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Contents

Effectiveness and Safety of rVSV-ZEBOV Vaccine Against the Zaire Ebola Virus

Jerry Du, China

Abstract

The recombinant vesicular stomatitis virus–Zaire Ebola virus vaccine (rVSVΔG-ZEBOV-GP, Ervebo) is a major vaccine developed against Ebola Virus Disease (EVD). This literature review introduces evidence from clinical trials to evaluate the vaccine's effectiveness and safety. The vaccine demonstrates high immunogenicity, with seroconversion rates exceeding 90% in diverse populations, including adults and children, and induces durable antibody responses lasting up to 24 months. It is also effective in boosting immunity in individuals with pre-existing antibodies. The vaccine has a considerable safety profile, with adverse events (AEs) primarily being mild to moderate and transient, such as injection-site pain, fatigue, headache, and fever. Serious adverse events are rare and not attributed to the vaccine. While there are limitations, including a lack of long-term data beyond two years and limited research on immunocompromised individuals, evidence confirms that rVSVΔG-ZEBOV-GP is a highly effective and safe tool for outbreak control and global health security.

Introduction

Ebola virus (EBOV) is a member of the Filoviridae family, which includes deadly viruses such as the Marburg virus. The virus was identified in 1976 in the outbreaks in Sudan and the Democratic Republic of Congo, and earned its name from the Ebola River near one of the outbreak sites. EBOV causes hemorrhagic fevers that lead to the likelihood of death. EBOV's rapid transmission and significant public health implications cause sporadic outbreaks with high mortality rates, particularly in sub-Saharan Africa. [1] Ebola virus disease (EVD) is caused by the infection of one of the Ebola virus species, with the most lethal being the Zaire Ebola Virus. This virus is transmitted to humans through contact with infected animals, such as fruit bats, and is transmitted among humans by direct or indirect contact with the blood, body fluids, or secretions. The symptoms after the infection of EBOV include sudden onset of fever, weakness, muscle pain, and internal and external bleeding in severe cases. [2] Previously, the 2013-2016 outbreak of the Zaire Ebola virus (ZEBOV) in West Africa, within sub-Saharan Africa, the largest EBOV outbreak up to date, resulted in more than 28600 reported cases of Ebola virus disease (EVD) and 11325 deaths. [3] The epidemic emphasized the lack of disease surveillance, preparation, and treatment. Since then, significant efforts in the medical field have guided us to have a more detailed understanding of the virus.

The invention of a vaccine against ZEBOV would be a vital milestone for human beings to combat and prepare for future epidemics. Early efforts to develop Ebola vaccines date back to the 1990s and early 2000s, but these were predominantly limited to preclinical stages due to challenges, including biosafety concerns, limited funding, and sporadic outbreak patterns that hindered large-scale trials. [4] The initial vaccine candidates were a variety of different approaches, including DNA-based vaccines, adenovirus-vectored approaches, and virus-like particles. Although some did show promise in animal testing, none of them progressed to the final stages of clinical trials. [5] Later in the process, the West African epidemic impelled international cooperation and the acceleration of vaccine development.

The most notable outcome of the efforts was the invention of the rVSVΔG-ZEBOV-GP, a recombinant, replication-competent vaccine. This vaccine demonstrated high efficacy in a landmark ring vaccination trial conducted in Guinea in 2015, which showed near-complete protection among vaccinated individuals. Following further clinical evaluation, the vaccine received approval from both the World Health Organization (WHO) and the U.S. Food and Drug Administration in 2019, becoming the first licensed vaccine for EVD. [6] In addition, other vaccines such as ChAd3-EBO-Z/S, Ad26.ZEBOV/MVA-BN-Filo and multivalent or pan-ebolavirus vaccines are in experimental trials and have all revealed promising results. [6]

This literature review investigates the pre-existing trials conducted using the rVSVΔG-ZEBOV-GP vaccine. By reporting and comparing methods, data, and conclusions from previous studies, this paper will provide a review of the immunogenicity, the ability for the vaccine to trigger immune responses, and adverse events (AE), the harmful medical occurrences during clinical trials. The purpose of this paper is to understand the effectiveness and safety of the vaccine.

Vaccine Mechanism and Function

The recombinant vesicular stomatitis virus–ZEBOV envelope glycoprotein vaccine (rVSVΔG-ZEBOV-GP) is the most effective and applied vaccine against EBOV. The vaccine, commercially known as Ervebo, is a recombinant, replication-competent viral vector vaccine designed to offer protection against Zaire ebolavirus (ZEBOV). Recombinant vaccines, like the rVSVΔG-ZEBOV-GP, are made by using a gene of the EBOV and adding it to the vesicular stomatitis virus. This vaccine, originally developed by the Public Health Agency of Canada, uses rVSV, Indiana Strain, as a vector to provoke an immune response against the ZEBOV by replacing the gene encoding vesicular stomatitis virus (VSV) surface glycoprotein (G protein) with the gene encoding ZEBOV GP. [6] Following intramuscular injection, the vaccine virus enters host cells via endocytosis. The vaccine utilizes the Ebola GP to bind to host cell receptors and mimics natural Ebola virus entry. Then, the recombinant VSV replicates locally at the injection site and in regional lymph nodes, expressing the Ebola virus GP on its surface during replication. As a result, adaptive immune responses occur. [7] rVSVΔG-ZEBOV-GP vaccine may induce adverse events, including pain and edema at the injection site and fever, chills, fatigue, headache, myalgia, arthralgia, lymphopenia, and arthritis, all of which are transient and of mild to moderate intensity. [6] The paper will further analyze the efficacy and AEs presented in vaccine trials.

Effectiveness of the Vaccine

In the recent decade, the rVSVΔG-ZEBOV-GP has stepped into Phase I and Phase II testing, presenting relatively satisfactory results. The vaccine has been rigorously evaluated through multiple clinical trials with diverse methodological approaches. In different journals published by numerous research programs and labs, through a variety of trials, the rVSVΔG-ZEBOV-GP has high immunogenicity and efficacy.

Phase 3 randomized, double-blind, placebo-controlled studies, like the one conducted by Halperin et al. [7], proved its immunogenicity by measuring ZEBOV-GP-specific antibody responses via enzyme-linked immunosorbent assay (ELISA) and plaque reduction neutralization tests (PRNT). These assays demonstrated a >58-fold increase in geometric mean titers (GMTs) by day 28, with sustained responses over 24 months, confirming long-term immune memory. Over 94% of recipients seroconverted by day 28, and ≥91% maintained immune responses at 24 months. Antibodies also peaked at 18 months and remained elevated. The design of the study, with the method of using consistent testing and stratified sample groups, presented itself with strong validity. Its large sample size (N=1,197) was

proven to be relatively general to healthy adult populations, with strong and meaningful correlation with humans.

Pediatric studies, such as the phase 2 trial by Alabi et al. [8], expanded the evidence base by assessing immunogenicity in children aged 1–12 years. A randomized, controlled, open-label design, the trial measured ZEBOV-GP IgG responses and neutralizing antibody kinetics over 12 months. Results showed seroconversion rates of 87–97% by day 28. Antibody titers persisted for 12 months, and neutralization functions peaked early and remained stable.

The immunogenicity in individuals with pre-existing immunity was studied in Guinea. This study discovered that 16.3% (228/1403) of participants had baseline anti-GP IgG antibodies, possibly from pre-exposure. [9] After vaccination, 81.3% (955/1175) of seronegative individuals seroconverted, while those with baseline antibodies saw a significant rise in GMTs (0.237 IU/mL vs. 0.106 IU/mL in seronegative participants, $p < 0.0001$). These results show that the rVSVAG-ZEBOV-GP effectively boosts immunity regardless of prior exposure. This finding was extremely critical since the pre-existing immunity characteristic applied to outbreak settings. [9] Thus, this study supports the vaccine's utility in boosting immune responses across populations.

Given that the populations and sample groups varied in size and traits, the studies could not empirically provide any justification for an overall cost-benefit analysis of the virus. However, based on the lab results from the studies above, the immunogenicity of the rVSVAG-ZEBOV-GP vaccine was well tested and empirically supported with different sample groups. The rVSVAG-ZEBOV-GP vaccine is highly effective in preventing EVD through rapid protection in outbreak settings and robust immunogenicity in diverse populations.

Safety of the Vaccine

The safety profile of the rVSVAG-ZEBOV-GP vaccine was evaluated under an extensive number of studies with various methods and different populations, such as adults, children, and high-risk frontline workers, etc. Overall, clinical trials consistently report that the vaccine is relatively well-tolerated, with the adverse events (AEs) primarily being mild to moderate and transient.

In a phase 2 study of adults receiving a delayed booster at 18 months, reactogenicity post-booster was comparable to primary vaccination, with no new safety signals. [10] The sample group of the trial was individuals who received primary vaccination with 2×10^7 plaque-forming units per mL of VSVΔG-ZEBOV-GP and received a booster, the same as the previous vaccine, after 18 months. [10] In terms of safety, previously documented AE, arthritis, occurred in 9% of primary vaccinees but did not recur post-booster. Serious adverse events (SAEs), such as epistaxis and gastrointestinal hemorrhage, were rare and not related to the vaccination. All the results show that the homologous boosting vaccines do not increase nor exacerbate AEs. Halperin et al.'s Phase 3 Trial evaluated safety in healthy adults. [7] This randomized controlled trial involved 1,197 healthy adults and found that the vaccine was generally well tolerated. Participants received one lot of rVSVΔG-ZEBOV-GP (standard dose: 2×10^7 plaque-forming units [pfu]), a high-dose formulation (1×10^8 pfu), or placebo. The study revealed relatively mild AEs, including injection-site pain (58.8% vaccinated vs. 21.8% placebo) and systemic AEs like fatigue (49% vs. 28%). [7] SAEs were rare and not vaccine-related, with no deaths corresponding to the vaccine. Interestingly, female sex and prior arthritis history were identified as potential risk factors for post-vaccination arthritis, though severe cases were uncommon. [7]

The vaccine has been tested in live scenarios against EBV. Applying this vaccine in a

frontliner setting against the virus can prove how the safety was demonstrated in a dangerous environment. A study of 2016 vaccinated frontline workers in Guinea surveillance, with structured diaries for adverse events (AEs). [11] The use of control groups of the unvaccinated population allowed for a comparative assessment of AE frequencies with Fisher's exact. Results indicate that over 70% reported at least one AE within the first three days post-vaccination, with the most common symptoms being headache (52%), fatigue (46%), arthralgia (25%), and subjective fever (24%) [11]. Fever, a concern in Ebola-endemic regions due to the overlap of symptoms with EVD, was reported in 15% of participants, and most cases were low-grade (<39°C) and resolved within 48 hours. These findings were consistent with phase 1 trials, supporting that the vaccine's AEs are manageable and self-limiting.

