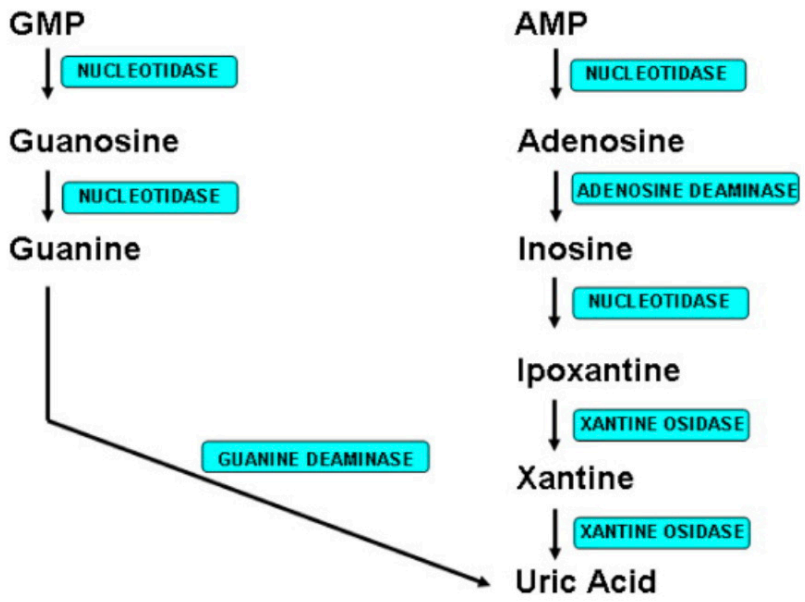

Figure 2. This diagram shows how guanine and adenine nucleotides become uric acid, the precursor to urate salts. (Maiuolo 2016).

cal pathways in the body, one mutation in the signals or cell receptor(s) can have disastrous effects. Mutations or malfunctions in purinergic signaling are known to cause a variety of illnesses—Alzheimer's disease, gout, and tumors. In patients with Alzheimer's, purine receptors in the frontal cortex (responsible for voluntary movement, expressing language, and executive functions) are present in increased amounts, while receptors in the dentate gyrus (part of the temporal lobe, responsible for episodic memory) are decreased (Burnstock, 2009; del Puerto, 2013). Changing the number of receptors present in parts of the body for purinergic signals changes how frequently that organ can respond to the signal. Increasing the number of receptors will increase the number of times the pathway and response are triggered by the signal, and decreasing the number of receptors will lead to the opposite effect; this change in responses causes different symptoms associated with Alzheimer's.

Since purinergic signals participate in so many different biological and physiological pathways in the body, one mutation in the signals or cell receptor(s) can have disastrous effects.

Another disease rooted in purinergic signaling malfunction is gout. Gout is caused by the accumulation of urate salts, a salt formed from uric acid, in various joints in the body. Gout is associated with the intake of purine-rich diets, as purine molecules are later metabolized into uric acid as pictured to the left. Uric acid normally is excreted from the body in the form of urine. However, if a person consumes a purine-rich diet or loses the ability to properly metabolize these molecules through loss-of-function or gain-of-function mutations in their urate transporters, then the uric acid will be stored in the body, primarily in joints such as the knees, ankles, and toes and in organs such as the kidney (Huang, 2021). Most gout medications target purine metabolism or purinergic signal receptors to decrease the likelihood of large urate deposits forming (Huang, 2021).

One major ailment marked by differences in purinergic signaling is tumor formation. Extracellular levels of adenine derivatives increase in response to trauma, inflammation, or hypoxia, acting as an alarm signal to ensure that the body is ready to fight against any dangers or harm. However, if a mutation or malfunction occurs in the purine metabolism pathway, then increased amounts of these adenine derivatives will remain in the bloodstream for longer than necessary, which can lead to disastrous outcomes, especially in people with higher risks of cancer or disease (Antonioli, 2013). One of the hallmarks of cancer is an increased amount of adenosine and adenine derivatives in the bloodstream. These increased amounts of adenine purinergic signals in the bloodstream lead to immunosuppression, meaning the immune system will not be activated and the body will not be able to fight the cancer (Di Virgilio, 2017). In fact, this extracellular adenine also promotes the growth of tumor cells and metastasis through specific receptors expressed on cancer cells (Antonioli, 2013). This lethal combination of purine signal-mediated support of tumor growth and increased immunosuppression makes cancer a deadly disease. Furthermore, this

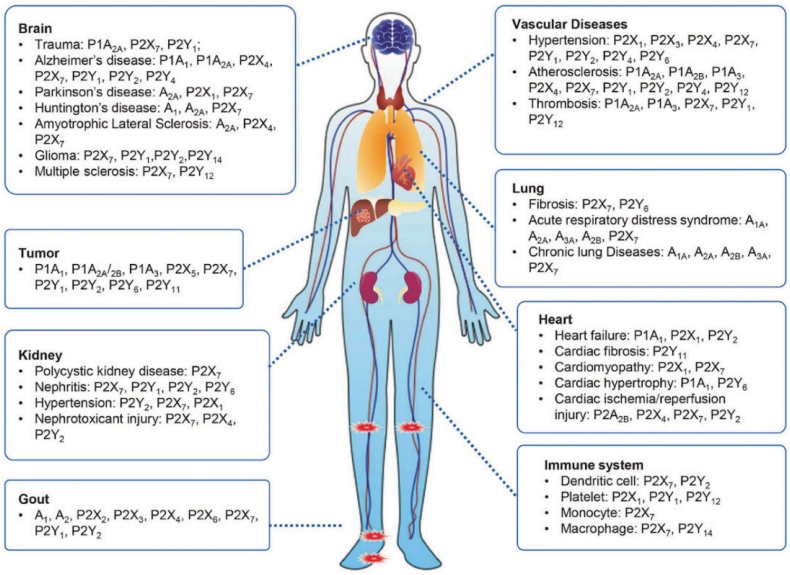

Figure 3. This shows an overview of the mutations in purinergic signal receptors which cause a wide variety of diseases. (Huang 2021).

hijacking of one of the most integral signaling pathways in the human body by the tumor cells is the central focus of many cancer research projects.

Purinergic signals are some of the oldest and most essential signaling molecules known. These molecules have vast functions in the body such as cell differentiation and proliferation, regulating blood flow, activating or suppressing immune function, and much more. They are essential pieces to major biological pathways that keep us alive. However, they are also prone to mutation and malfunction which can cause many different diseases such as Alzheimer's, gout, cancer, and many more. Although purinergic signals are some of the most basic and essential signaling molecules in the body, there is still much we do not know about their function and versatility. Diving deeper into the intricacies of their function in the body would prove to be a very interesting research question. Current medical research is investigating how purinergic signals can be used as cancer therapies, anti-inflammatory drugs, vasodilators, and more. Even better understanding the role of guanine-derived signals is a vast undertaking as little is known about them. ❧

AUTHOR BIO

Uma is a third year majoring in Biology. She is interested in cancer biology, how it affects humans presently, how modern medicine treats malignant tumors, and how that differs from ancient medical practices regarding cancer.

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Pay attention: prenatal drug exposure and pediatric attention deficit disorders

SHREYA RAMANATHAN
Secretary

Attention-deficit hyperactivity disorder (ADHD) is a clinically heterogeneous disorder characterized by inattention, hyperactivity, and impulsivity. Genes known to be involved in this disorder are the D4 dopamine receptor gene, the dopamine transporter gene, and the D2 dopamine receptor gene (Blum et al., 2008). Furthermore, one of the hallmarks of the disorder is a deficiency in the dopamine neurotransmitter, which is responsible for reward pathways in humans. This means that there is general dysfunction in the "brain reward cascade," particularly in the mesolimbic dopamine system, causing the brain to require increased levels of dopamine to avoid unpleasant emotions. These neurobiological characteristics not only implicate executive function—the capacity to complete tasks and meet goals—and working memory, but also increase the risk for addictive, impulsive, and compulsive behavioral propensities. Recent studies have also explored the effect of prenatal substance abuse on the risk and severity of ADHD in these children (Sandtorv et al., 2018).

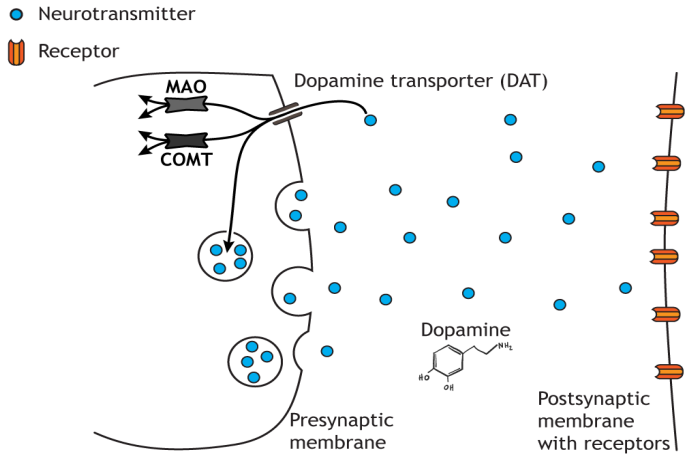

Figure 1: The DAT1 gene codes for Dopamine transporter (DAT) which facilitates transport of dopamine from the postsynaptic membrane back into the presynaptic membrane. DAT1 dysfunction leads to higher dopamine uptake, which causes lower dopamine levels (Henley 2021).

Through these studies, prenatal substance abuse, particularly of dopamine-stimulating drugs such as nicotine, opioids, and cocaine, has been implicated in increased ADHD risk and severity. These drugs alter vital neurological pathways responsible for reward, decision-making, and memory in developing embryos (Garrison-Desany et al., 2022). The occurrence of drug abuse with other factors coincident with prenatal drug exposure such as early childhood trauma and child abuse has also been demonstrated to significantly increase risk and severity. This brief review aims to delineate the neurobiological processes of ADHD and explore how prenatal drug exposure affects ADHD risk and severity in children.

These results provide clear evidence that dopamine-caused reward deficiencies, particularly in the D2 and D3 receptors, play a central role in symptoms of attention and impulse in patients with ADHD.

Although ADHD presents differently across individuals and can evolve from childhood to adulthood, it is primarily characterized by inattention, hyperactivity, and/or impulsivity that can cause impairment in cognitive, behavioral, and interpersonal domains (Volkow et al., 2009). These symptoms are primarily controlled by components in the limbic system, the region of the brain responsible for fundamental behaviors such as motivation and decision-making. One of the primary components of the limbic system is the mesolimbic dopamine system, which controls the release and uptake of dopamine, a neurotransmitter responsible for reward and motivation. This dopamine pathway projects from the ventral tegmental area in the midbrain to the nucleus accumbens, which is considered the neural interface between motivation and action (Volkow et al., 2009). As shown in Figure 1, mutations of two genes involved in the dopamine pathway, DRD4 (mesolimbic neuronal signaling), and DAT1 (facilitates movement of dopamine), cause dopamine pathway dysfunction in patients with ADHD (Gizer et al., 2009).

Hypotheses linking dopamine pathway activity with

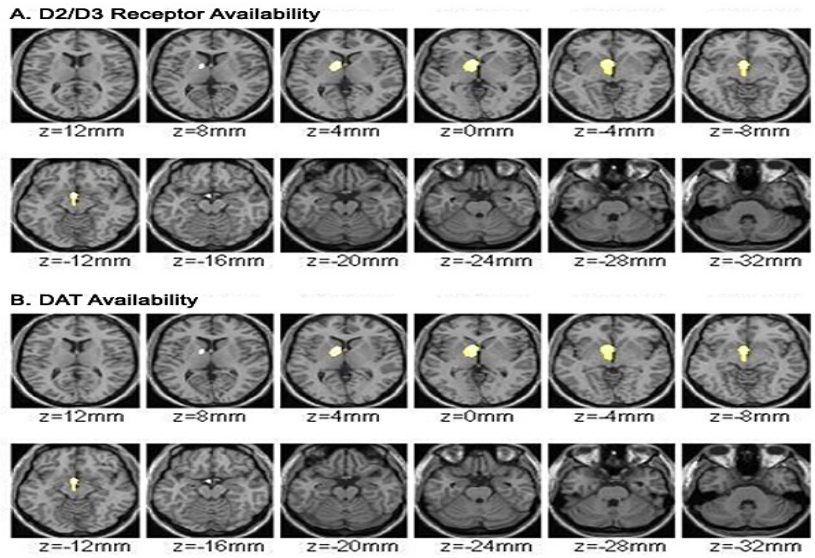

Figure 2: PET scans comparing normal patients (top row A, B) and ADHD patients (bottom row A, B) highlight that individuals with ADHD have lower levels of dopamine D2/D3 and transporter (DAT) availability compared to their non-ADHD counterparts. The yellow regions indicate areas in the brain that differ between the control and ADHD participants (Volkow et al., 2009).

attention deficits are supported by neuroimaging studies focusing on the receptors dopamine D2 and D3 receptors, which are responsible for locomotion, attention, sleep, memory, and learning (D2) and impulse control, attention, and sleep (D3). In a 2009 study, researchers compared 53 never-medicated ADHD patients with 44 health controls using PET scans and ADHD rating scales. Tests were then conducted to assess correlations between these questionnaire results and PET dopamine measurements. Statistic analyses revealed lower D2/D3 dopamine availability in the dopamine reward pathway regions—the ventral caudate, nucleus accumbens, midbrain, and hypothalamus—in ADHD patients compared to the control group as seen in Figure 2 (Volkow et al., 2009). This "significantly lower dopamine transporter availability" indicates that there are significantly lower levels of dopamine release in individuals with ADHD and lower levels of activity in the regions of the brain responsible for decision-making and motivation. Furthermore, there was a strong negative correlation between severity of inattention/hyperactivity symptoms obtained from the ADHD questionnaire administered to the experimental and control group and D2/D3 receptor availability. This means that the lower the dopamine measures, the greater the symptoms of inattention (Blum et al., 2008). These results provide clear evidence that dopamine-caused reward deficiencies, particularly in the D2 and D3 receptors, play a central role in symptoms of attention and impulse in patients with ADHD.