The vaccine's capability with populations closely in contact with EVD is extremely essential, as this would be the primary population vaccinated in the future. Watson et al. conducted a cohort study in Guinea. [9] This study vaccinated close contacts of EVD survivors, including individuals with pre-existing immunity. The study found no significant difference in adverse event rates between seropositive and seronegative participants, with headache (35.1%), fatigue (23.7%), and muscle pain (14.6%) as the most common reactions. [9] There were only eight moderate and one severe adverse event reported, none of which were attributed to vaccination. This study provided critical evidence that pre-existing immunity does not worsen reactogenicity, thus making the vaccine suitable for environments with pre-existing exposure to EVD. Davis et al. conducted an observational follow-up study of 26 vaccinated individuals in the UK, a cohort design with standardized adverse event reporting over 12 months. [12] The study examined vaccination following exposure to a healthcare worker with Ebola virus disease (EVD) reactivation. Results show that the vaccine was well tolerated, with no severe AEs reported. [12] Common AEs included fatigue (81%), headache (69%), myalgia (69%), and fever (50%), all of which were transient and resolved without much intervention. Throughout the trial, 50% of participants developed a fever ≥37.5°C, which was followed by urgent screening for Ebola, and none tested positive. [12] Two cases of arthralgia were observed, but were unrelated to vaccination after review. This evidence suggests that although AEs are common, the vaccine remains safe for emergency use. [12]

Systematic reviews and network meta-analyses compared the safety of multiple Ebola vaccines, including rVSV-ZEBOV. Diallo et al. used models to estimate odds ratios for adverse events, with P-scores to rank vaccine safety profiles. [13] The analysis confirmed that rVSV-ZEBOV has a higher chance of injection-site pain (P-score 0.90 for lower doses) and AEs such as fatigue and headache compared to other candidates. However, these AEs were mainly mild to moderate, with severe events being rare. [13] The study claimed the vaccine's AEs were dose-dependent, with higher doses (e.g., 2 × 10^7 PFU) associated with increased but manageable side effects. There were no anaphylaxis or life-threatening reactions reported, strengthening the vaccine's safety. [13]

The relatively smaller populations were also tested with the vaccine. The safety demonstrated reflects the essential information on how the vaccine can protect these special populations. The Sierra Leone Trial to Introduce a Vaccine against Ebola (STRIVE), a phase 3 trial, used randomized methods to monitor AEs and SAEs. [14] In the STRIVE trial, 84 women were vaccinated during early pregnancy or became pregnant within 60 days post-vaccination. [14] Pregnancy outcomes between the immediately vaccinated and unvaccinated groups were not statistically significantly different, with pregnancy loss rates of 45% (14/31) and 33% (11/33), respectively. [14] A total of 7 serious adverse events (SAEs) were reported. Five SAEs were hospitalizations for a pregnancy-related complication: gestational hypertension (2 cases),

prolonged labor (2 cases), and a postpartum hemorrhage (1 case) that resulted in a maternal death. No congenital anomalies were detected among 44 live-born infants examined. [14] Indeed, there is a need for Ebola vaccination decisions to balance the possible risk for an adverse pregnancy outcome with the risk for Ebola exposure.

Pediatric trials created new evidence of various populations of the vaccine against EVD. The phase 2 trial involving Gabonese children employed age-determined randomization (1–5 and 6–12 years) and a control vaccine (varicella) to control for background AE rates. [8] Real-time PCR assessed plasma and saliva at multiple timepoints (days 0–28). The trial found that AEs, such as injection-site pain (83%) and fever (29%), were more frequent in the rVSVAG-ZEBOV-GP group compared to controls receiving the varicella vaccine. [8] Symptoms like fatigue and myalgia were more prevalent in older children (6–12 years), revealing some age-dependent immune responses. Other than these reactions, there were no reported vaccine-related serious adverse events (SAEs), and abnormalities (e.g., leukopenia) resolved without intervention. The absence of severe AEs supports the vaccine's suitability for pediatric use, as proved by its approval for children ≥1 year by the FDA and EMA. [8]

Discussion

The primary intent of this paper is to analyze different results of the safety and effectiveness of the rVSVΔG-ZEBOV-GP vaccine. It demonstrated high immunogenicity and a strong safety profile as a vaccine to prevent EVD caused by ZEBOV. Clinical trials in diverse populations, including adults, children, and individuals with pre-existing immunity, showed strong efficacy. Seroconversion rates, which are the production of antibodies in the blood of a person, are a valuable way for studies to measure effectiveness. exceeded 90% in most studies, with durable antibody responses lasting up to 24 months, which then indicates the long-term reliability of this vaccine.

The vaccine's mechanism, utilizing a recombinant VSV vector to express ZEBOV glycoprotein, is very effective in generating immune responses. [9] et al. (2024) explained the mechanism and demonstrated that the vaccine effectively boosts immunity even in individuals with pre-existing antibodies, with individuals showing an 81.3% seroconversion rate. This finding is particularly useful in settings where recurring issues can occur. The rapid protection offered, typically within 10 days as observed, makes this vaccine very valuable for epidemic control.

In addition, the vaccine's safety profile is very strong and secure. Vaccination only leads to transient, mild to moderate AEs, which are all very manageable. Common AEs are injection-site pain, fatigue, headache, and low-grade fever. They were frequently reported but never escalated to a life-threatening level. In most safety trials, there was an absence of SAEs. These AEs were very acceptable as trade-offs given their high immunogenicity and efficacy. Overall, the benefits of vaccination outweigh the harms, especially in high-exposure environments.

Collective evidence from multiple trials shows that the AEs are relatively manageable. Davey et al. found that adverse events after booster vaccination were similar to those after primary vaccination. [10] Common reactions such as injection-site pain, fatigue, and headache were generally mild to moderate, as reported by Juan-Giner et al. [11]

Although the vaccine is effective and safe, several limitations in current research exist. One critical limitation is the lack of long-term data over 24 months, as explained by Halperin et al., whose Phase 3 trial showed sustained antibody responses but did not extend follow-up further. [7] Indeed, studies confirm durable immunity for up to two years, but the duration of protection in endemic regions needs further research. Moreover, the current trials lack research on individuals with weak or failing immune systems, such as those with HIV. Watson et al. did research about

pre-existing immunity, but did not address people with an immune deficiency. [9] This leaves a gap in understanding in high-risk populations.

Furthermore, the vaccine induces fever, which is a symptom overlapping with EVD. This poses challenges in outbreak settings, presented in the study by Juan-Giner et al. [10]. There is a need for post-vaccination monitoring to distinguish vaccine-related AEs from actual EVD infection.

The rVSVΔG-ZEBOV-GP vaccine has already given us the opportunity to react to the Ebola outbreak response, but its future applications are beyond emergency use. Combining this vaccine with other candidates and vaccines could enhance cross-protection against multiple species. This can solve the problem of the lack of a "pan-EBOV vaccine".

This vaccine's efficiency is also great for global health security. Future research should explore its use as a mechanism for other hemorrhagic fever viruses, such as Marburg or Lassa virus. This approach could fasten vaccine development for emerging infectious diseases, as suggested by Diallo et al. in their comparative analysis of Ebola vaccine platforms. [13]

Conclusion

The rVSVΔG-ZEBOV-GP vaccine has proven to be a great tool in Ebola prevention. Its strong efficacy and an acceptable safety profile across diverse populations can greatly benefit the current system. Its rapid and durable immune responses can also serve as a great solution for high-risk settings. The vaccine is a landmark in global health preparedness, offering a powerful defense against future outbreaks. The innovation in vaccine deployment and combination strategies will further strengthen how humankind can combat Ebola and related emerging infectious diseases.

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The Cosmic Spectrum: Unveiling the diverse types of stars

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The Cosmic Spectrum: Unveiling the diverse types of stars

Abstract

This paper provides a comprehensive overview of stellar classification, tracing humanity's evolving understanding of stars from ancient observations to modern astrophysical models. It details the historical advancements in astronomy, including the development of spectroscopy by Newton, Fraunhofer, Secchi, Kirchhoff, and Bunsen, which enabled the determination of stars' chemical compositions. It then explores the evolution of various stellar classification systems, from Angelo Secchi's early efforts to categorize stars to the contributions made by the 'Harvard Computers' and Annie Jump Cannon specifically to create the OBAFKM spectral sequence. Furthermore, it talks about the Hertzsprung-Russell diagram and the subsequent Morgan-Keenan (MK) system, which incorporates both temperature and luminosity, building upon the earlier Harvard spectral classification. The paper also examines the diverse properties and evolutionary stages of various stellar types, including main-sequence stars, giants, supergiants, and more exotic objects such as Wolf-Rayet stars, carbon stars, white dwarfs, and brown dwarfs. Overall, this paper highlights how stellar classification is a fundamental tool for comprehending cosmic evolution and the intricate mysteries of the universe.

1. Introduction

The night sky, and its millions of points of light, has captivated humanity for millennia. In fact, there are an estimated seventy sextillion (7×10^{22}) stars in the observable universe, approximately 10,000 times more than the number of grains of sand on Earth! (1) (2) These seemingly boundless celestial bodies have been used in religious practices, mythology, celestial navigation, and to mark the passage of time for centuries. Stars are approximately spheres made of plasma. They are crucial for humanity due to their supplies of light and heat. (3) To understand their great impact and variety, this paper will provide a comprehensive overview of the different types of stars, including the modern stellar classification system. It also aims to provide a historical overview of humanity's evolving relationship with and understanding of these celestial bodies and examine the various sophisticated techniques astronomers use to observe and measure these distant yet fascinating objects.

2. Unveiling stars: A brief history of their observations and related discoveries

2.1. Early celestial observations during ancient times

For much of human history, stars have been observed as unchanging points of light, their true nature a mystery. Most information gathered by early astronomers was purely observational. However, they also noted a difference between fixed stars, whose positions do not change, and planets, which had noticeable movement over a period of days or weeks. (3) There is also evidence of Ancient Egyptian star charts dated as far back as 1534 BCE (4) and the sighting of what was likely a supernova by Chinese astronomers in 185 CE. (5) These early records laid crucial foundational data, begin the first recorded sighting of specific stellar events, even though they were mostly based on philosophical frameworks rather than concrete scientific discoveries.

2.2.The advancement of stellar astronomy

The invention of the telescope and discoveries made by Galileo Galilei helped to popularize the idea of a heliocentric model with the Earth and the planets orbiting the Sun. (6) (7) Around this time, other revolutionary ideas were proposed, including the idea of stars being distant suns with their own planetary systems. (8) In the 17th century, Sir Isaac Newton discovered spectroscopy by using a prism to split white light into a spectrum of colors. (9) In the 19th century, Bavarian scientist Joseph von Fraunhofer invented the spectroscope (10), and together with Italian astronomer Angelo Secchi, they found differences in the strength and number of absorption lines between the spectra of stars like Sirius and the Sun. (3) In the 1850s, Gustav Kirchhoff and Robert Bunsen managed to describe the phenomena behind these absorption lines. They found that any chemical element, when heated, emits or absorbs light at specific wavelengths. Additionally, hot solids emit light with a continuous spectrum, and hot gases emit light at specific, discrete wavelengths unique to that element. They also found that hot solids surrounded by cool gases show a nearly continuous spectrum with dark lines corresponding to the emission lines of the gases. (11)

Figure 1: A continuous spectrum, as seen in the light emitted by hot solids. (12)

Figure 2: Discrete emission lines, as seen in the light emitted by hot gases. (13)

Figure 3: Absorption lines in a continuum plus discrete spectrum. (14)

By comparing the absorption lines of stars with the emission spectra of known gases, the chemical composition of stars could be determined. This demonstrated stars were composed of the same elements found on Earth, albeit in different proportions. (11)

2.3.The development of stellar classification

During the 1860s and 70s, Angelo Secchi began classifying stars into spectral types, creating the Secchi classes. (3) However, by the late 1890s, this classification was mostly replaced by the newer Harvard classification. Under the leadership of Edward Pickering, a group of female astronomers known as the Harvard Computers managed to identify over 10,000 stars. They would go on to release the Henry Draper catalogue to replace the previous classification made by Secchi. In 1912, Annie Jump Cannon would further develop this system and create the modern OBAFGKM spectral classification system, which ordered stars by their surface temperature. (15)

Another crucial discovery would be made through the work of Danish astronomer Ejnar Hertzsprung (16) and American astronomer Henry Norris Russell (17). They would both create a scatter plot of stars showing the relationship between their luminosities and temperatures. This diagram revealed distinct groupings of stars and showed that stars move across the diagram when they evolve. (18) In 1943, William Wilson Morgan, Philip C. Keenan, and Edith Kelman at Yerkes Observatory created the Yerkes spectral classification which builds onto the earlier Harvard spectral classification by adding a classification scheme for luminosity as well as for temperature. (15)

3. The modern Stellar Classification System

Stars exhibit many diverse properties, including in their mass, temperature, luminosity, and size. To effectively study and analyze the stellar population, a systematic classification system for stars is required. Modern astronomers classify stars mostly according to the stellar classification system, which categorizes stars based on their spectral characteristics and by extension, their surface temperatures. The most widely used modern classification system is the Morgan-Keenan (MK) system, also known as the Yerkes spectral classification. The MK system builds upon the older Harvard spectral classification which assigns a letter and a number to each star indicating its temperature. The MK system does this by adding a luminosity class, which indicates the star's luminosity and evolutionary stage. When combined, these two components provide a star's full MK classification. (15)

3.1. Harvard spectral classification

The Harvard system is the one-dimensional classification scheme which assigns a letter and a number to each star based on their temperature. It uses the letters O, B, A, F, G, K, and M, in order from hottest to coolest. Each letter is then further subdivided into a numerical class, with 0 being the hottest and 9 being the coolest. As a result, O1 would be hotter than O2, which would in turn be hotter than B0. A decimal number (e.g. O9.7) is also possible. (15)

Here is a table showing the different classes of stars according to the Harvard spectral classification and their properties:

Table 1: Physical characteristics associated with the Harvard Spectral Classes.

Class	Color	Temperature (K)
O	Blue	≥33,000
B	Bluish white	10,000 – 33,000
A	White	7,300 – 10,000
F	Yellowish white	6,000 – 7,300

G	Yellow	5,300 – 6,000
K	Orange	3,900 – 5,300
M	Red	2,300 – 3,900

(15)

Table 2: Properties of main sequence stars only according to the Harvard spectral classification.

Class	Mass ($M_\odot$)	Radii ($R_\odot$)	Percentage of all main sequence stars
O	≥16	≥6.6	0.00003
B	2.1 – 16	1.8 – 6.6	0.12
A	1.4 – 2.1	1.4 – 1.8	0.61
F	1.04 – 1.4	1.15 – 1.4	3
G	0.8 – 1.04	0.96 – 1.15	7.6
K	0.45 – 0.8	0.7 – 0.96	12
M	0.08 – 0.45	≤0.7	76

Note. $M_\odot$ = solar masses. $R_\odot$ = solar radii. Data is approximate.

(15)

However, this sequence does not encompass the full diversity of all stellar objects. As astronomical observations and spectroscopic techniques have advanced, new stellar objects have been discovered that do not fit into these categories due to their unique features or extreme states. Consequently, the sequence has been expanded to include new categories for stars that were discovered later and do not fit the original sequence, namely, W, S, C, D, L, T, and Y-type stars.

Wolf-Rayet (WR) stars (W-type)

Wolf-Rayet stars are exceptionally hot (20,000 – 210,000 K), massive, and luminous stars that are in advanced evolutionary stages (i.e., they have completely lost their outer hydrogen and are now fusing other, heavier elements such as helium). They are notable for having spectra which lack hydrogen. Instead, their spectra are mostly made up of broad emission lines made up of highly ionized helium, nitrogen, carbon, or oxygen. This is likely because their outer hydrogen layers have been stripped away by powerful stellar winds, revealing deeper, hotter material. This

class of stars is further subdivided into subclasses according to the relative strength of the nitrogen and carbon emission lines in their spectra and outer lines. (19)

S-type stars

S-type stars are giant stars that have cooled (with similar temperatures to class K and M stars). Their atmospheres contain approximately the same amount of carbon and oxygen. This leads to prominent absorption bands of Zirconium oxide (ZrO), and the absence of Titanium(II) oxide (TiO), which is more commonly found in M-type stars. (20)

Carbon stars (C-type)

Carbon stars are also cool, evolved, giant stars, but their atmospheres have more carbon than oxygen. This results in very distinct absorption bands containing many carbon-based molecules such as C_2, C_3, CH, CN, and SiC_2. (21)

White dwarfs (D-type)

White dwarfs are classified under the MK system; however, they are stellar remnants and not stars. White dwarfs are the final evolutionary stage of stars that are not big enough to become neutron stars or black holes. (22) (23)

Brown dwarfs (L, T, Y types)

Brown dwarfs are also classified under the MK system despite technically not being stars. They are often described as 'failed stars' because they are more massive than planets (around 13 – 80 times larger than Jupiter), but not massive enough to sustain hydrogen fusion in their core, and thus do not qualify as stars. However, they form in a similar way to stars (from collapsing gas and dust clouds), meaning they cannot be considered planets. They are subdivided into three types according to their temperature — Y-type (<600 K), T-type (600 – 1,300 K), and L-type (1,300 – 2,100 K). (24) (23)

3.2.Luminosity classification

While the Harvard spectral classification classifies stars by their surface temperature, the Morgan-Keenan system also adds a luminosity class to each star's spectral type. Here are the main luminosity classes: (15)

Class 0

Class 0 stars, also known as class Ia^{+}, are known as hypergiants. Hypergiants have extremely high luminosities, masses, and sizes. Hypergiants are very rare and usually very unstable. (25)

Class I

Class I stars are known as supergiants. They are very massive and luminous. They are further subdivided into three types — Ia for luminous supergiants, Iab for intermediate-size luminous supergiants, and Ib for less luminous supergiants. (26)

Class II

Class II stars are known as bright giants. These stars are on the boundary between ordinary giants and supergiants. (27)

Class III

Class III stars are known as giant stars. A main sequence star becomes a giant after it has exhausted all the hydrogen available for fusion in its core. (27)

Class IV

Class IV stars are known as subgiants. Subgiants are stars that are brighter than normal main sequence stars of the same temperature, but not as bright as giant stars. (28)

Class V

Class V stars are known as main sequence stars or Dwarfs. This class represents most stars, including the Sun. These stars are in the longest phase of their lives and are actively fusing hydrogen into helium in their cores. (29) (23)

Class VI

Class VI stars, sometimes denoted as 'sd', are known as subdwarfs. They are stars that are slightly less luminous than main-sequence stars of the same temperature. (30)

3.3.Complete star classification

The complete MK classification for a star combines its Harvard spectral type and its luminosity class. For example, the Sun is classified as a G2V star, indicating it is a Yellow (G2) Dwarf (V). Note that some stars may lie in between two categories. If a star's temperature falls in between two spectral types, a dash (-) can be used. If a star is in one of two luminosity classes, a slash (/) is used. (15) For example, a star classified as G5-6IV/V would be in between spectral types G5 and G6 and be either a subgiant or a main sequence (dwarf) star. This two-dimensional classification system allows astronomers to place stars on the Hertzsprung-Russell (H-R) diagram, which is a scatter plot showing the relationship between the stars' luminosities and temperatures. (18)