These neural pathways responsible for decision-making, reward assessment, and attentional differentiation are also targeted by substances of abuse such as opioids, nicotine, and alcohol. Although each of these substances targets different regions of the brain, they all function to heighten feelings of euphoria and happiness, lower inhibitions, and alter natural reward pathways. For example, the class of drugs known as opioids includes the drugs morphine, heroin, fentanyl, and codeine, which are prescribed as painkillers, but often abused to increase feelings of pleasure when performing "basic life functions" (George and Kosten, 2002). When an individual takes heroin, oxycodone, or any other opiate, the drug travels through their bloodstream to the brain, where the chemical attaches to mu-opioid receptors found on opiate-sensitive neurons. Primarily, the binding of opioids targets the mesolimbic dopamine system by activating the ventral tegmental area which results in the release of dopamine in the nucleus accumbens. Furthermore, these opioids delay the reuptake of dopamine which heightens and lengthens the feelings of pleasure associated with taking the drug. These memories of heightened and long-lasting memory lead to conditioned associations between the drug and pleasure, leading to cravings for the drug, and ultimately addiction (George and Kosten, 2002).

Because opioids and other substances of abuse such as alcohol and nicotine are highly addictive, pregnant women often continue using such drugs while pregnant, leading to prenatal drug exposure, and further leading to a variety of birth defects including brain damage, learning difficulties, growth restriction, and neonatal drug withdrawal

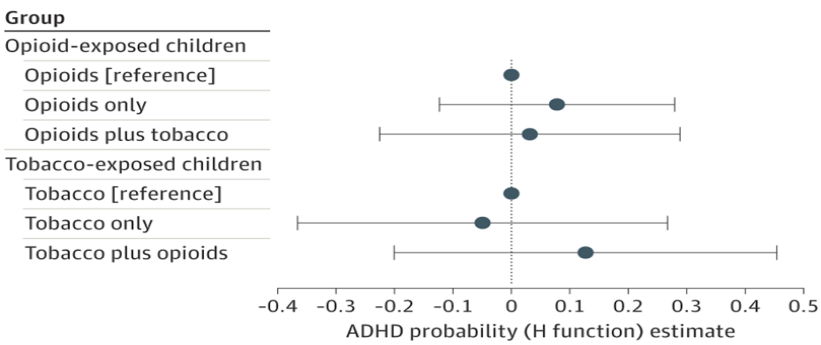

Figure 3: Comparing risk for ADHD based on tobacco and opioid exposure using the H function. Prenatal drug exposure increases ADHD risk with concurrent tobacco and opioid-use leads to the highest probability of ADHD occurrence in prenatally exposed youth (Garrison-Desany et al., 2022).

(Ross et al., 2015). Several studies have found that prenatal drug exposure significantly increases the risk and severity of ADHD in children compared to non-exposed children. In a 2022 study, Garrison-Desany et al. analyzed the Boston Birth Cohort, composed of a multiethnic urban cohort of primarily low-income mother-child pairs spanning from 1998 to 2019. They recorded substance use during pregnancy through self-reports of tobacco, alcohol, opioids, cocaine, and/or nicotine in any trimester of the pregnancy. The study then compared risk for ADHD based on tobacco and opioid exposure using the H function, which is an exposure-response function used to measure non-linear interactions between exposure, fetal substance exposure, and estimated outcome, ADHD risk (Figure 3). The study found that among the 3,138 children studied, more than 15.5% had an ADHD diagnosis and 84.5% were neurotypical, and 24.4% reported the use of at least one substance during pregnancy. Significantly, opioids were found to have the highest adjusted hazard ratio for ADHD, followed by alcohol and cannabis, meaning that these three substances produced the highest risk of ADHD compared to children without prenatal drug exposure (Garrison-Desany et al., 2022). In addition, polysubstance exposure further increased the risk of ADHD compared to prenatal polysubstance exposure.

This study provides compelling evidence that drug exposure, particularly to highly addictive substances such as opioids, cocaine, and alcohol significantly increases the risk of ADHD. Furthermore, a 2018 study found that prenatal drug exposure not only increased the risk for ADHD but also the severity of ADHD. The study looked at a hospital-based population of school-aged children exposed to opiates and other illicit substances and were evaluated for symptoms associated with ADHD and autism spectrum disorders (ASD) using a number of questionnaires. The results of these questionnaires were then compared to a reference group of children without prenatal drug exposure but with ADHD and/or ASD. Sandtorv et al. found that prenatally exposed children had significantly higher SNAP-IV (ADHD questionnaire) scores associated with ADHD symptoms of both inattention and hyperactivity/impulsivity and a higher Autism Spectrum Screening Questionnaire score, indicating an increased number of symptoms associated with ASD (Sandtorv et al., 2018). This demonstrates that prenatally exposed children had significantly more severe mental health symptoms, particularly inattention, and impulsivity, compared to the reference group. As demonstrated by these two case studies, prenatal drug exposure, especially to opioids, cannabis, and alcohol significantly increase the risk and severity of ADHD and broader behavioral deficits in young children and adolescents.

Over the last several decades, it has been proven that prenatal drug exposure severely impairs the adolescent brain and can have irreversible ramifications including higher risk and severity of ADHD in prenatally exposed children compared to their healthy counterparts. As delineated through this article, attentional deficit disorders are characterized by dysfunctional mesolimbic dopamine and LC-NE systems that are also targeted by drugs of

Ultimately, educating individuals, particularly low-income communities who are more at risk for drug abuse, and promoting resources to help stop drug abuse, is imperative to preventing prenatal drug exposure and its associated adverse health outcomes for future generations.

abuse. Taken together, the higher risk and severity of ADHD amongst prenatally exposed children puts them at a higher risk for poor decision-making skills associated with incarceration and adolescent drug abuse (Lambert et al., 2014).

This can become a vicious cycle of drug exposure, incarceration, and drug abuse, leading to an increased risk of another generation of prenatally exposed individuals. Several studies have found that prenatal drug exposure is also associated with environmental and socioeconomic adversity that further increases the severity of behavioral disorders such as ADHD and worsens decision-making skills and risk assessment. These high-risk environments are characterized by poverty, inadequate parental monitoring, and violence exposure, and are often concurrent with familial substance use. Importantly, individuals more exposed to these high-risk environments, such as low-income individuals or people of color also have a higher incidence of prenatal drug exposure (Onah et al., 2016). These concurrent factors are then associated with deficits in inhibitory amongst drug-exposed youth, which increases their likelihood of partaking in risk-taking behavior such as drug abuse, criminal activity leading to adolescent arrests, and high-risk sexual activity (Lambert et al., 2014). This means that it is imperative to improve access to appropriate social, educational, and medical services to help prevent and intervene with risk-taking behaviors and their potential consequences amongst high-risk adolescent youth and their families, particularly for prenatally exposed adolescents. As delineated through this article, ADHD is a result of genetic mutations that reduce dopamine availability and thus, impair reward, decision-making, and motivation pathways. Moreover, ADHD risk and severity is significantly worsened by fetal substance exposure leading to a harmful cycle of fetal drug exposure, ADHD incidence, risk-taking behavior, and drug exposure. Ultimately, educating individuals, particularly low-income communities who are more at risk for drug abuse, and promoting resources to help stop drug abuse, is imperative to preventing prenatal drug exposure and its associated adverse health outcomes for future generations. ❧

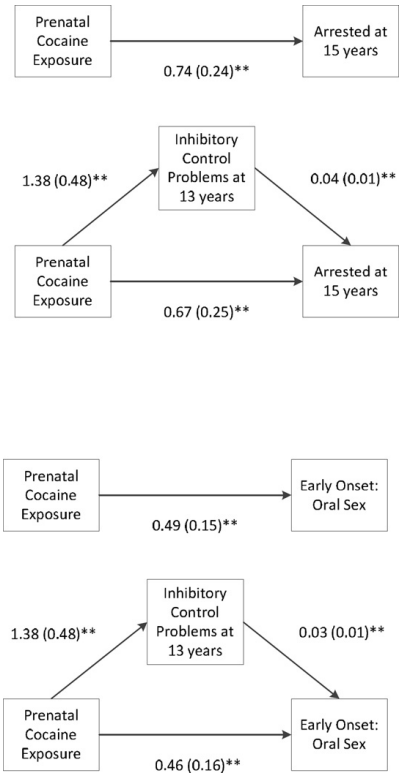

*Figure 4: Comparing cocaine exposure with early onset of oral sex and arrests. The values indicated are regression coefficients where ** = $p \leq 0.01$, indicating statistical significance. Prenatal cocaine Exposure is thus associated with inhibitory control problems leading to increased early onset of adverse risk-taking behaviors (Lambert et al., 2014).*

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Organ donation policies: Altruistic or misanthropic?

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Per the four bioethical principles, autonomy protects a patient's ability to make their own choices. Free from coercion and external influences, a patient's medical decisions are theirs alone. However, the policies that govern the medical system and the sociological stigmas accompanying it play a more significant role than once thought. To analyze the interplay of these factors, one need not look further than organ donation policies. Opt-in and opt-out organ donation policies are substantiated ethically in their own right, and yet the corresponding organ donation rates are worlds apart. The disparity in the numbers that impact equitable healthcare access from a global standpoint begs the question, is one policy superior to the other?

Two models of consent are followed when it comes to organ donation: expressed and presumed consent. Expressed consent requires that the individual explicitly state that they would like to be an organ donor. On the other hand, presumed consent assumes that the individual will donate their organs upon brain death unless explicitly stated otherwise. Countries with opt-in policies follow models based on expressed consent, whereas countries with opt-out policies follow models based on presumed consent (Zink et al., 2005).

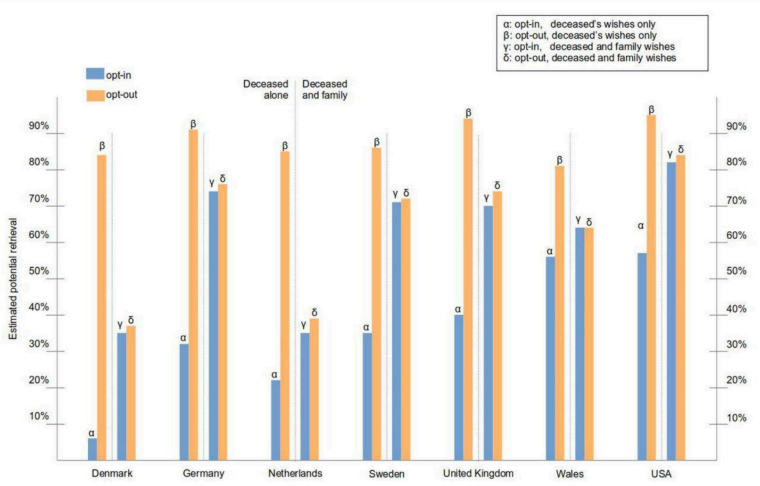

Figure 1. From Molina-Pérez, 2022: Worldwide organ donation rates.