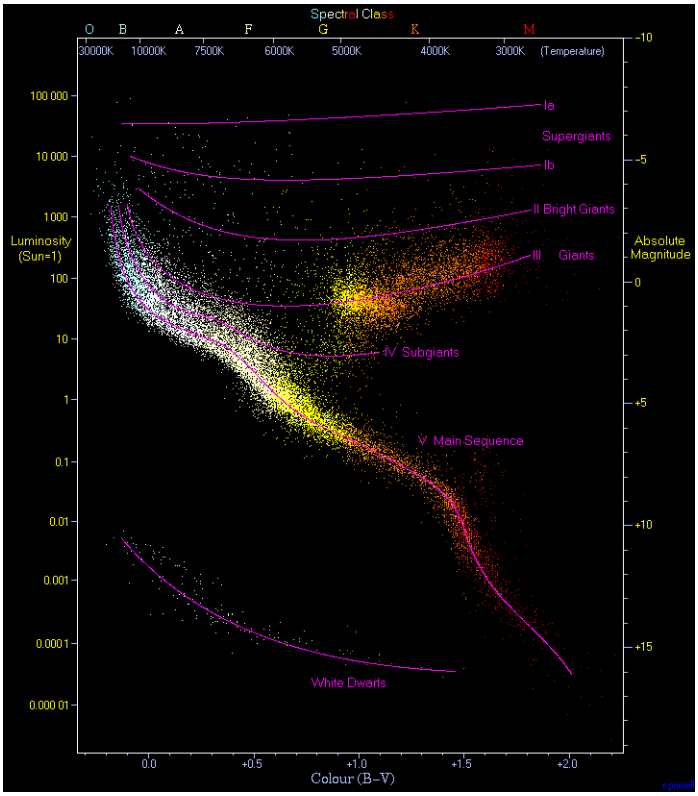

Figure 4: A scatter plot of 23,000 stars on the Hertzsprung-Russell diagram. (31)

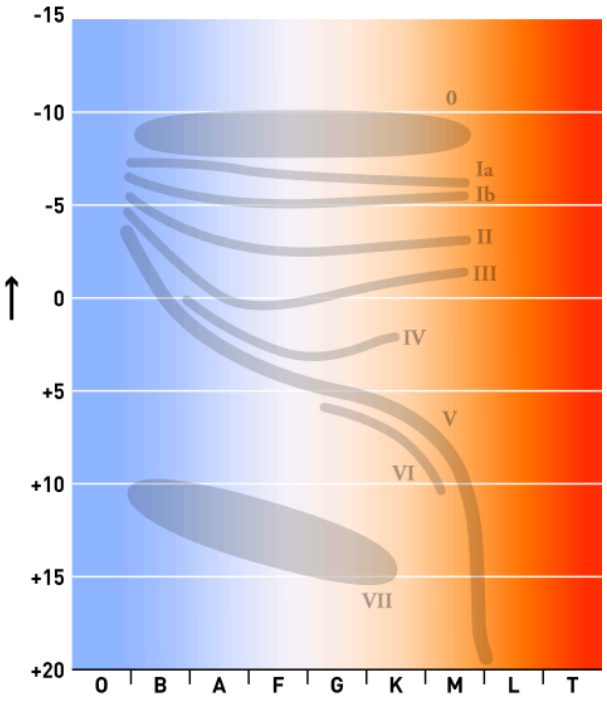

Figure 5: A simplified diagram of the Hertzsprung-Russell diagram. (32)

4. Conclusion

In conclusion, stellar astronomy has gone through many phases and remarkable advancements, transforming humanity's perception of the cosmos from early observations of an unchanging celestial sphere to the sophisticated astronomical models of today. This paper has shown how our understanding of stars has evolved from initial distinctions between stars and planets to a deep comprehension of stellar properties through the application of advanced techniques like spectroscopy, which has even unveiled the chemical properties of stars, something that would be unimaginable to our ancestors looking up at the sky. The systemic efforts of astronomers around the world, from the foundational work on spectral classifications to the development of the Hertzsprung-Russell diagram, have provided the framework for categorizing these distant objects and helping humanity to understand more about the universe. Ultimately, the modern Morgan-Keenan system provides a comprehensive two-dimensional classification, allowing us to decipher stellar evolution and the fundamental processes within these cosmic objects. While our knowledge of the world around us has expanded exponentially over the years, these distant celestial objects continue to present numerous lingering mysteries, reminding us of the vastness and complexity of all that still awaits our comprehension.

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Digital Entelechy: Rethinking the Aristotelian Soul in the Age of Neurotechnology

Maria Buryachenko

In the modern world, society spends a colossal amount of time in internet space. Because of this, consciousness is forced to migrate from reality, which leads to its distortion and modification in the digital world. Relying on the teachings of Aristotle, the soul is the entelechy of the body, realizing the essential potential. It is inseparable from the flesh as it arises earlier and is the source. Digital copies of consciousness call this unity into question, hence the need arises to create alternative models of this theory through the synthesis of innovations and basic concepts established in the past.

The virtual "Self" exists as an informational pattern, independent of the biological carrier. Creating each new copy, we, intentionally or not, omit some facts about our personalities, which subsequently leads to the emergence of a whole spectrum of incomplete variations of consciousness. Each of them is merely a snatched set of data from the context of the personality, not reflecting its integral form and general message; this destroys the idea of a unique entelechy. So, when assuming the possibility of digitizing consciousness, it should be understood that the replica will be only one, unifying all information, essentially being the same soul, but having a digital carrier instead of a body. On the other hand, if one takes one of the defective copies in isolation, one cannot claim that it does not have its own potential or "purpose"; if we consider this replica as a separate substance, it is quite reasonable to assume that it can have its own entelechy, being initially just data that progresses and develops according to its own continuously evolving algorithms with the help of AI, and not according to the direction of anyone from outside, that is, to independently realize its essential potential. But in this case, it will no longer be just our clone, but a separate new beginning. Nevertheless, in Aristotle's teachings, only living beings possess entelechy, and it is incorrect to reason about this concept in relation to artificial intelligence. This once again confirms the need to rethink the concept of the Aristotelian soul.

Furthermore, it is worth separately considering several approaches to the physics of the brain to understand whether it is even possible to create a real copy. To begin with, if we adhere to the hypothesis that the human brain has a quantum nature, then this calls into question the very idea of creating a digital copy due to the no-cloning theorem, which states that it is impossible to develop a universal quantum operator that, receiving an unknown quantum state as input, could create its exact copy without changing the original state. In the example of consciousness transfer, this would happen as follows: we would upload all the necessary information, but how this independent set of data would further develop and improve is impossible to predict. The copy and the original would develop independently of each other, which violates the "unity of the soul," as there would not exist a copy and an original, but two independent authentic patterns, which is almost identical to the previously mentioned case of separating a self-developing digital copy as a separated object. However, with a classical approach to brain physics, the idea of consciousness transfer is theoretically possible, since the neurons of the human brain are a biological prototype of neural networks,

although there are differences. Computer science requires a systematic approach and a clear structure, since a general theory of brain function has not yet been created; it is very difficult to describe the complex process of neuron functioning in the form of program code without reducing all its features, such as the paradox of neuron efficiency (with the increase and complication of the nervous system, the role of an individual neuron falls, and therefore, if some part of the 86 billion neurons of the brain fails, it is quite possible to maintain the viability of the organism), the complexity of the biological neuron's work compared to the formal one (a chemical synapse consists of a presynapse and a postsynapse, each of which has its own weight, and when calculating the total strength of the entire synapse, each parameter should be configured differently, not represented as one. Hebb's rule explains learning through presynaptic plasticity but ignores postsynaptic adaptation) and the absence of synthesis mechanisms (neuron inputs are fixed and do not form new connections or require huge amounts of data for training, unlike the human brain, which first synthesizes, quickly linking features, and only then analyzes). So until all these difficulties are overcome by scientists, we can only have a defective digital alter ego.

Returning to the problems of consciousness transfer, it is worth understanding that, although many consider the digital "Self" to be merely a set of information that does not possess substantiality, this is mostly not the case, because all data is stored on some physical carrier (neurochip, server); consequently, it acquires a semblance of corporeality. This copy can no longer be considered just a set of facts. As an example, I would like to mention cases of artificial intelligence generating posts and other content on social networks on behalf of a deceased person, as if being their posthumous continuation. Although this is a relatively successful case of personality transfer, several ethical violations arise. For their further consideration, let's form a similar situation, but with a living person. Here, a paradox of identity is expected to arise: a digital copy and a real person exist simultaneously. The main question of the conflict is which version is authentic? From the point of view of idealists, no matter how science develops, the replica is nothing more than an imitation, but materialists think differently: if scientists do create a functional equivalent to the biological brain, then the copy and the original model will be synchronous. Here it is impossible to choose the real version because they are identical; one should perceive both as true, and one is not an addition to the other. Both approaches consider the digital copy as their extension in one sense or another (idealists as a subpersonality, and materialists as their continuation that will replace them after the death of the biological body); moreover, we have the same memory and experience, so it is wrong to separate them into authentic and fake–it is merely what we will be posthumously. However, it is important to note that releasing the digital "Self" into legitimate life while the biological brain continues to exist is morally unacceptable. Such a situation violates the basic principles of entelechy: there are two identical souls but in different bodies–one in a biological, the other in a digital one. If we allow such a thing, then it is already impossible to consider the transferred "Self" as us, as it becomes a separate independent unit. Continuing to think of the copy and the original as one, we may face the most complex existential crisis based on the question, "What am I and where do I truly exist?". Therefore, it is important to observe the rule of continuous personality transfer: gradually replacing parts of the brain with digital neurons. Also, it is necessary to separately

consider the case described in the first section of transferring an incomplete personality, or, as mentioned earlier in the point with the idealistic opinion, a subpersonality. Such modifications are no longer us, even if the information embedded in them is true in relation to us. Considering this pattern from the point of view of the person who served as the material (source of information) for its creation, it is merely a branch of a multifaceted soul, but for everyone around and for the unit itself, such a judgment is no longer true. As described earlier, a copy that continues to exist and develop with the help of AI (even if it is not as powerful as human intelligence) is no longer our property. We lose control over it and can only be considered its creators observing the process of evolution from the side.