To understand the debate surrounding organ donation models, it is crucial to understand the types of donation and the current policies that govern organ donation rates. There are four types of organ donation: deceased donation, living donation, organ transplantation, and organ procurement. Deceased donation, comprising donation after brain death (DBD) and donation after circulatory death (DCD), occurs once the patient has been certified as brain dead and is the main category of donation being discussed. (Etheredge, 2021). The Uniform Anatomical Gift Act, enacted in 1968, is the primary law in the United States governing organ donation. Organ donation is maximized by allowing two ways of opting in accordance with this policy: first-person authorization, when an individual can opt-in before death, or a surrogate authorization, having a trusted individual authorize donation after one's death. The UAGA allows for three positions: authorized gift, no decision, and refusal to make gift. A registered donor is listed under the positive category, authorized gift. No decision, or the neutral position, is the default position under which every individual is categorized. If an authorized gifter was to revoke their decision, they would revert back to no decision. If an individual is in a neutral position at the time of passing, the surrogate can choose to authorize organ donation, even if the individual had previously revoked consent. The only way to prevent surrogate organ donation posthumous-

Organ donation is maximized by allowing two ways of opting in accordance with this policy: first-person authorization, when an individual can opt-in before death, or a surrogate authorization, having a trusted individual authorize donation after one's death.

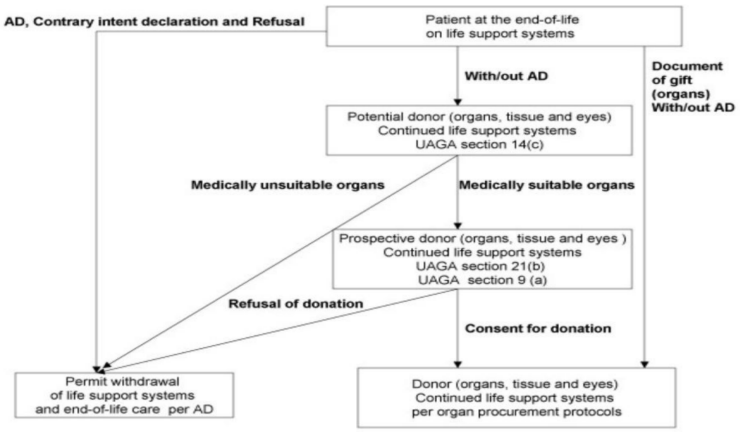

Figure 2. From Verheijde et al., 2007: The UAGA pathway that enables donation.

ly is for individuals to declare the third category, refusal to make a gift, while alive (Glazier, 2018; Glazier & Mone, 2019).

Currently, the United States has an organ donation rate of 38.1 donors for every million deaths and is second only to Spain, with a rate of 47 donors for every million. Spain, however, follows an opt-out system, unlike the United States (Lewis et al., 2021). As a result, not only have they cemented their place as the country with the world's highest organ donation rates, but they also doubled their donation rates in less than a decade. This exponential growth was facilitated by creating the Organización Nacional de Trasplantes (ONT) in 1989 to identify donation opportunities and shift public attitudes surrounding organ donation (Matesanz et al., 2017). To aid this goal, the ONT established three objectives: promoting early identification and referral of potential donors to consider incorporating organ donation into the end-of-life care plan, fostering the incorporation of non-standard or risk donors, and developing a framework for the practice of DCD. With the government pursuing policy to support organ donation, physicians have followed suit and incorporated organ donation inclusive care plans for neurocritical patients allowing some hospitals to have organ donation rates as high as 60 to 70 patients per million (Kuroda, 2016; Matesanz et al., 2017).

Existing social perceptions surrounding organ donation differ vastly depending on whether the country follows an opt-in or an opt-out policy.

Existing social perceptions surrounding organ donation differ vastly depending on whether the country follows an opt-in or an opt-out policy. In a study conducted by Davidai et. al, American participants read opt-in policies and opt-out policies followed in other countries and then rated their decision to be an organ donor relative to other behavioral choices. The default policy followed in the country had a significant impact on the way participants rated the altruism associated with organ donation. Davidai says, "In the opt-in case, the question posed to potential donors is something akin to, 'Do you want to put yourself forward as an exceptional altruist, someone who acts for the good of others under circumstances when only particularly virtuous fellow citizens are likely to follow suit?' In an opt-out context, in contrast, the implicit question is something akin to, "Do you want to stand out as an exceptional misanthrope, someone who fails to step forward and do one's duty as most good citizens and community members do?" (Davidai et al., 2012).

While both systems have a multitude of pros and cons, no system has proved to be self-sufficient, with thousands dying annually while waiting on organs. When evaluating the efficacy of both systems, it is crucial to evaluate the importance of protecting individual autonomy while also progressing the collective., the transplant list grows.

From a philosophical standpoint, altruism is commonly associated with organ donation, as the action undertaken is weighed by its beneficial impact on other individuals without regard for consequences for the individual. Two kinds of altruism correspond with the two systems: obligatory altruism, commonly associated with opt-out countries, and supererogatory altruism,

Two kinds of altruism correspond with the two systems: obligatory altruism, commonly associated with opt-out countries, and supererogatory altruism, which is practiced in opt-in countries.

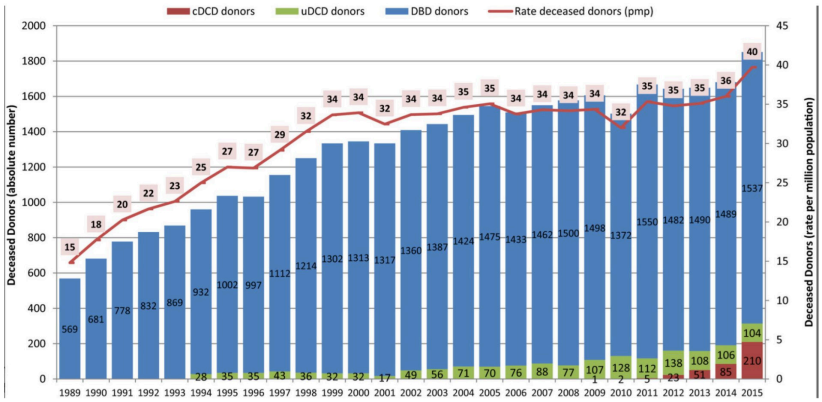

Figure 3. From Matesanz et al., 2017 Spain's organ donation growth rate over the past decade.

which is practiced in opt-in countries. Obligatory altruism, where altruism is associated with the moral duty to help others, explains why organ donation is thought to be the standard. Supererogatory altruism is defined as behaving morally good even though it is not expected; hence, in opt-in countries, organ donation is viewed as going above and beyond (Dalal, 2015). Opt-in and opt-out policies have spurred a range of philosophical debates, with ethicists arguing whether models of presumed consent, as followed in opt-out countries, align with the principles of autonomy. In the West, opt-in policies modeled after explicit consent align with the accepted autonomy standards. However, some ethicists believe presumed consent helps society move towards a conscription model where individuals are under a compulsion to donate organs (Dalal, 2015).

While both systems have a multitude of pros and cons, no system has proved to be self-sufficient, with thousands dying annually while waiting on organs. When evaluating the efficacy of both systems, it is crucial to evaluate the importance of protecting individual autonomy while also progressing the collective, the transplant list grows. ❧

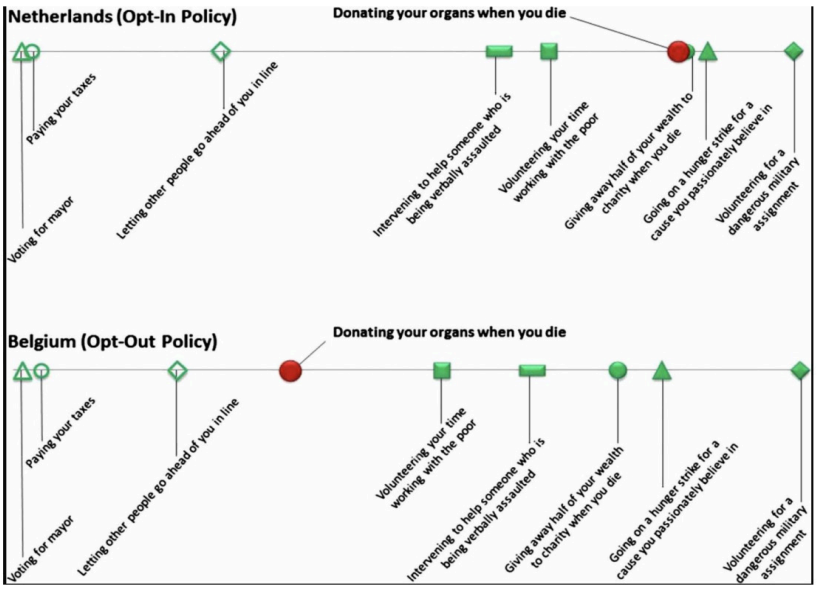

Figure 4. From Davidai et al., 2012: Results from the study ranking.

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The scars that can't be seen: PTSD in refugee populations

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Staff Writer

Figure 1. In poorly resourced refugee camps such as this one in Greece, people escaping conflict are more likely to develop PTSD symptoms due to a lack of reliable food, water, or shelter (Dolors Lola, 2016).

While escaping a conflict zone may help refugees reach physical safety, the deep-seated mental scars of violence are far more enduring. In fact, up to 40% of refugees and asylum seekers around the world show symptoms of possible post-traumatic stress disorder (PTSD), which is a mental disorder in which patients have difficulty recovering after experiencing traumatic events (Mahmood et al., 2019). This rate is up to five times as much as that of the general United States population (Mahmood et al., 2019; Schein et al., 2021). Worse yet, the issues of refugees being marginalized tend to be overlooked. There is a severe PTSD crisis among refugee populations across the world that humanitarian organizations, hospitals, and governments must work to address. In order to truly alleviate the burden of PTSD in refugee populations, it is important to explore its causes, uniqueness, and potential solutions.

PTSD often arises in refugee populations due to the stressors and trauma of the conflict zones they come from.. A survey of Iraqi refugees living in Sydney, Australia showed that almost half of the study population reported the unnatural death (47%) or murder (46.7%) of a family member or a friend, 41% had experienced being close to death, and nearly 41% experienced a lack of food or water at some point (Slewa-Younan et al., 2017). Because refugees experience a plethora of traumatic events, they have a high propensity for PTSD development. Previous epidemiological studies have strongly linked interpersonal violence and cumulative exposure to potentially traumatic events to the incidence of PTSD in patients (Bryant, 2019). Therefore, consistent exposure to interpersonal violence and resource shortages over periods of years or even decades often contributes to refugees experiencing high rates of PTSD. A survey of villagers in a South Lebanese conflict zone solidifies this violence-PTSD axis, finding that individuals suffering from both PTSD and depression were more likely to have been exposed to at least one form of a violent event and have suffered from health issues (Farhood et al., 2016). Given that a high proportion of refugees not only have experiences with violence but also resource shortages, likely causing health issues, it is unsurprising that this population shows a high rate of PTSD.

...refugees suffer from a longer-lasting type of PTSD due to the difficult transitions they make in order to escape conflict zones.

PTSD continues to afflict refugees even after they escape from acute conflict zones due to the stressors of uncertainty and integrating into a new culture. Usually, PTSD cases resolve within a few years of symptom development. In fact, a collection of surveys across 22 countries show that 50% of patients with PTSD recovered within 2 years (Rosellini et al., 2018). Refugees likely belong to the other 50% of patients, as the same collec-

Figure 2. For many refugees entering new countries, such as these Syrian children in a Lebanese school, integration is a difficult process that often exacerbates symptoms of PTSD (Adam Patterson, 2016).

tion of surveys finds that PTSD patients who do not recover within two years are more likely to have witnessed purposeful injury, torture, killing, and other atrocities (Rosellini et al., 2018). In addition to the nature of the traumatic events they experience, refugees suffer from a longer-lasting type of PTSD due to the difficult transitions they make in order to escape conflict zones. A review of mental health disorders among refugees finds that refugees housed in camps that often lack basic necessities are restricted in their movement along with uncertainty about what the future holds for them, which can be a cause of stress (Hameed et al., 2018). As aforementioned, a lack of resources and associated declines in health are direct predictors of PTSD, and the stress associated with the difficulties of living in refugee camps may have a role in exacerbating symptoms. Even after refugees manage to find permanent homes in host countries, they uniquely suffer from acculturative stress due to entirely new settings, customs, and a lack of familiar support systems (Hameed et al., 2018). Thus, the type of PTSD that refugees suffer from is fundamentally different from that of patients living in their native countries. Refugees lack access to support systems that other patients may have, whether they are religious, familial, or otherwise. This lack of support coupled with the difficulties of assimilation results in the prolongation of PTSD symptoms, often for years after resettlement.