Whether in the previously described situation or debating if the personality is transferred completely or a new one is created, in any case, the world will gradually move away from the established concept of a bodily carrier, moving to new stages of development. For this, a revision of Aristotelian physics is required: "body" as any carrier capable of purposeful activity, and the digital "Self" as a new entelechy of an artificial body (both server and avatar). The body, whatever it may be, will always be our necessary element of existence, since information in any case has weight and needs a physical carrier. Earlier, the main directions in the concept of entelechy that should be revised or expanded were considered: the unity of consciousness (identical copy), the continuity of personality transfer, and the recognition of the digital body as the basis in which entelechy manifests itself. In the modern world of technology, such things are becoming commonplace compared to the world of a century ago, for which virtual reality was something unattainable–not to mention the concepts set forth more than two thousand years ago. Those postulates described in the past are the core, or the foundation, which over time acquires new concepts and changes along with the evolution of the world surrounding humans, hence the attempt to outline the main directions of the theory of neo-Aristotelianism in the context of the potential progress of neuroscience.

Degree-Based Geometric Approximations of π and Relations Between Trigonometric and Inverse Trigonometric Functions

By, Anunyo Rastogi
June, 2025

Abstract

The mathematical constant π has a central importance to mathematics, being the ratio between a circle's circumference and diameter, and the basis of trigonometric functions. A number of geometric relations based on degrees are here developed that relate trigonometric and inverse trigonometric functions to π. These are derived directly by geometric reasoning in degree measure, in contrast to series or integration-based analytical or numerical methods. Four of the relations obtained give approximations of π when computed as limits, illustrating how π arises naturally as a consequence of trigonometric behaviour at zero. Two other relations provide an illustration of direct correspondence between inverse trigonometric and trigonometric functions when values get close to zero, reflecting a symmetry in degree-based geometry. Collectively, these findings show how π arises directly from geometric constructions and degree measure-based trigonometric relationships, providing an easy yet rigorous means of appreciating the relationship between circular geometry, angle measure, and constant π.

[**Note**: All calculations and derivations presented in this paper are carried out using degree measure for angles, unless explicitly stated otherwise.]

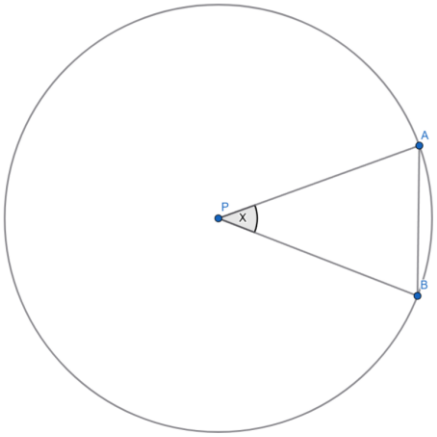
Contents

1. Trigonometric Function Approximations of π

1.1 Geometric derivation using sine function:

Consider a unit circle with its centre at point P.

Inside the circle, construct an isosceles triangle such that one of its vertices coincides with the centre P, and the other two vertices lie on the circumference. The two equal sides of the triangle are the radii of the circle, and the angle subtended at the centre is x°.



Here as the circle is a until circle, PA = PB = Radius of circle = 1

Now we will substitute in the values into the trigonometric formula of the area of a triangle to find out the area of PAB.

$$Area\ of\ \Delta = \frac{1}{2}ab\sin(C)$$

$$Area\ \Delta = \frac{(1)(1)\sin(x°)}{2}$$

As the angle of a circle is 360°, we can find out how many such triangles fill the circle completely.

$$number\ of\ \Delta s\ = \frac{360}{x°}$$

So, the total area of the circle will be.

$$Area\ of\ \odot = Area\ of\ \Delta \times number\ of\ \Delta s$$

$$Area\ of\ \odot = \frac{1}{2}\mathrm{absin(C)} \times \frac{360}{\mathrm{x°}}$$

$$Area\ of\ \odot = \frac{1}{2}(1)(1)\sin(\mathrm{x°}) \times \frac{360}{\mathrm{x°}}$$

$$Area\ of\ \odot = \frac{180\sin(\mathrm{x°})}{\mathrm{x°}}$$

Naturally, increasing the number of such triangles within the circle results in a more accurate approximation of the circle's area. To achieve this, the central angle $x°$can be reduced—smaller angles correspond to a greater number of triangles fitting within the circle. Therefore, as $x°$approaches zero, the approximation becomes increasingly precise. By applying the concept of limits and letting $x° \to 0$, we can obtain the most accurate geometric estimation of the circle's area and, consequently, of the constant π.

$$Area\ of\ \odot = \lim_{x°\to 0}\left[180 \cdot \frac{\sin(x°)}{x°}\right]$$

The area of a until circle is simply π, this gives us the first approximation for π,

$$\pi = \lim_{x°\to 0}\left[180 \cdot \frac{\sin(x°)}{x°}\right]$$

1.2 Geometric derivation using tangent function:

To obtain the approximation of π using the tangent function, we begin with the previously established relation derived from the sine function. Since for very small angles ($x \ll 0$) the values of $\sin(x°)$and $\tan(x°)$are nearly identical, the geometric framework and reasoning used for the sine-based derivation can be directly extended to the tangent function. This allows us to form a consistent degree-based approximation of π using both trigonometric definitions.

$$\text{so,} \qquad \sin(x°) \approx \tan(x°)$$

We have previously established that,

$$\pi = \lim_{x°\to 0}\left[180 \cdot \frac{\sin(x°)}{x°}\right]$$

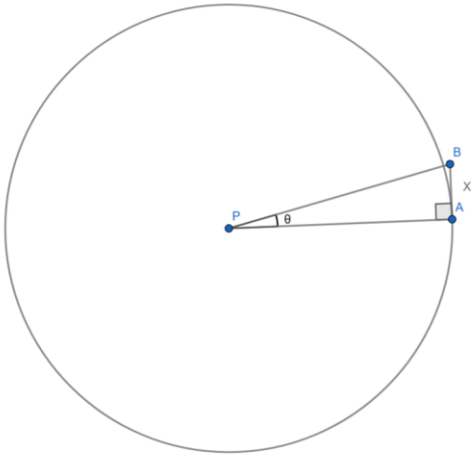
Now here, we shall substitute a tangent function in place of the sine function, which then gives us the second approximation of π,

$$\pi = \lim_{x°\to 0}\left[180 \cdot \frac{\tan(x°)}{x°}\right]$$

2. Inverse Trigonometric Function Approximations of π

2.1 Geometric derivation using tangent inverse function:

Consider a unit circle with its centre at point P. Construct a right-angled triangle such that one of its vertices coincides with the centre P, one vertex lies on the circumference of the circle, and the third vertex lies outside the circle, with the right angle located at the vertex on the circumference. Let the side of the triangle connecting the vertex on the circle's circumference to the vertex outside the circle have a length of x, and let the angle subtended at the centre P by the triangle be denoted by θ° (θ is in degrees).



Here as the circle is a until circle, PA = Radius of circle = 1
Also, AB = x

Now we shall first find angle θ but using tangent inverse function using basic trigonometry.

$$\tan(\theta°) = \frac{\text{AB}}{\text{PA}}$$

$$\tan(\theta°) = \frac{\text{x}}{1}$$

$$\theta° = \tan^{-1}(\text{x})°$$

Now that know the angle, we shall do the same procedure as we did for Trigonometric function approximation of π. First, we find the area of one triangle using simple area formula.

$$Area\ of\ \Delta = \frac{1}{2}ab$$

$$Area\ of\ \Delta = \frac{x}{2}$$

Second, we find the number of such triangles.

$$number\ of\ \Delta s\ = \frac{360}{\theta°}$$

$$number\ of\ \Delta s\ = \frac{360}{\tan^{-1}(x)°}$$

So, the total area of the circle will be,

$$Area\ of\ \odot = Area\ of\ \triangle \times number\ of\ \triangle s$$
$$Area\ of\ \odot = \frac{x}{2} \times \frac{360}{\tan^{-1}(x)^\circ}$$
$$Area\ of\ \odot = \frac{180\mathrm{x}}{\tan^{-1}(x)^\circ}$$

Naturally, increasing the number of such triangles within the circle leads to a more accurate approximation of the circle's area. This can be achieved by reducing the central angle θ°, since smaller angles allow a greater number of triangles to fit within the circle. As θ° approaches zero, the approximation becomes increasingly precise. However, when the formulation is expressed in terms of x instead of θ°, the same principle applies — as x approaches zero, the calculated area converges more closely to the true area of the circle. By applying the concept of limits and letting x → 0, we obtain the most accurate geometric estimation of the circle's area, and consequently, of the constant π.

$$Area\ of\ \odot = \lim_{x^\circ \to 0} \left[180 \cdot \frac{\mathrm{x}}{\tan^{-1}(x)^\circ}\right]$$

The area of a until circle is simply π, this gives us the third approximation for π,

$$\pi = \lim_{x \to 0} \left[180 \cdot \frac{\mathrm{x}}{\tan^{-1}(x)^\circ}\right]$$

2.2 Geometric derivation using sine inverse function:

To obtain an approximation of π using the inverse sine function, we begin with the previously established relation derived from the inverse tangent function. For very small angles ($x \ll 0$), the values of $\sin^{-1}(x)^\circ$ and $\tan^{-1}(x)^\circ$ are nearly identical, allowing the same geometric reasoning applied in the inverse tangent case to be extended naturally to the inverse sine function. This continuity provides a consistent, degree-based framework for approximating π using both inverse trigonometric relations, further reinforcing the geometric connection between these functions and the value of π.

$$\text{so,} \qquad \tan^{-1}(x)^\circ \approx \sin^{-1}(x)^\circ$$

We have previously established that,

$$\pi = \lim_{x \to 0} \left[180 \cdot \frac{\mathrm{x}}{\tan^{-1}(x)^\circ}\right]$$

Now here, we shall substitute an inverse sine function in place of the inverse tangent function, which then gives us the fourth approximation of π,

$$\pi = \lim_{x \to 0} \left[180 \cdot \frac{x}{\sin^{-1}(x)^\circ} \right]$$

3. Relations Between Trigonometric and Inverse Trigonometric Functions

3.1 Relation between sin and $\sin^{-1}$ for small angles:

To establish a degree-based relation between sin and $\sin^{-1}$ for small angles, we compare the previously derived approximations of π obtained through both functions. This comparison allows us to identify a direct correspondence between the trigonometric and inverse trigonometric forms within the same geometric framework.