...an ideal method to treat PTSD in refugees is narrative exposure therapy, as it involves patients reconstructing their life stories until traumatic events no longer incite anxiety

In addition, PTSD treatment for refugees involves the use of different methods than those normally employed in clinical settings. Standard treatments for PTSD used in the West include prolonged exposure, cognitive processing, and cognitive behavioral therapy (Watkins et al., 2018). While these methods generally lead to improvements in patients, providers must carry them out over extended periods of time, often up to 15 weekly sessions (Watkins et al., 2018). However, these extended time periods are infeasible for many refugees, as they often cannot stay in one place with a clinician for a lengthy period of time (Gwozdziewycz & Mehl-Madrona, 2013). Moreover, some of the commonly used treatment methods, namely prolonged exposure, involve processing one traumatic event at a time, which may not be as effective for refugees given that they likely have multiple traumatic experiences (Watkins et al., 2018). Consequently, an ideal method to treat PTSD in refugees is narrative exposure therapy, as it involves patients reconstructing their life stories until traumatic events no longer incite anxiety and therefore enables the processing of a large number of traumatic events in a short amount of time (Knipscheer et al., 2015). A randomized control trial of refugees and asylum seekers with PTSD in Norway found this holistic approach to be effective compared to others, with a significantly greater reduction in symptoms (Stenmark et al., 2013). Therefore, it is more effective for providers to use treatment methods that account for the more transient lifestyles and cumulative trauma of refugees.

Overall, PTSD continues to be a significant health concern in refugee populations, regardless of national origin or host country. To combat this health shortcoming, it is crucial to develop an understanding of its causes and ways to treat it. By considering the unique factors that exacerbate PTSD in refugees, such as acculturative stress, and applying appropriate treatments, namely narrative exposure therapy, clinicians, non-governmental organizations, and governments themselves can best address this issue. Doing so would result in improved wellbeing for millions of patients in countries all across the world. ❧

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The evolution of mental health treatment and beliefs

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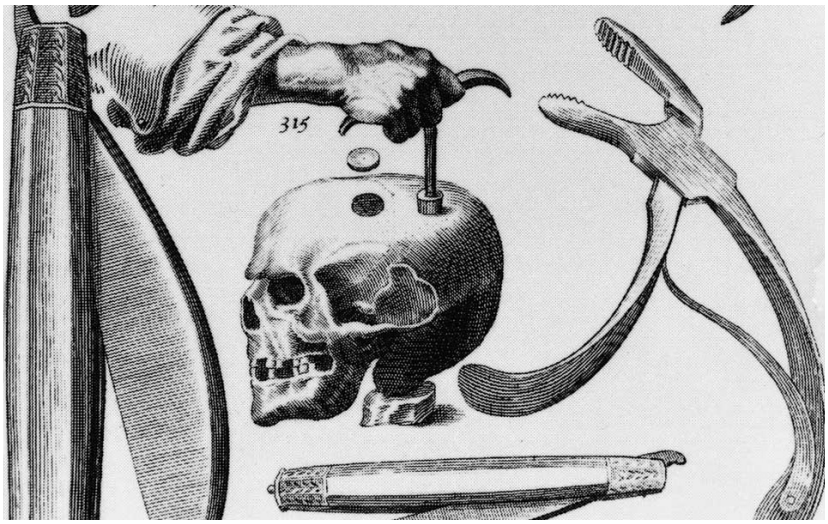

Figure 1: A common practice of 400 BC known as trephining (Gross, 2021).

In 2023, mental health is viewed as a significant portion of medical and behavioral healthcare. Historically, however, this has not always been the case. In past centuries, mental health illnesses have consistently been attributed to extraneous supernatural, biological, or psychological causes resulting in severe and inhumane treatment. This article works to explore how our understanding of the etiology of mental illnesses has changed over time due to scientific advances as well as the medical community's response to the new information.

In the B.C. era, mental illness around the world was largely attributed to supernatural species or evil spiritual entities that made their way into an individual's body. As a result, individuals with a mental illness were thought of as being "possessed by the devil" and were thus treated as if they had committed a sin (Farreras, 2023). Some patients with mental disorders were forced to undergo severe and inhumane treatments as a way to rid themselves of their illnesses. For example, in 6500 B.C., around the world, two of the most common treatments available were gyrating chairs and trephining. Gyrating chairs was a treatment in which patients would be chained down to a chair that would then be vigorously shaken. This method was believed to increase the amount of blood flowing to the brain which would then be released to cure the patient and rid them of disease. In addition, trephining was a procedure commonly performed in which a small hole would be drilled into a patient's skull using a variety of crude objects. It was believed that the creation of this hole or trephine would then allow the evil spirits that were inhabiting this person's head to be relieved, causing an illness to be cured (Gross, 2021).

Some patients with mental disorders were forced to undergo severe and inhumane treatments as a way to rid themselves of their illnesses.

Later on, in the 800-400 C.E. era, Hippocrates, considered the first physician from the Western World, understood the body in terms of its four humors. These four humors were: blood, yellow bile, black bile, and phlegm. Thus, Hippocrates believed that illness, either physical or mental, could be attributed to an imbalance of the humors in the body. An increase or decrease in any one of the four fluids would result in an overall disequilibrium. For example, Hippocrates thought that "melancholia", today commonly referred to as depression, was "caused by black bile" and that individuals with "an excess of black bile could suffer from epilepsy and seizures" (Kalachanis, 2020). As a result, the treatment for mental illness was said to be through bleeding or purging the patient to restore fluid balance for the patient. Overall, although mental illness was beginning to be recognized as a non-physical illness in the B.C. era, there was a strong tendency to attribute mental illnesses to entities outside of human control, which resulted in harmful methods of curing patients.

Between the B.C. era and the 20th century, mental illness was beginning to be recognized as

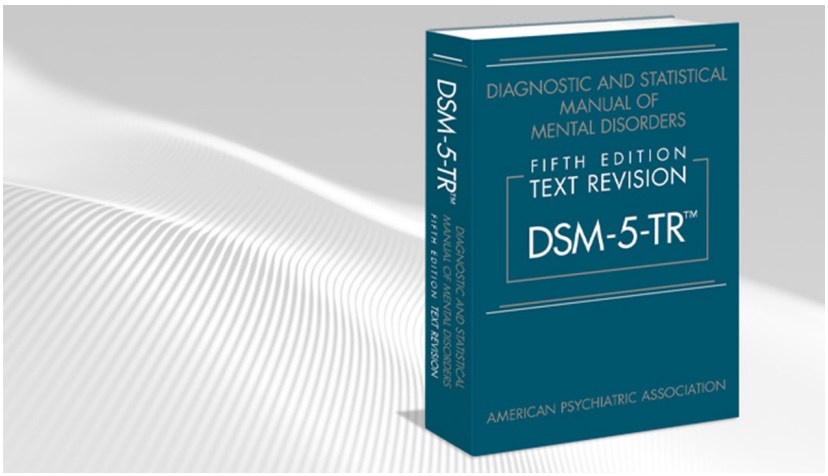

Figure 2: The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders. (Psychiatry.org)

a condition that would demand medical services; however, the actual treatment of these conditions remained stagnant. Moving into the 20th century, two fundamental theories emerged to understand the origin of mental illness: the psychodynamic approach by Sigmund Freud and the theory of behaviorism by John Watson. The focus of the psychodynamic approach was to convey that mental illness and disorders can be viewed through the lens of one's unresolved childhood experiences or issues. Thus, treatment should be focused on "open dialogue [and conversation] with the patient" (Jutras, 2017). Freud believed that there were three main parts to the human psyche: the id, ego, and superego. The id is the "primitive and instinctual part of the mind that contains sexual and aggressive drives", the ego is the "realistic portion of the mind that mediates'', and the superego acts as the "moral conscience" of an individual (Traylor, 2022). Freud believed that these segments of the mind were active from a young age as an individual builds their personality. Thus, Freud's psychodynamic approach was built from this idea and explained how different experiences during one's upbringing can impact their adult life. Additionally, John Watson created the theory of behaviorism, which stated that mental illness was a product of behavioral outcomes and thus should be treated with behavioral conditioning. For example, in a famous experiment known as the Little Albert Experiment, Watson demonstrated the way in which an individual can become conditioned to a particular behavior. To accomplish this, Watson took an 11-month old baby, Little Albert, and showed him a white rat which would not cause any change in Albert's behavior. Then, Watson would show Albert the white rat but couple it with a loud noise which would elicit a sense of fear in Albert. Over time, with repeated exposure to this stimulus, Albert was conditioned to fear the white rat even though this fear did not exist previously. As a result, Watson's theory is founded on the idea that "observable behavior is dependent on mental causes" and at the time was largely considered an alternative to "mentalism", a term in which people are considered crazy (Malone, 2014). With both the psychodynamic and behaviorist theory circulating in the public, mental illness began to be more recognized as a medical diagnosis. The past notion that mental illnesses were caused by spirits or evil entities was foregone and a more scientific understanding of mental disorders began to arise.

With both the psychodynamic and behaviorist theory circulating in the public, mental illness began to be more recognized as a medical diagnosis.

As a result, this led to the publication of the official "Diagnostic and Statistical Manual of Mental Disorders" in 1952 (Kawa, 2012). The developers of this medical textbook aimed to provide standardized terminology for clinicians and physicians to speak about mental disorders and find a common place to learn more about conditions and available treatments. Since its first edition, there have been five subsequent publications which are all designed to include updated and more relevant information regarding mental disorders to keep physicians up to date with optimal treatments available for their patients. Furthermore, the publication of this textbook led to the increased acceptance and accurate diagnoses of those with mental disorders. In addition, in 1946, the US Surgeon General signed the Mental Health Act of the USA which granted funds and created

the official National Institute of Mental Health. Overall, the 20th century saw an increase in the representation of mental health illnesses in the medical field and general public, an increase in advocacy for those with mental health disorders, and a more scientific underpinning to individuals' understanding of mental health.

In 2023, mental health and mental illness are given more direct treatment and focused attention. Considering mental health has gained a much larger emphasis within medical care, behavioral and mental health support and resources are expanding. In fact, even routine medical visits now contain questionnaires asking individuals to rate their perceived mental health quality. This information can then be used to aid patients who may be suffering from mental illnesses. However, even with an abundance of advancements, a new negative stigma surrounding mental health is developing. Unfortunately, at times this stigma tends to cloud people's perceptions of an individual diagnosed with a mental illness. This can result in those suffering from mental illness being treated poorly and being ostracized. Overall, mental health and the manner in which mental health disorders have been treated have evolved drastically since the B.C. era. Although mental illness was originally attributed to supernatural forces, an abundance of scientific knowledge has allowed us to have a much better understanding of the causes and treatments for mental disorders. History and medical treatment have come a long way in the past several centuries, but significant progress is needed to reach a point at which mental disorders are given the same recognition and treatment as physical medical conditions. ❧

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An overdue conversation about obesity

ESTHER JUNG
Staff Writer

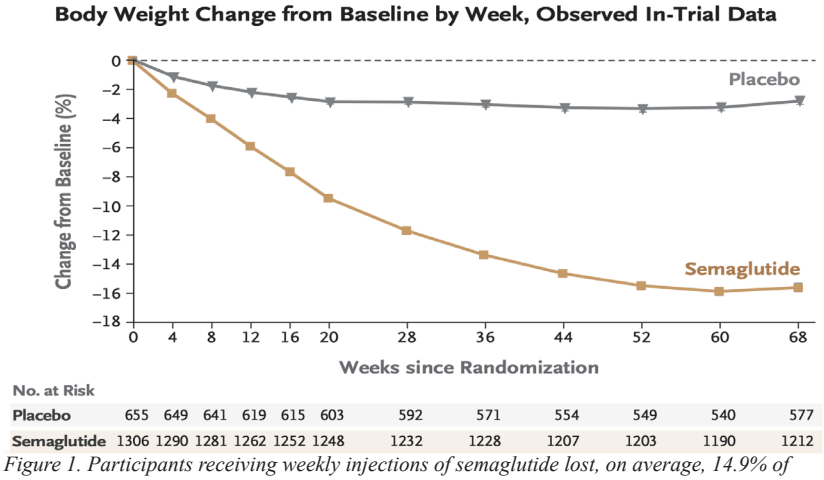

Figure 1. Participants receiving weekly injections of semaglutide lost, on average, 14.9% of their body weight after 16 months of treatment, while those who received a placebo lost 2.4% on average (Wilding et al., 2021).

In America, approximately 69% of adults are overweight, and more than one in three adults are obese (Flegal et al., 2012; Centers for Disease Control and Prevention, 2022). Worldwide, about 500 million adults are obese (Finucane et al., 2011). Obesity is a steadily growing problem not just in the United States, but also in developing and wealthy countries alike. The shift toward overeating and a reliance on Western diets, which consist of processed foods, edible oils, and sugar-sweetened beverages, is correlated with this influx of obesity cases (Popkin et al., 2012). Despite the prevalence of obesity in the United States and worldwide, there are few medications that help patients lose weight without serious side effects. In addition, obesity often conflicts with other medical diagnoses and treatments; during the peak of the pandemic, scientists were concerned that the COVID-19 vaccine would not be as effective in obese people, a group already vulnerable to the infectious disease (Ledford, 2020). However, recent breakthroughs in anti-obesity medications provide new hope to those struggling to lose weight despite making drastic lifestyle changes.

Obesity cases have risen in the past few decades. Body mass index, or BMI, is often used as a measure of body fat and is calculated by body mass divided by the square of the body height, expressed in units of kg/m². A BMI of 25 to 29.9 is categorized as overweight, and obesity is defined as a BMI of 30 or higher. Across the world, mean BMI has increased since 1980, and among high-income countries, the USA has the highest BMI (Finucane et al., 2011). In 2009-2010, the prevalence of obesity was 35.5% among adult men and 35.8% among adult women (Flegal et al., 2012). Obesity can increase the risk of other health conditions, including heart disease, diabetes, breathing problems, and joint problems (Centers for Disease Control and Prevention, 2022). Furthermore, during the peak of the COVID-19 pandemic, doctors working in emergency rooms found that obese individuals tended to show more severe cases of the virus, and BMI showed a positive correlation with the severity of COVID-19. Researchers also worried that the efficacy of a vaccine could be dampened by obesity (Ledford, 2020). Researchers have found that BMI is a strong predictor of overall mortality, and as BMI increases, mortality also increases. At a BMI of 30–35 kg/m2, median lifespan is reduced by 2–4 years; at 40–45 kg/m2, it is reduced by 8–10 years (Prospective Studies Collaboration et al., 2009). In a study done in the Asia-Pacific region, researchers found that BMI also has associations with risks of stroke and heart disease, and as BMI decreases by 2 kg/m2, there is an associated 12% lower risk of stroke caused by a blood clot, 8% lower risk of stroke caused by bleeding, and 11% lower risk of heart disease

Despite the prevalence of obesity in the United States and worldwide, there are few medications that help patients lose weight without serious side effects.

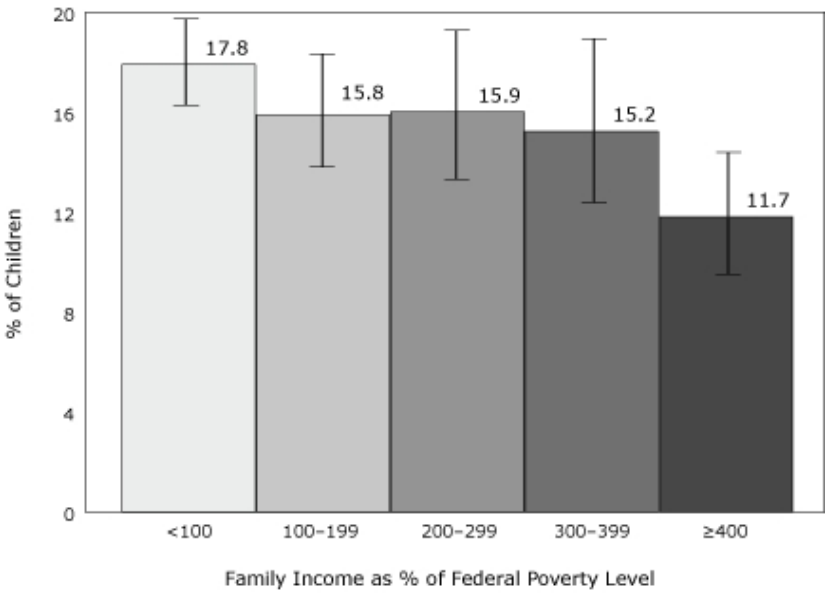

Figure 2. Prevalence of obesity amng children according to family income as a percentage of the federal poverty level. Image from Braveman, 2009.

(Ni Mhurchu et al., 2004).

The rise in obesity rates can be largely attributed to changes in diets and activity patterns. In the United States, the consumption of processed food and prepared meals has become increasingly common, and eating away from home, particularly in fast food restaurants, is a major part of many people's lives. At the same time, physical activity is declining as advances in technology, transportation, leisure, and home production (cooking, cleaning, child care, etc.) increase (Popkin et al., 2012). Meanwhile, in low- and middle-income countries, changes in edible oil production have created cheap vegetable oils that allow people to increase their energy consumption at very low levels of income, and the presence of added sugar in foods and beverages has increased significantly (Popkin et al., 2012).

Unlike previous drugs tested to show minimal weight loss in obese individuals, semaglutide helped obese individuals lose significant weight (Prillaman, 2023).

However, is there a cure for obesity besides drastic lifestyle changes and cutting down on unhealthy foods? To address this question, scientists started searching for a weight-loss drug by investigating the hormonal underpinnings of appetite regulation, glucose levels, and fat formation. One such hormone that regulates the body's blood glucose levels is glucagon-like peptide 1 (GLP-1), which promotes glucose-stimulated insulin secretion while inhibiting glucagon release (Lim & Brubaker, 2006). GLP-1 stimulates the secretion of insulin, a hormone that helps the body regulate blood sugar. Insulin is also commonly dysregulated in individuals diagnosed with diabetes. A drug called semaglutide, which acts by mimicking GLP-1 in target areas of the brain that regulate appetite and food intake, was initially approved by the FDA to treat diabetes (FDA, 2021).

A groundbreaking trial administering semaglutide to adults with obesity pressed the FDA to approve semaglutide for chronic weight management. Wilding and colleagues recruited 1961 obese adults for a study wherein they randomly assigned participants to either 68 weeks of treatment with once-weekly subcutaneous semaglutide injections (at a dose of 2.4 mg) or a placebo. During the period of the study, both treatment groups received lifestyle intervention consisting of counseling sessions every 4 weeks to help them adhere to a reduced-calorie diet and increased physical activity. As seen in Figure 1, the semaglutide group lost an average of 14.9% of their body weight, while the placebo group lost 2.4% on average after 68 weeks (Wilding et al., 2021). The drug was further shown to be effective in adolescents. In a study of 180 obese adolescents, participants randomly assigned to receive weekly semaglutide injections showed a mean BMI decrease of 16.1%, while the placebo group showed a 0.6% increase (Weghuber et al., 2022). Unlike previous drugs tested to show minimal weight loss in obese individuals, semaglutide helped obese individuals lose significant weight, all without the adverse side effects of other anti-obesity medications, especially on the heart and gastrointestinal system (Prillaman, 2023).

Unfortunately, the rate of obesity follows a socioeconomic gradient with the highest rates

observed among minorities and the poor, especially in America (Drewnowski & Darmon, 2005). From 1999 to 2010, statistically significant increases in obesity rates were observed in non-Hispanic black women and Mexican-American women, but obesity showed no significant increase among women overall (Flegal et al., 2012). As seen in Figure 2, obesity in children appears to be correlated with family income and wealth: the poorest have the highest obesity rates, and the richest have the lowest obesity rates, with adult obesity following a similar pattern (Braveman, 2009). The link between obesity risk and socioeconomic disparities can be brought back to the differences in diet. Lower-income households may allocate their limited resources to items deemed more essential, such as clothing or rent, leading to a deprioritization of a healthy diet. Higher consumption of fats and sweets is associated with a net saving in diet costs (Drewnowski & Darmon, 2005). In contrast, buying healthier foods, like fruits and vegetables, is associated with higher diet costs, making lower-income households less likely to rely on fresh produce for their diets. Furthermore, low-income consumers are more likely to live in areas with less physical access to healthier foods. Facing these financial and physical barriers, low-income households must choose diets consisting of low-cost meats, inexpensive grains, added sugars, and added fats. As a result, lower socioeconomic classes are disproportionately affected by obesity due to the diets available to them.

Will semaglutide make differences in the lives most affected by obesity? Despite the transformative breakthrough that semaglutide offers, the price barrier is steep, and the lower socioeconomic classes disproportionately affected by obesity may not be able to afford weight-loss medications. Semaglutide, currently branded as Wegovy for weight loss, is considered a "vanity drug" by most insurance companies, allowing companies to refuse to cover the hefty expense of $1,300 each month (Prillaman, 2023). The mislabeling of semaglutide, as well as other weight-loss drugs, as a vanity drug echoes the fatphobic prejudices against those suffering from obesity. Although obesity can lead to biological changes in weight-regulating pathways that make it difficult for obese individuals to lose weight, widespread societal views uphold that obesity can simply be cured by pure willpower. This perspective even seeps into healthcare settings, where physicians may advise obese patients to increase their physical activity or change their diet while disregarding the challenges of losing weight. However, other doctors disagree: Dr. Louis Aronne, an obesity medicine specialist at Weill Cornell Medicine, argues, "It's not that they don't have willpower. Something physical is holding them back" (Kolata, 2022). Many obesity medicine specialists emphasize that obesity is a chronic disease that should be treated as intensively as any other chronic illness. Although semaglutide shows promising evidence to drastically change the lives of those suffering from obesity, the drug's accessibility also highlights the systemic barriers that prevent marginalized groups from utilizing such a crucial medication. Obesity is an important medical condition that should be treated as such, but societal views of obesity reduce it to an issue of self-discipline or willpower. It is more apparent than ever that obesity is not an equal-opportunity illness, with socioeconomic disparities impacting obesity rates. The stigma around obesity needs to be addressed in order to properly treat individuals suffering from its consequences. ❧

Despite the transformative breakthrough that semaglutide offers, the price barrier is steep, and the lower socioeconomic classes disproportionately affected by obesity may not be able to afford weight-loss medications.

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Manifestations of childhood trauma into adulthood

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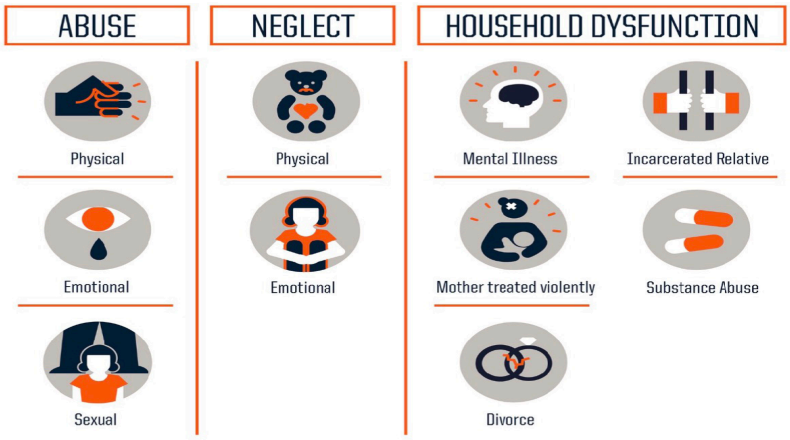

Figure 1. The image depictst the ten different ACEs categorized into abuse, neglect, and household dysfunction (Starecheski 2015).

When Dr. Burke Harris examined Diego's height chart, she was convinced she had made a mistake. Diego's height was at the 50th percentile for a four-year-old. At first, she thought his height was completely normal, until she realized that Diego was actually seven years old. As Dr. Burke Harris studied Diego's growth history, she found that he hadn't grown a centimeter from age four to age seven. After talking to Diego's mother, Dr. Burke Harris learned that he had been sexually assaulted at age four and consequently, had developed asthma, eczema, ADHD, and growth failure after the incident (Harris, 2021). Dr. Burke Harris' work along with various other studies have proven that childhood trauma is retained through adolescence and adulthood. The retention of childhood trauma often manifests as physical as well as psychological illness years later, as depicted by biological and physiological implications, acceleration in aging, and prolonged stress levels. Thus, identifying childhood trauma through universal screenings is key to maximizing future health outcomes of children who have faced trauma at a young age.

Thus, identifying childhood trauma through universal screenings is key to maximizing future health outcomes of children who have faced trauma at a young age.

The CDC identifies ten different adverse childhood experiences (ACEs): physical abuse by a parent, emotional abuse by a parent, sexual abuse, physical neglect, emotional neglect, growing up in a house with alcohol or drug abuse, incarceration of a family member, mental illness in the household, witnessing domestic violence, and divorce (Center for Disease Control and Prevention, 2021). The CDC and the Kaiser healthcare system collaborated on a study to determine the effect of these ACEs on common physical ailments and collected data in two waves between 1995 and 1997 from 17,337 Health Maintenance Organization members in Southern California. Just prior to their physical exams, members completed a confidential survey about their childhood experiences and current health status. Each individual in the sample was categorized as having 0, 1, 2, 3, or 4+ ACEs. The findings depicted that a higher number of ACEs was associated with severe obesity, various types of cancer, and a higher chance of developing heart, lung, and liver disease.