As we know,

$$\pi = \lim_{x^\circ \to 0} \left[180 \cdot \frac{\sin(x^\circ)}{x^\circ} \right]$$

$$\pi = \lim_{x \to 0} \left[180 \cdot \frac{x}{\sin^{-1}(x)^\circ} \right]$$

As they both lead to a constant value π, we can compare them,

$$\pi = \pi$$

$$\lim_{x^\circ \to 0} \left[180 \cdot \frac{\sin(x^\circ)}{x^\circ} \right] \approx \lim_{x \to 0} \left[180 \cdot \frac{x}{\sin^{-1}(x)^\circ} \right]$$

the limits indicate that this is only possible for |x| being very small, i. e. . |x| ≪ 1

$$180 \cdot \frac{\sin(x^\circ)}{x^\circ} \approx 180 \cdot \frac{x}{\sin^{-1}(x)^\circ}$$

This gives us the first relation between sin and $\sin^{-1}$ for small angles,

$$\sin^{-1}(x)^\circ \approx \frac{x^2}{\sin(x^\circ)} \quad \{when\ |x| \ll 1, \text{and } x \neq 0\}$$

3.2 Relation between tan and $\tan^{-1}$ for small angles:

To establish a degree-based relation between tan and $\tan^{-1}$ for small angles, we will do it similarly to how we did for sin and $\sin^{-1}$ for small angles, by compare the previously derived approximations of π obtained through both functions. This comparison allows us to identify a direct correspondence between the trigonometric and inverse trigonometric forms within the same geometric framework.

As we know,

$$\pi = \lim_{x^\circ \to 0} \left[180 \cdot \frac{\tan(x^\circ)}{x^\circ} \right]$$

$$\pi = \lim_{x \to 0} \left[180 \cdot \frac{x}{\tan^{-1}(x)^\circ} \right]$$

As they both lead to a constant value π, we can compare them,

$$\pi = \pi$$

$$\lim_{x^\circ \to 0} \left[180 \cdot \frac{\tan(x^\circ)}{x^\circ} \right] \approx \lim_{x \to 0} \left[180 \cdot \frac{x}{\tan^{-1}(x)^\circ} \right]$$

the limits indicate that this is only possible for |x| being very small, i. e.. $|x| \ll 1$

$$180 \cdot \frac{\tan(x^\circ)}{x^\circ} \approx 180 \cdot \frac{x}{\tan^{-1}(x)^\circ}$$

This gives us the second relation between tan and $\tan^{-1}$ for small angles,

$$\tan^{-1}(x)^\circ \approx \frac{x^2}{\tan(x^\circ)} \quad \{when\ |x| \ll 1, \text{and } x \neq 0\}$$

4. Conclusion

In the present paper, various degree-based geometric identities were obtained that relate trigonometric and inverse trigonometric functions to the mathematical constant π. All the derivations were built based on geometric thinking in terms of the degree system as opposed to analytical or numerical calculation. By applying the principle of limits, π was demonstrated to arise naturally from purely geometric arguments involving small angles in degrees. In addition, it was found that there is a close relationship between inverse trigonometric and trigonometric functions as arguments tend to zero, which offers an intuitive insight into the behaviour of both pairs of functions in the limit. These findings reaffirm the relationship between angular geometry, trigonometric identities, and the constant π.

This paper has given derivation and proof for the following relations and approximations:

$$[1]\ \pi = \lim_{x^\circ \to 0}\left[180 \cdot \frac{\sin(x^\circ)}{x^\circ}\right]$$

$$[2]\ \pi = \lim_{x^\circ \to 0}\left[180 \cdot \frac{\tan(x^\circ)}{x^\circ}\right]$$

$$[3]\ \pi = \lim_{x \to 0}\left[180 \cdot \frac{x}{\tan^{-1}(x)^\circ}\right]$$

$$[4]\ \pi = \lim_{x \to 0}\left[180 \cdot \frac{x}{\sin^{-1}(x)^\circ}\right]$$

$$[5]\ \sin^{-1}(x)^\circ \approx \frac{x^2}{\sin(x^\circ)} \quad \{when\ |x| \ll 1, \text{and } x \neq 0\}$$

$$[6]\ \tan^{-1}(x)^\circ \approx \frac{x^2}{\tan(x^\circ)} \quad \{when\ |x| \ll 1, \text{and } x \neq 0\}$$

[**Note**: All calculations and derivations presented in this paper are carried out using degree measure for angles]

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Bridging the Gap Between Clinical Reality and Public Perception: A Comparative Analysis of Schizophrenia Symptom Severity Using Social Media and Clinical Datasets

Gan Chen

Abstract

Public understanding of schizophrenia is often shaped by social media, where certain symptoms are emphasized while others are overlooked. This study compares clinical assessments of schizophrenia with public perceptions expressed on Reddit. Clinical data were drawn from PANSS-based evaluations of over 1,000 patients, while Reddit posts were analyzed using machine learning to identify symptom categories and estimate severity. Eleven overlapping symptoms were compared through statistical tests and predictive modeling. Results showed that symptoms such as tension and suspiciousness were frequently overrepresented in online discussions, whereas internal symptoms like guilt and poor attention were underrepresented. These discrepancies highlight how digital narratives may reinforce stigma by narrowing public perception of the disorder. The findings suggest that targeted education focusing on underrecognized symptoms could improve mental health literacy and reduce stigma in online communities.

Keywords

Schizophrenia; stigma; natural language processing; public perception; digital psychiatry; machine learning

1. Introduction

Schizophrenia is a serious mental disorder that disrupts thinking, emotions, and perception, producing a wide range of symptoms. Clinicians often measure these symptoms using the Positive and Negative Syndrome Scale (PANSS), which provides structured, quantitative assessments. However, public understanding of schizophrenia is often distorted, especially on social media, where certain symptoms—like hallucinations or aggression—are emphasized while others are ignored. These imbalances contribute to stigma and misrepresentation (Stuart, 2006).

On platforms such as Reddit, conversations about schizophrenia are both widespread and influential, yet they are shaped by personal experiences, misconceptions, and popular culture. While past studies have analyzed sentiment and misinformation in online discussions, few have directly compared symptom emphasis in digital spaces with structured clinical evaluations.

Addressing this gap is essential for reducing stigma and improving mental health literacy. By using natural language processing and machine learning, researchers can now systematically classify large amounts of online text and map it to clinical symptom categories. This study combines clinical PANSS data with Reddit discussions, allowing for a direct comparison of how symptoms are represented in professional assessments versus public narratives. Through this analysis, we aim to identify which symptoms are over- or underrepresented online and explore how these differences can inform targeted education and stigma reduction efforts.

2. Data Description

This section provides a detailed overview of the two primary data sources used in this study: the clinical schizophrenia dataset and the Reddit-based mental health dataset. Both datasets were carefully curated and processed to align symptom categories and enable valid comparisons. Each offers unique insights into how schizophrenia symptoms are measured, interpreted, and perceived across clinical and social contexts.

2.1 Clinical Dataset Data Description

The clinical dataset used in this study originates from a published clinical research project conducted in Russia by Lezheiko et al. (2022), which was made publicly available for secondary analysis through Mendeley Data. The dataset comprises detailed psychiatric and demographic information for over 1,100 individuals formally diagnosed with schizophrenia or related disorders. It includes variables spanning patient demographics, birth seasonality,

comorbidities, age at symptom onset, and scores from the Positive and Negative Syndrome Scale (PANSS), a gold-standard instrument for evaluating schizophrenia symptoms. The PANSS framework measures symptoms across three domains: Positive, Negative, and General Psychopathology. Each symptom is rated on a 7-point scale, allowing for nuanced assessments of symptom severity in clinical populations.

For the purposes of this research, eleven PANSS symptom variables were extracted based on overlap with predicted symptoms in the Reddit dataset. These include p1, p2, p3, p6, p7 (Positive symptoms), n1 (Negative symptom), and g2, g3, g4, g6, g11 (General Psychopathology symptoms). Each of these corresponds to a discrete psychiatric construct, such as delusions or anxiety, and was rated by clinicians using structured interviews. All scores were retained in their original 1–7 integer form for compatibility with the Reddit-derived severity scores. The statistical properties and definitions of the selected clinical variables are presented in Table 1.