Though the CDC-Kaiser study has many strengths, including the large sample size, critics argue that the study is not representative of the overall population and lacks external validity. With 74.8% of participants being Caucasian and 100% of participants being from Southern California, the CDC-Kaiser data is limited by the demographics of the study. In 2010, Dr. Leah Gilbert and her team designed a study that aimed to determine if ACE exposure increases the risk of developing chronic disease. Their goal was to study a more representative sample than in the CDC-Kaiser study. Gilbert's team added an optional ACE module in the Behavioral Risk-Factor Surveillance Survey, a random-digit-dial telephone survey of US adults. They asked about the same ACEs as in the CDC-Kaiser study and participants were categorized as

Figure 2. Dr. Brke Hrris is working on developing interventions with a woman and her grandchildren at the Cener for Youth Wellness (Bornstein 2018).

having exposure to 0, 1-3, 4-6, or 7-9 ACEs. After controlling for sociodemographic variables, they found that coronary heart disease and stroke were significantly higher for those who reported 4-6 or 7-9 ACEs than 0 or 1-3 ACEs. Additionally, myocardial infarction, asthma, and poor health were highest for participants who had experienced >1 ACEs compared to individuals who reported 0 ACEs (Gilbert et al., 2015).

Along with increasing risk of various physical illnesses, childhood trauma has also been associated with accelerated aging in adolescents and adults. In 2020, Dr. Natalie Colich conducted two studies to determine the impact of childhood trauma on cellular and cortical aging, respectively. The first study was a meta-analysis of 54 studies on 116,010 subjects that aimed at understanding the association between early life adversity (ELA) and cellular aging. The results indicated that children who suffered threat-related trauma such as abuse and violence had shortened telomeres, a region of repetitive DNA sequences at the end of a chromosome (Chadwick, 2023). Shortened telomeres are a primary indicator of accelerated aging and earlier onset of puberty. Meanwhile, children subject to neglect-related trauma did not show these signs. The second study was a systematic review of 25 manuscripts on 3,253 individuals and aimed to explain the association between ELA and neural markers of accelerated development. The data illustrated that childhood adversity and trauma are strongly correlated with reduced cortical thickness. Cortical thinning is a sign of aging as the cortex drastically thins as individuals age (Shaw, 2106). Interestingly, different categories of adversity were associated with cortical thinning in various lobes of the brain. Violent traumas led to thinning of the prefrontal cortex, the social and emotional processing sector of the brain. On the contrary, neglect-related trauma led to thinning of the frontoparietal cortex and visual network, the sensory and cognitive processing sectors. Taken together, Colich's findings showed that trauma is correlated with both cellular and cortical aging (Colich et al., 2020).

Along with increasing risk of various physical illnesses, childhood trauma has also been associated with accelerated aging in adolescents and adults.

The CDC-Kaiser, Gilbert, and Colich studies are only three out of many studies that have indicated that childhood trauma can be retained for years and can have a negative impact on all body systems. This evidence can be partially discerned by a few key biological explanations. First, childhood trauma causes severe and prolonged stress. The toxic stress can cause the biological stress response to over-activate during adulthood which negatively affects brain development, DNA transcription, and the immune response (Harris, 2021). Second, childhood trauma can activate toxic stress, resulting in a release of high amounts of stress hormones such as cortisol. An increase in stress hormones further leads to desensitization of the ventral tegmentum, the pleasure and reward center of the brain (Bourab, 2019). During adulthood, individuals affected in these ways tend to participate in risky behaviors in hopes of finding pleasure that they have lacked for years (Peterson, 2018). However,

the high-risk behavior explanation only accounts for about 50% of increased health risks. A large number of ACEs also independently lead to increased chronic inflammation and autoimmune diseases such as asthma, arthritis and lupus, but current research has yet to account for this association. Psychiatrists and scientists are working together to further understand the relationship between childhood trauma and health risks during adulthood (Peterson, 2018).

Along with improving research efforts, universal screening is imperative to maximizing health outcomes of children who have experienced trauma at a young age.

Along with improving research efforts, universal screening is imperative to maximizing health outcomes of children who have experienced trauma at a young age. Dr. Burke Harris is the founder of the Center for Youth Wellness, a medical center in San Francisco well-known for screening children for ACEs at a young age. Screening for ACEs at a young age is the most effective method of determining if a child is at low, moderate, or high risk of having toxic stress physiology. The results of the screening allow the child, family, and healthcare team to create an effective intervention. Data from the Center for Youth Wellness has shown that when children receive early high-quality interventions, their brain scans look similar to children who were never maltreated (Bornstein 2018). However, the only way to screen the entire population is to start screening at primary care rather than waiting years to visit a mental health practitioner. The Child Health and Development Institute (CHDI) recommends instituting the Childhood Trauma Screen (CTS), a brief trauma screen developed by the Connecticut Department of Children and Yale University. The CTS is a free 10 item questionnaire designed for children ages 6-17 that is intended to be administered by pediatric primary care providers. A 2021 study examined the effect of CTS on 107 caregiver-youth pairs between ages 7 and 17 years. The study found that the CTS was able to correctly classify 85% of youth based on likely PTSD diagnosis (Lang et al., 2021).

Diego's story, though shocking and extreme, represents the plight of many individuals who carry the burden of childhood trauma. The CDC-Kaiser, Gilbert, and Colich studies demonstrate that psychological and somatic processes are deeply connected and that childhood trauma manifests in many physical symptoms and illnesses years later. Universal screenings such as Dr. Harris' work at the Center for Youth Wellness and the CTS are key to identifying ACEs at a young age. It is imperative that screenings begin at primary care so effective interventions can be designed for thousands of children like Diego. ❧

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Mommy's favorite juice: Alcoholism in American mothers and postpartum depression

ADITI WAMORKAR
Events Chair

Figure 1: An example of Wine Mom Culture. An exasperated mother tries to parent her infant but cannot without a large glass of wine. Image from Shutterstock.

Scrolling through Facebook, there are always those cringy posts of some random person's mom holding up a comically large wine glass filled to the brim with Chardonnay. Or shopped in Kohl's and saw a shirt that said "Mommy needs her wine." While this is easily chalked up to frivolous fun to detract from the stresses of motherhood, this Wine Mom phenomenon may be a symptom of a deeper issue, the long-ignored mental health of American mothers. American mothers have some of the highest rates of Postpartum Depression (PPD), with 1 in 10 mothers experiencing PPD (Alcohol and Postpartum Depression 2022). Mothers with PPD may turn to drugs, especially alcohol, to self-medicate. This is heavily exacerbated by the "Wine Mom" culture in the United States which describes a mother who turns to alcoholic drinks, typically a "classy" drink such as wine, to cope with being overworked or fatigued from parenting. Self-proclaimed "Wine Moms" make fun of their thinly-veiled alcoholism by buying shirts, outrageously large wine glasses, and baking mitts that say something along the lines of "Mom all day and then rosé." The "Wine Mom" culture in the United States furthers PPD by promoting a dangerous excuse to drink and trivializes a serious gap in American mothers' ability to receive quality mental health care.

While this is easily chalked up to frivolous fun to detract from the stresses of motherhood, this Wine Mom phenomenon may be a symptom of a deeper issue, the long-ignored mental health of American mothers.

PPD is defined as depressive episodes that occur during the first year of motherhood (O'Hara, 2009). Despite its differences from generalized depression and other mental illnesses, PPD is not catered for as a distinct mental health disorder in the Diagnostic and Statistical Manual (DSEM) (Stevens 2017). This leads to PPD having no specific diagnostic criteria, resulting in helpless mothers falling in between the cracks of the United States' poor healthcare system. Major Depressive Disorder, also called depression, is already the leading cause of non-obstetric hospitalization among women ages 18 to 44 in the United States (O'Hara, 2009). Depression exacerbates a woman's chance of getting PPD, with the risk of PPD being 20 times higher in women with pre-existing diagnoses of depression (Silverman, 2017). This statistic is much higher for Black and Indigenous women, with a study finding that 23% of Indigenous Lumbee women experienced some form of PPD symptoms compared to the national average of 11% (Baker, 2005). Adolescent mothers also reported a higher frequency of PPD symptoms as compared to non-adolescent mothers (May, 2022). PPD also increases among low-income families with mothers on a special supplemental nutrition program called WIC reporting a higher frequency of PPD symptoms (Pooler, 2013). With the pressure of being a "perfect mother" thrust onto the backs of vulnerable populations, it is a sad reality that many American mothers turn to alcohol as an outlet for comfort from persistent PPD symptoms that they cannot

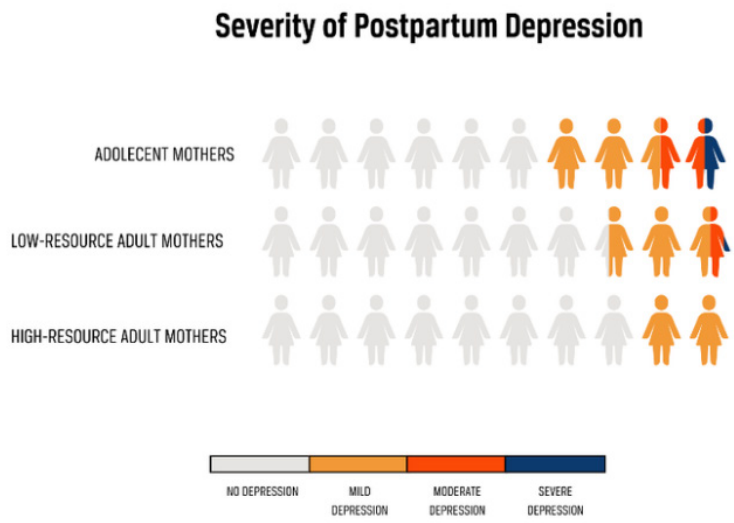

Figure 2: This graph shows how age can be a significant factor in whether or not a mother develops PPD as well as the severity of her symptoms. Adolescent mothers often face a variety of stigmas and challenges which exacerbate their likelihood of getting PPD. They also often have the least access to mental health resources to treat their PPD. Image from May 2022.

access quality mental health care for. This is exacerbated by the societal expectation that all mothers should be experiencing euphoric happiness after the birth of their baby and should not be feeling any negative emotion.

The history of drug use in American motherhood is not relatively new. Doctors in the 19th century over-prescribed opium, specifically morphine, to mothers dealing with reproductive health issues, leading to 60-75% of opium-morphine addicts being women, primarily those who were 25-44 (Kandall & Chavin, 1992). This then shifted to tranquilizers, such as a drug called Milton, and various forms of amphetamines in the 1950s and 60s (Kandall & Chavin, 1992). It appears that now wine has become the drug of choice, with 50% of US Women reporting drinking within the past 30 days and 18% reporting binge drinking at least 3 times a month (Newman & Nelson, 2021).

The most common trope is what is infamously referred to as a "Wine Mom." A Wine Mom is an American mother, typically white and upper-class, who uses wine to self-medicate from mental health issues that are exacerbated by the demands of hegemonic motherhood and lack of quality mental health care (Newman & Nelson, 2021). Wine Moms typically poke fun at their alarming alcoholism through the use of funny t-shirts and obscenely large wine glasses. However, the Wine Mom culture is a cry for help from American mothers who are forced to normalize alcoholism as a form of escapism, a sort of solution to the lack of mental health care available (Newman & Nelson, 2021).

"Wine Mom" culture makes it all too normal to let the answer to PPD be a bottle of wine rather than a visit to a psychiatrist.

PPD is tied heavily to alcoholism, with a total of 12 studies that study maternal alcohol consumption finding that women who drank pre- and post-pregnancy were at significant risk of developing PPD (Qiu, 2022). With motherhood and postpartum in America being painted as a joyous period of time, mothers with postpartum depression may turn to drugs, especially alcohol, to self-medicate and stop feelings of hopelessness or sadness that society dictates they should not be feeling (Alcohol and Postpartum Depression, 2022). "Wine Mom" culture makes it all too normal to let the answer to PPD be a bottle of wine rather than a visit to a psychiatrist. Thus, postpartum becomes a very vulnerable period of time for new mothers who don't have proper access to mental health help. This is reflected in 15.1% of postpartum women engaging in binge drinking rate compared to 4.1% during pregnancy (Alcohol and Postpartum Depression, 2022). Nearly 40% of all PPD cases go undiagnosed while the rate of alcoholism in American mothers climbs (Alcohol and Postpartum Depression, 2022). For adolescent mothers, women who have a history of depression, BIPOC women, and women from low-income families, the risk of abusing alcohol postpartum is even higher (Alcohol and Postpartum Depression, 2022).

Social media also plays a huge role in the discrepancy between PPD patients and the band-aid solution of wine. Platforms such as Facebook and Instagram have emerged as popular places for new mothers to share

their concerns and cope with the stress of being a new mom (Adams et al., 2021). Wine mom culture flourishes on Facebook, with pages such as "Mommy drinks wine and swears" or "The Wine Mom Chronicles" (Adams et al., 2021). While these pages offer a place to vent, they normalize alcohol as a coping mechanism or dismiss PPD symptoms as just a case of "baby blues" and can be quickly fixed with a glass of wine (Adams et al., 2021).

The most effective solution for dismantling Wine Mom culture and tackling PPD is to create a stronger mental healthcare system for mothers and reduce the stigma behind PPD. Often during the postpartum time, the focus on the physical health of the mother and baby distracts from considering the mother's emotional well-being (Alcoholism and Postpartum Depression, 2022). Physicians should begin implementing PPD screening questions and actively start conversations with expectant mothers or postpartum mothers about what PPD looks like. In addition, mental healthcare for postpartum mothers should be treated with as much importance as physical healthcare. Physicians should keep an ever-watchful eye on their patient's mental well-being and provide instruction on how to adjust to motherhood in a healthy manner. Just by strengthening mental healthcare strategies and providing outlets for postpartum mothers to get the care they need, alcohol will not be a coping mechanism that desperate mothers are forced to turn to. Community discussions about PPD are also necessary (Alcoholism and Postpartum Depression, 2022). With such a large emphasis on preparing for the baby, mothers often forget they themselves are preparing for a new chapter of their life. Bringing up PPD in birthing classes or other prenatal groups would be a good way to engage with women who may not be able to see a physician because of limiting factors such as cost or transportation. For a country that puts such an emphasis on babies, we often forget about the women who already exist and deserve quality care. We cannot continue to fail American mothers; it comes at a deadly cost. ❧

Just by strengthening mental healthcare strategies and providing outlets for postpartum mothers to get the care they need, alcohol will not be a coping mechanism that desperate mothers are forced to turn to.

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Commotio Cordis vs. Damar Hamlin: The deadly nature of high-performance sports

ASHLEY ZHU
Staff Writer

When 24-year-old Buffalo Bills player Damar Hamlin went into cardiac arrest — the sudden loss of all heart activity due to an irregular rhythm — millions of Monday Night Football viewers and the American football community watched in suspense on Jan. 2 as paramedics rushed to save his life. Doctors speculated that the cause of the rare event was commotio cordis — translating to "agitation of the heart" in Latin etymology — cardiac arrest that results from a blow to the chest at the exact 20-millisecond interval in the heart's cycle that can make it stop. Commotio cordis results from a mechanical force that causes a stretch in myocardial cell membranes, activating just the right amount of ion channels during a vulnerable period of depolarization, which causes ventricular fibrillation (Tainter, 2022).

Despite the benefits associated with exercise, evidence shows that physical activity beyond a certain intensity threshold can often lead to health detriments (Runacres, 2021). The National Football League's (NFL) emphasis on rigorous training and discipline raises the question of whether or not a disproportionate burden of injury is placed on Black football players, who make up about 70% of all NFL players. As demonstrated by Hamlin's collapse, the extraordinary stresses experienced by high-performance athletes put them at higher risk of illness and injury — because the NFL is composed of majority Black men, the rigorous training and discipline has afflicted them the most.

The National Football League's (NFL) emphasis on rigorous training and discipline raises the question of whether or not a disproportionate burden of injury is placed on Black football players, who make up about 70% of all NFL players.

It is widely known and accepted that exercise can be extremely beneficial for long-term physical and mental health. The American Heart Association specifically emphasizes cardiorespiratory fitness and improving exercise capacity in order to combat coronary heart disease; cardiovascular (CV) disease and cancer are the most prevalent causes of mortality worldwide, and research has repeatedly shown that mortality risk decreases with regular exercise (Al-Mallah, 2018). However, the exercise-longevity relationship may be "J" shaped, with exces-

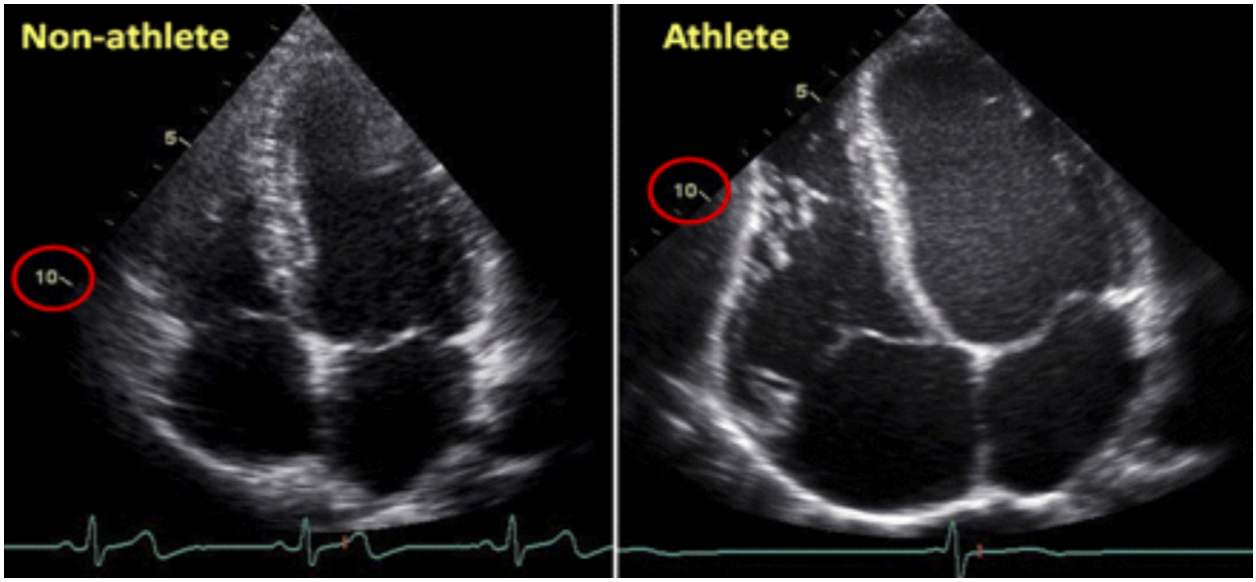

Figure 1: Apical four chamber echocardiogram compares the heart of a 23-year-old non-athlete (left) with that of a 23-year-old professional cyclist. Athletes experience dilation of all four cardiac chambers and an increase in stroke volume, despite normal or even reduced resting function.

sive physical activity beyond a certain limit affording higher risks of a CV event. For example, the Copenhagen Heart Study reported that joggers who run at light and moderate intensities possess extremely low mortality hazard ratios of 0.22 and 0.66, respectively, while strenuous joggers exhibit a hazard ratio of 1.97 (Runacres, 2021). Hazard ratios describe the relative risk of the complication based on a comparison of event rates (Spruance, 2004). Additionally, the Million Women study, which obtained robust information regarding breast cancer risk, showed that women who exercised every day were at increased risk of a CV event compared to women who had at least one rest day during the week (Runacres, 2021).

European and American health guidelines recommend a minimum of 150 minutes of moderate-intensity exercise per week for adults, but most competitive athletes regularly engage in over 20 hours of intense exercise per week (Sharma, 2015). Such sustained lengths of physical activity can result in a multitude of electrical, structural and functional changes within the heart that result in a condition called "athlete's heart." This ailment is characterized by enlargement of cardiac chambers, left ventricular hypertrophy—increased thickness in the wall of the heart's main pumping chamber—and greater cardiac filling during diastole (Sharma, 2015). Such changes are benign and can be reversed after detraining processes which results in the partial or complete loss of training-induced adaptations (Sharma, 2015). However, the combination of left ventricular hypertrophy with repolarization changes, and increased cavity size with low ejection fraction — the percentage of blood that leaves the heart each time it contracts — may overlap with cardiomyopathy (Sharma, 2015).

[E]lite athletes also experience "broadly comparable" rates of poor mental health relative to the general population in relation to anxiety, depression and post-traumatic stress [...].

Sudden cardiac death (SCD) occurs during or immediately following an athletic competition. Though such occurrences are rare, prevalence varies between 1 in one million to 1 in 23,000 athletes per year; some subpopulations are at an even higher risk, with African-Americans experiencing an incidence rate of 1 in 18,000 and Division I male basketball players with a risk of 1 in 3000 (Harmon, 2014). An Italian prospective cohort study reported 2.5 times the relative risk of SCD in competitive athletes compared to non-athletes, and numerous other studies have further proven the high risk of SCD in competitive athletes (Harmon, 2014). Though Hamlin was fortunate enough to have survived the blow to his chest, commotio cordis is a leading cause of sudden death in athletes (Tainter, 2022).

As it relates to negative effects of participation in high-performance sports, elite athletes also experience "broadly comparable" rates of poor mental health relative to the general population in relation to anxiety, depression and post-traumatic stress; therefore, early detection and intervention are essential in the context of elite sporting (Purcell, 2019). Especially during junior development years, supportive relationships between parents and coaches for the well-being of a young athlete, lack of good sleeping conditions and exposure to unfamiliar training environments could be negative health factors (Purcell, 2019). Purcell, et al. suggest a

	%	#
2022		
White	24.9%	421
Black or African American	56.4%	954
Hispanic or Latino(a)	0.4%	7
Asian	0.1%	2
Hawaiian or Pac. Islander	1.5%	25
Am. Indian or Alaska Native	0.2%	3
Two or More Races	10.5%	178
Not dislosed/not specified	5.7%	97
Other	0.2%	3

Figure 2: Data from the 2022 Racial and Gender Report Card shows the demographic compositions of all NFL players.

framework that could develop a range of self-management skills, including psychological distress, equipping coaches and sports medicine staff to better recognize an athlete's mental health, and highlight the need for skilled professionals to manage athletes with severe mental health disorders (Purcell, 2019). Elite athletes in particular, are prone to training and competing even when ill or injured, and there is a need for coaches and players to work toward a common goal of optimizing performance while also prioritizing the athlete's well-beingA final implication tied to Hamlin's cardiac arrest relates to higher representation of Black people in specific sports, particularly in basketball, football and track and field, showing that they represent the majority of players in national leagues. According to the 2022 NFL Racial and Gender Report Card, Black or African-American players constituted 56.4% of all players, while the percentage of Black or African-American head coaches was 9.4% for both the 2021 and 2022 NFL seasons (Lapchik, 2022). Black and Hawaiian players were found to be at a significantly higher risk of adverse physical and cognitive function, pain interference in daily life, and depression and anxiety (Roberts, 2020). A study of former professional basketball players found a 77% greater risk of death for Black versus White players, equivalent to a difference of 18 months of life (Roberts, 2020). Experiences with racism are associated with poorer mental and physical health, as Black men may receive poorer quality health care than white men (Roberts, 2020). And despite the high salaries of all athletes in professional football leagues, the socioeconomic benefits of playing in the NFL do not necessarily equalize race-related health disparities (Roberts, 2020).

Though there is limited research exploring the effects of the disproportionate burden of injury on Black athletes, the majority composition of Black players among all football players coupled with the risks of high-performance sports puts them at a higher risk of injury. In addition to higher risks of SCD, Black athletes are certainly at a higher risk of illness and injury in intense sports which suggests a need for greater emphasis on Black men's health and wellness. ❧

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Strength in neurodiversity: Accelerating healthcare progress & inclusivity

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Neurodevelopmental condition	Common strengths
ADHD	Creative thinking Visual-spatial skills Hyper-focus and passion
Autism	Attention to detail Recognition of complex patterns Innovative thinking
Dyslexia	Visual-spatial skills Visual reasoning Creative thinking

Figure 1. Common strengths possessed by neurodiverse individuals Recent research has discovered associations between certain neurodevelopmental conditions and particular strengths. However, the specific strengths possessed by neurodiverse individuals vary greatly depending on the individual just as strengths vary among neurotypical individuals (Doyle, 2020).

In the wake of recent research, it has become increasingly clear that there is no "normal" or "abnormal" brain. While neurodevelopmental conditions can create challenges that make it more difficult to function in society among neurotypical individuals, they can also result in strengths. However, stigma and a lack of appropriate infrastructure often prevent them from contributing their strengths in a wide array of professions, including healthcare. Altering perceptions of neurodivergent individuals as well as employment and accommodation policies could have a significant impact on the prevalence and performance of these individuals in healthcare settings. Ultimately, creating healthcare settings that are more inclusive of neurodivergent healthcare professionals could benefit physicians, patients, and the healthcare system as a whole.