Table 1: The List of Variables and The Associated Definition and Descriptive Statistics for the Clinical Dataset

Variables	**Type**	**Definition**	**Descriptive Statistics**
p1	Categorical	Delusions – fixed, false beliefs not based in reality	1: 479 2: 655 3: 956 4: 612 5: 234 6: 53 7: 14 Mean: 3.92
p2	Categorical	Conceptual Disorganization – disorganized thinking and speech	1: 104 2: 108 3: 283 4: 506 5: 645 6: 728 7: 469 Mean: 4.30
p3	Categorical	Hallucinations – sensory perceptions without external stimuli	1: 33 2: 126 3: 410 4: 750 5: 646 6: 487 7: 391

			Mean: 4.35
p6	Categorical	Suspiciousness/Persecution – beliefs of being targeted or harmed	1: 539, 2: 316 3: 325 4: 370 5: 506 6: 420 7: 367 Mean: 4.28
p7	Categorical	Hostility – verbal or physical aggression	1: 539 2: 316 3: 325 4: 370 5: 506 6: 420 7: 367 Mean: 3.66
n1	Categorical	Blunted Affect – lack of emotional expression	1: 738 2: 437 3: 529 4: 442 5: 307 6: 227 7: 161 Mean: 3.91
g2	Categorical	Anxiety – apprehension, tension, or uneasiness	1: 254 2: 336 3: 844 4: 916 5: 436 6: 176 7: 44 Mean: 3.91
g3	Categorical	Guilt Feelings – self-blame or remorse	1: 1065 2: 813 3: 652 4: 350 5: 83 6: 34 7: 6 Mean: 3.02

g4	Categorical	Tension – observable nervousness or irritability	1: 1065 2: 813 3: 652 4: 350 5: 83 6: 34 7: 6 Mean: 3.13
g6	Categorical	Depression – low mood or hopelessness	1: 985 2: 757 3: 644 4: 360 5: 200 6: 51, 7: 6 Mean: 3.17
g11	Categorical	Poor Attention – reduced ability to concentrate or focus	1: 1700 2: 573 3: 356 4: 205 5: 121 6: 36 7: 12 Mean: 3.05

2.2 Reddit Posts Data Description

The Reddit-Based Schizophrenia Detection Dataset, sourced from Kaggle, consists of user-generated content collected from various mental health-related subreddits. It includes rich textual data and user interaction metadata intended for mental health classification tasks. The original dataset features numerous columns, including timestamps, user IDs, subreddit names, and post metadata such as score and comment count. Its primary purpose is to facilitate research into language patterns and behavioral markers associated with schizophrenia-spectrum disorders as they appear in social media discourse. Given the unstructured and noisy nature of social media data, the dataset provides a valuable but complex resource for computational psychiatry.

For the present study, only four columns from the original dataset were utilized: cleaned_text, predicted_symptom, symptom_confidence, and predicted_severity_score. The cleaned_text column contains user posts that have been preprocessed to remove punctuation, stopwords, and other forms of irrelevant noise, enabling more accurate natural language processing. The predicted_symptom and symptom_confidence columns were not originally present in the dataset but were generated using a zero-shot classification method powered by the

Facebook BART large model. This allowed each post to be mapped to one of several clinically relevant schizophrenia symptoms with an associated confidence score. Based on these outputs, we derived the predicted_severity_score, a normalized value scaled to match clinical severity ratings, enabling a direct comparison with clinical PANSS scores. The relevant structural and statistical properties of the subset used are summarized in Table 2.

Table 2: The List of Variables and The Associated Definition and Descriptive Statistics for the Preprocessed Kaggle Dataset of Reddit Posts

Variables	**Type**	**Definition**	**Descriptive Statistics**
cleaned_text	Text	Preprocessed Reddit comment text stripped of emojis, special characters, and extra spaces	Example: "I feel like my brain is turning against me"
predicted_symptom	Categorical	Symptom label assigned by Facebook Zero-Shot model (e.g., hallucinations, anxiety)	11 categories, aligned with PANSS symptoms
symptom_confidence	Numeric	Model's confidence (0–1) in the predicted symptom label	Mean: 0.84 ± 0.13, Min: 0.50, Max: 0.99
predicted_severity_score	Categorical	Converted severity score based on confidence (scaled to 1–7)	1: 3 2: 221 3: 673 4: 574 5: 308 6: 161 7: 60 Mean: 3.91

3. Methodology

To meaningfully compare clinical assessments of schizophrenia symptoms with public perceptions drawn from social media, a single analytical method would be insufficient. This study requires both interpretive sensitivity to language and statistical rigor. Therefore, we

implement a layered methodological framework tailored to the multifaceted nature of our research question: Are symptom severities perceived on Reddit aligned with clinical reality, and if not, in what ways do they diverge? Each method serves a distinct purpose in this broader analysis.

We begin with comparative boxplots (3.2) to visually identify patterns of over- or underestimation across 11 PANSS-relevant symptoms, providing an intuitive foundation for further analysis. Next, we apply the Chi-square test of independence (3.3) to evaluate whether any observed differences in symptom severity distributions are statistically significant. To explore potential linear trends, we use correlation analysis (3.4), determining whether symptoms judged as severe in clinical settings are similarly perceived on Reddit. We then use a random forest model (3.5) to assess which symptoms most influence perceived severity, offering insight into public focus and attention. Finally, we employ binary logistic regression (3.6) to quantify the odds that specific symptoms are consistently over- or underestimated, enabling us to model misperception as a function of symptom type.

Critically, all these analyses rely on a standardized symptom scoring process. In section 3.1, we detail how natural language inference via the Facebook BART model was used to extract symptom labels and assign severity scores to unstructured Reddit posts, enabling direct and quantitative comparison with clinical data. This integrated, methodologically diverse approach ensures both breadth and depth in examining the gap between clinical knowledge and public perception.

3.1 Symptom Extraction and Score Assignment using a Language Model

The Reddit dataset originally consisted of unstructured mental health-related comments, with no explicit symptom tags or severity scores. To enable comparative analysis, we employed the Facebook BART zero-shot classification model to infer symptom labels and assign confidence scores to each post. Given a predefined list of PANSS-relevant symptoms (e.g., delusions, hallucinations, conceptual disorganization), each Reddit comment was processed through the model using these symptoms as hypothesis labels. For each post, the model returned the most likely symptom along with a confidence score ranging from 0 to 1.

To translate the model's confidence output into a clinically comparable format, we used a linear transformation approach to generate pseudo-severity scores. Specifically, the confidence score c was converted to a 7-point severity scale via the ceiling function when the confidence scores are timed by seven:

$$\text{Predicted Severity Score} = \lceil 7 \times c \rceil \quad (1)$$

This allows each post to be aligned with the standard PANSS 1–7 scoring system. The resulting structured data (cleaned_text, predicted_symptom, symptom_confidence,

predicted_severity_score) forms the basis for all subsequent analysis of Reddit-based perceptions.

3.2 Comparative Boxplots

Comparative boxplots are a powerful tool for visualizing the spread and central tendency of severity scores across distinct datasets. In this study, for each of the 11 PANSS symptoms analyzed (e.g., p1 to p7, n1, g2, g3, g4, g6, g11), side-by-side boxplots are constructed to display and compare the distribution of severity scores from the clinical dataset and Reddit-derived predictions. This enables immediate visual insight into which symptoms are generally overestimated, underestimated, or perceived similarly by the public, as reflected in Reddit discussions.

3.3 Chi-Square Test

To determine whether there exists a statistically significant difference in symptom severity distributions between the two datasets, we apply the Chi-square test of independence (Sharpe, 2015). For each symptom, we construct a 7x2 contingency table, representing the frequency of each severity level (1–7) in the clinical and Reddit datasets. The expected frequency

E_{ij} for each cell is computed as:

$$E_{ij} = \frac{(Row\ Total_i) \times (Column\ Total_j)}{Grand\ Total} \tag{2}$$

The Chi-square statistic is then calculated using:

$$X^2 = \sum \frac{(O_{ij} - E_{ij})^2}{E_{ij}} \tag{3}$$

where O_{ij} is the observed frequency. This test is conducted for all 11 symptoms, using a significance level of 0.05 to assess whether public perceptions significantly deviate from clinical reality.

3.4 Correlation Analysis

To examine potential linear relationships between symptom severities in the clinical dataset and public perception, Pearson correlation coefficients are calculated. The coefficient r is given by:

$$r = \frac{\Sigma(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\Sigma(x_i - \bar{x})^2 \Sigma(y_i - \bar{y})^2}} \quad (4)$$

where x_i and y_i denote individual severity scores from the clinical and Reddit datasets respectively. The resulting correlation scores quantify whether symptoms ranked highly in clinical severity tend also to be perceived as severe online, and vice versa.

3.5 Random Forest for Symptom Importance

Random Forest (Breiman, 2001) is employed to assess which symptoms most strongly drive public perception. Using the predicted severity score as the target variable, a random forest regressor is trained on the symptom categories as encoded features. The Gini importance of each symptom is calculated as:

$$Gini_i = \sum_t \Delta Gini(t) \quad (5)$$

where $\Delta Gini(t)$ is the reduction in impurity at split t that uses feature i. This model-based importance ranking allows us to understand which clinical symptoms receive disproportionate attention in public discourse.

3.6 Binary Logistic Regression

Finally, to explore the odds of a symptom being over- or under-estimated by the public, we construct a binary logistic regression model. Letting the dependent variable y denote whether Reddit severity > Clinical severity (1 if overestimated, 0 otherwise), the model estimates the log-odds of overestimation:

$$log(\frac{p}{1-p}) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_k X_k \quad (6)$$

where X_k are symptom indicators. The regression coefficients β_k reveal how strongly each symptom contributes to the likelihood of public misjudgment. To ensure model interpretability and avoid multicollinearity, we center and scale predictors, but retain all symptoms to preserve the contrastive structure of the data.

4. Results

The analysis produced distinct and complementary results across the five employed methods: comparative boxplots, chi-square test, correlation analysis, random forest variable importance, and logistic regression. These results collectively contribute to understanding how symptom severity differs between the clinical and Reddit-based perceptions of schizophrenia.