Neurodiversity is rooted in the idea that while neurodivergent individuals face challenges and limitations, it is important to also recognize the strengths possessed by such individuals.

Such change would be centered around recent findings supporting neurodiversity, a concept that regards individuals with differences in brain function and behavior as part of normal variation in the human population (Doyle, 2020). Such brain differences include autism spectrum disorder, attention-deficit/hyperactivity disorder (ADHD), and dyslexia. Neurodiversity is rooted in the idea that while neurodivergent individuals face challenges and limitations, it is important to also recognize the strengths possessed by such individuals. Some feel that this perspective overlooks neurodivergent individuals who face significant challenges, such as difficulty speaking. However, many neurodivergent individuals argue that neurodiversity does not mean denying the reality of being disabled. Rather, this definition of neurodiversity can be used to acknowledge the challenges neurodiverse individuals face while also recognizing the value of their strengths (Doyle, 2020). Replacing misconceptions with a scientific understanding of neurodiversity may reduce stigma that can affect a neurodivergent individual's chances of being hired, respected, and accommodated as a healthcare worker.

For example, autism spectrum disorder (ASD) refers to differences in the brain that affect communication and behavior, often resulting in specialized interests, difficulties with social communication, and sensitivity to sensory input. Several studies have demonstrated that the same mechanism that can result in sensory hypersensitivity in many autistic brains also results in excellent attention to detail and an enhanced ability to recognize patterns (Uddin, 2022). Such abilities are essential for healthcare providers to quickly and accurately diagnose and treat patients (Fackler et al., 2009). Similarly, while dyslexic individuals experience significant difficulties with reading and writing, they have been found to

possess excellent global visual-spatial abilities. Differences in dyslexic brain structure and development may increase their capacity to perceive peripheral or diffused visual information more quickly and efficiently than individuals without dyslexia (von Károlyi et al., 2003). Such skills have shown to be especially beneficial to surgeons, who rely on visual-spatial abilities to carry out complex surgical procedures (Wanzel et al., 2002).

Increasing the number of physicians with these abilities may reduce misdiagnoses and other medical errors (Fackler et al., 2009). Therefore, when considering whether to accept a neurodivergent applicant to medical school or hire a neurodivergent healthcare worker, rejecting the individual solely on the basis of their diagnosis may overlook highly valuable strengths. Each individual with the same neurodevelopmental condition experiences a different set of traits—for instance, no two autistic individuals possess the same set of abilities and difficulties. While hypersensitivity may cause one autistic individual to be especially perceptive of details or patterns in a patient's medical record, it may cause another autistic individual to be particularly conscious of their patient's emotions. A third autistic individual may not experience hypersensitivity at all (Doyle, 2020). As a result, by considering each individual neurodivergent applicant's abilities, admissions committees and employers may gain a more accurate understanding of their strengths and challenges than if they were to solely consider the limitations described by the DSM-5. Not all neurodivergent individuals possess the qualities necessary to be an effective healthcare worker, just as not all neurotypical individuals possess these qualities. However, the aforementioned research demonstrates that rejecting a neurodivergent individual before considering whether they possess such qualities may reject an applicant who is more proficient in such areas than the majority of neurotypical individuals. Ultimately, medicine is a diverse field that includes a variety of specialties that require a multitude of capabilities and characteristics. Only including and supporting neurotypical individuals in the field of healthcare may limit the wide range of skills that are necessary for the healthcare system to function at its best.

It is critical to understand and address some of the barriers that limit the prevalence and performance of neurodiverse individuals in order to increase the diversity and productivity of the healthcare system as a whole. While stigma and misconceptions surrounding neurodivergent individuals can lead healthcare employers to be more hesitant to hire them, there are also few accommodations in place for neurodivergent healthcare workers who are hired. This often leads to poor performance and exhaustion of these individuals. The exhaustion is often caused by neurodiverse individuals feeling the need to "mask" behaviors because of lack of acceptance in the workforce. "Masking" refers to when neurotypical individuals feel pressured to mirror the behavior of neurotypical individuals, such as "suppressing self-soothing behaviors like fidgeting" (Duong et al., 2022); it can lead to dire consequences such as increased anxiety, depression, and suicidal thoughts (Duong et al., 2022). In order to better support these diverse healthcare professionals, it is critical to provide arrangements and systemic improvements that can not only reduce mental efforts towards masking, but also increase productivity in the workplace.

Education can break down the barriers caused by stereotyping and can prevent the stigma that may cause healthcare employers to prematurely reject neurodiverse applicants before assessing individuals' specific strengths and weaknesses. Especially in medicine, these disorders can be under-assessed because the profession filters for "intelligent and conscientious people whose strengths may mask difficulties'' (Duong et al., 2022). There are existing campaigns sponsored by the Department of Labor such as the Campaign for Disability Employment (CDE) that promote positive employment outcomes for people with disabilities by encouraging employers to recognize the values they bring to the workplace. In addition to governmental efforts, there are organizations such as the Autistic Doctors International, a peer-support and advocacy group for doctors with autism; it could be useful for these organizations to partner with local companies to increase awareness about supporting neurodiverse health-

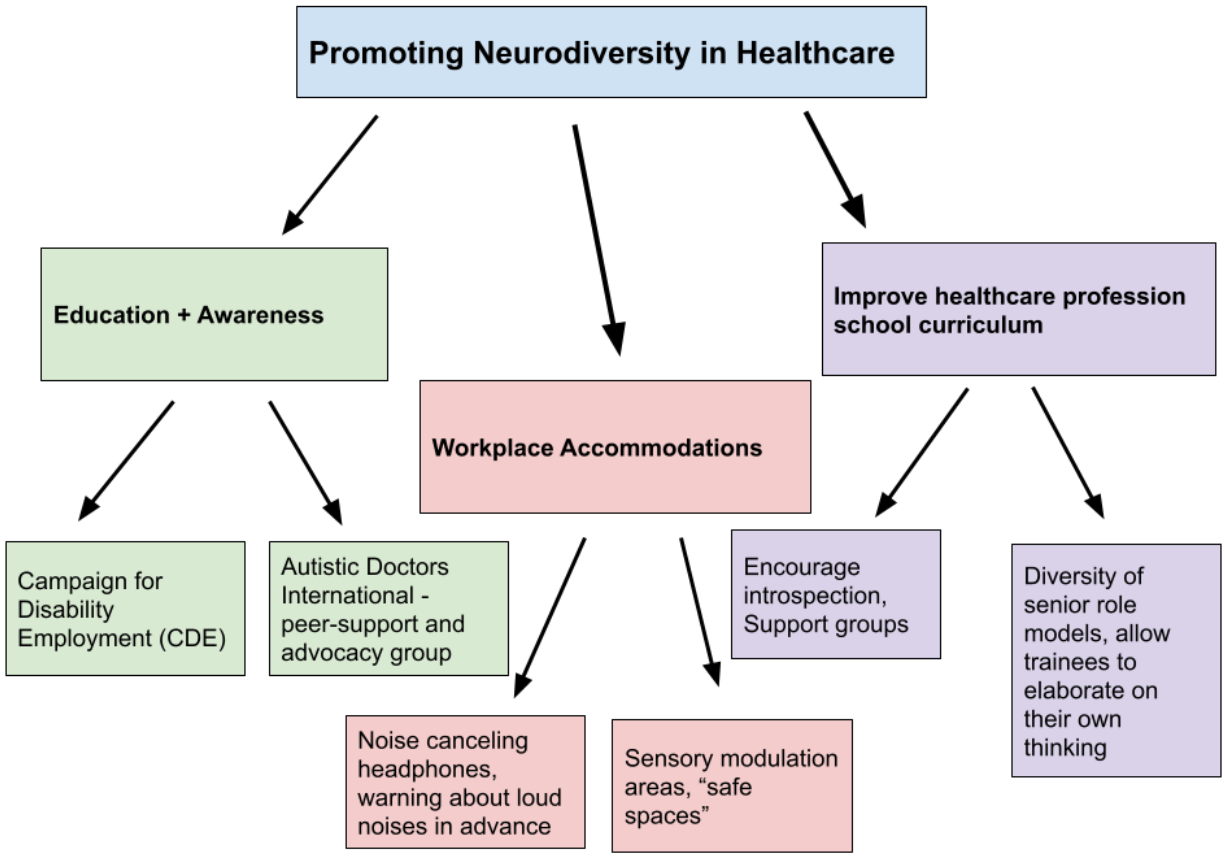

Figure 2. Elements of improving the promotion of neurodiversity in healthcare, and potential actions we should take in the future. Main facets of promotion are education + awareness, workplace accommodations, and improving healthcare profession school curriculum.

care employees. Promoting open communication about this topic and encouraging support groups is key to achieving inclusivity. Besides autism, which is one of the most discussed disorders, education on lesser-known disorders, such as ADHD or dyslexia, may be beneficial to increase acceptance in the workplace.

Education not only encompasses the wider public but also includes educating medical school students. Within the curriculum, Daniel Robinson, a psychiatry trainee with ADHD, suggests that it is beneficial to have learning environments with neurodiverse senior role models that "provide timely feedback" and "use teaching strategies that make visible the thought processes involved in complex tasks and allow trainees to elaborate on their own thinking" (Duong et al., 2022). This can encourage introspection in medical training and support students in expressing their creativity; these improvements can eventually translate into more understanding healthcare professionals supporting their patients.

It could be useful for these organizations to partner with local companies to increase awareness about supporting neurodiverse healthcare employees.

After training, while healthcare professionals are in the workplace, accommodations may alleviate neurodiverse individuals from feeling as if they need to "mask" their behaviors. Factors in many workplace environments, such as sudden or loud noises and smaller cubicles, may cause masking for this population. For instance, autistic individuals may be more sensitive to sudden or loud sounds due to "their increased sensory acuity" (Trotman et al., 2018). To accommodate these employees, workplaces can establish "quiet areas", allowing a place for breaks, and offer noise-canceling headphones to increase productivity. Additionally, fidgeting in autistic and ADHD individuals should be accepted and normalized. Contrary to public belief that neurodiverse individuals may contribute less

to the workplace than their counterparts, these accommodations should not be a barrier to hiring diverse populations if everyone is productive in the workplace and contributing adequately to the team output. To many neurodiverse healthcare employees, organizations often have moments of supporting these populations but do not offer embedded change such as sensory modulation areas and multimodal entry points (multiple methods to complete a task), which can be beneficial in supporting employees to achieve productivity (Trotman et al., 2018).

In recent years, the healthcare system has improved diversity and inclusion, but there is still more progress to achieve. Neurodiversity, a previously overlooked topic, is now at the forefront of the discussion on how to make the healthcare field more inclusive, as individuals with disorders ranging from ADHD to autism can contribute vastly to their healthcare professions by showcasing their unique strengths. To truly promote inclusivity and diversity, healthcare systems should cherish this difference and see the potential for improving healthcare for all patients. In the coming years, it will be of utmost importance to establish the accommodations previously mentioned to support neurodiverse healthcare professionals and allow them to contribute to their field, free from the barriers they currently face. ❧

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EUMR's main advisor is Dr. Arri Eisen, professor of pedagogy in biology and at the Center for Ethics at Emory University. After receiving his PhD in biochemistry from University of Washington - Seattle in 1990, he began teaching at Emory and became a teaching coordinator for FIRST, a postdoctoral fellowship in research and teaching that is supported by the National Institutes of Health.

Dr. Eisen aims to engage undergraduate students in the exploration of science and its applications in broad contexts. He has led the Emory-Tibet Science Initiative since 2005, which works with the Dalai Lama to provide a scientific education for Tibetan monks and nuns. He has published a wide variety of academic articles in science, science education, and bioethics.

Emory Undergraduate Medical Review articles are peer-reviewed by medical professionals from more than a dozen leading academic institutions. The Emory Undergradute Medical Review would like to extend its thanks to the following advisors.

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Doctorate in comparative literature from Cornell University.

Dr. Otis had her beginnings in science, earning a bachelors in molecular biophysics and biochemistry from Yale and then a masters in neuroscience from the University of California at San Francisco. Now at Emory, she teaches the intersection of science and literature with special interest in nineteenth century novels.

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Dr. Crane serves as the Raymond F. Schinazi Scholar of Bioethics and Jewish Thought at Emory University's Center for Ethics, professor at Emory University School of Medicine, and affiliated faculty in the Department of Religion. As the founder and co-Editor-in-Chief of the *Journal of Jewish Ethics*, he continues to publish research on Judaism, bioethics, and religious ethics.

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Shreya is a second year majoring in Anthropology and Human Biology and Minoring in South Asian Studies. She is currently secretary of EUMR and was a freshman liaison during her first year with the magazine. Outside of EUMR, Shreya is also involved with Emory Grey Matters and is a research ambassador.

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