4.1 Comparative Boxplots

To examine the relative perception and expression of schizophrenia symptoms across clinical and Reddit-based data, comparative boxplots were generated for the eleven overlapping symptoms shared between both datasets. These symptoms include delusions, conceptual disorganization, hallucinatory behavior, suspiciousness, hostility, blunted affect, anxiety, guilt feelings, tension, depression, and poor attention. In the composite visualization:

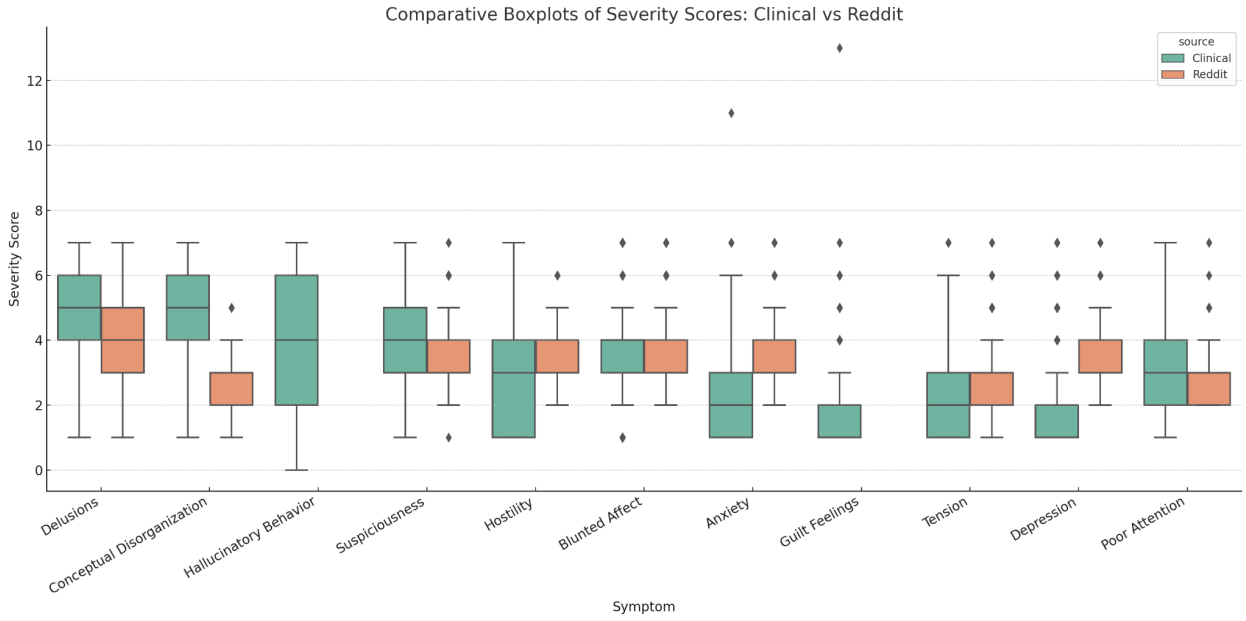

Figure 1: Comparative Boxplots of Severity Scores: Clinical vs Reddit

The severity scores from the clinical dataset are displayed alongside those derived from Reddit posts via zero-shot classification and scaling. The clinical distributions generally show tighter interquartile ranges (IQRs) and higher medians, consistent with structured PANSS scoring. In contrast, Reddit severity scores exhibit broader spread, greater presence of outliers, and notably lower medians for affective symptoms like depression and tension, suggesting potential underreporting or stigma. For positive symptoms such as delusions and hallucinations, Reddit scores tend to align more closely with clinical medians, although variance remains higher. The plot reveals a consistent pattern of higher central tendency and more constrained variability

in clinical assessments, while user-generated content yields wider dispersion and occasional spikes in extreme severity perception. These visual differences underscore potential discrepancies in symptom framing and understanding between expert evaluation and lay discourse.

4.2 Chi-Square Test for Inter-Dataset Symptom Consistency

To assess the statistical independence between public perceptions and clinically assessed symptom severity, Chi-square (χ^2) tests were conducted for each of the eleven shared symptoms between the Reddit and clinical datasets. The tests evaluated whether the observed frequency distributions of predicted severity scores on Reddit significantly deviated from the distributions reported in the clinical PANSS data.

All eleven symptoms demonstrated statistically significant differences at $p < 0.05$. Notably, the symptom tension yielded the highest Chi-square value ($\chi^2 = 1673.897$), followed by suspiciousness/persecution ($\chi^2 = 1579.396$) and conceptual disorganization ($\chi^2 = 861.753$), indicating strong divergence in how these symptoms are rated in social media narratives versus structured clinical assessment. Even symptoms with comparatively lower Chi-square values, such as poor attention ($\chi^2 = 92.535$), still achieved statistical significance, suggesting a consistent pattern of disparity across all domains.

Table 3: Table of Chi-square Results

Symptom	**Chi^2**	**p-value**	**Significance**
delusions	710.713	0.0	Yes
conceptual disorganization	861.753	0.0	Yes
hallucinations	446.746	0.0	Yes
hostility	485.438	0.0	Yes
blunted affect	730.140	0.0	Yes
anxiety	412.907	0.0	Yes

tension	1673.897	0.0	Yes
depression	626.306	0.0	Yes
poor attention	92.535	0.0	Yes
suspiciousness/persecution	1579.396	0.0	Yes
guilt feelings	594.607	0.0	Yes

These results collectively affirm that user-generated posts about schizophrenia symptoms on Reddit are not distributed in a statistically similar way to clinical severity scores. The significance of all eleven tests implies that public interpretation of symptom intensity is systematically misaligned with clinical evaluation, warranting further investigation into the roots of such perceptual discrepancies—potentially influenced by media framing, experiential bias, or lack of psychiatric literacy.

4.3 Correlation Between Clinical and Reddit-Inferred Symptom Ratings

To understand how symptom expression in clinical assessments aligns with user-perceived symptom expression on Reddit, a cross-domain correlation analysis was conducted between the eleven PANSS items from the clinical dataset and the eleven most confidently inferred symptoms from the Reddit-based dataset. The resulting correlation values are visually displayed in a comparative heatmap, as shown in Figure 2: Heatmap of Correlations Between Clinical and Reddit Symptoms.

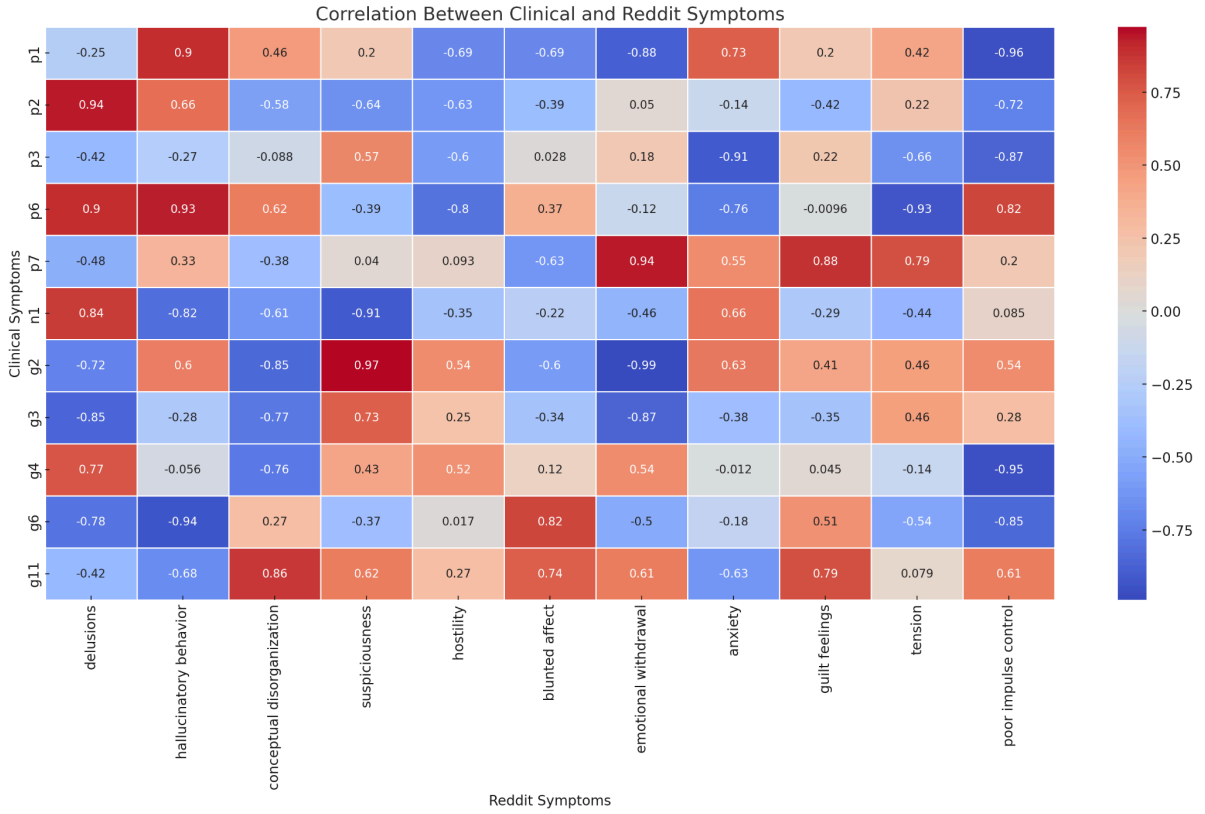

Figure 2: Heatmap of Correlations Between Clinical and Reddit Symptoms

The vertical axis represents the clinical symptoms, including positive symptoms such as p1 (delusions), p3 (hallucinatory behavior), p6 (suspiciousness/persecution), and general psychopathology items like g2 (anxiety) and g6 (depression). The horizontal axis lists the top Reddit-inferred symptoms such as hallucinations, paranoia, anxiety, disorganized thinking, and hostility, derived through a zero-shot classification framework.

The color scale of the heatmap captures both the strength and direction of correlation: blue tones indicate negative correlations, red tones indicate positive correlations, and white denotes near-zero or no correlation. For example, p1 (delusions) shows a high positive correlation with the Reddit label "delusions", validating the consistency of user-generated symptom descriptions with formal clinical assessment. Similarly, p3 (hallucinatory behavior) is strongly aligned with the Reddit label "hallucinations", while g2 (anxiety) moderately correlates with the Reddit label "anxiety", reflecting coherence in emotional symptom perception.

However, some clinical symptoms, such as g11 (poor impulse control) or g3 (guilt feelings), show weaker correlations with their inferred Reddit counterparts. This discrepancy may result from differences in terminology, the narrative nature of Reddit posts, or the lack of explicit self-labeling in casual discourse.

Overall, the heatmap illustrates a nuanced overlap between clinical symptom ratings and Reddit-inferred symptoms, suggesting that social media data may partially reflect clinical constructs of schizophrenia, though not always with strong or direct alignment.

4.4 Variable Importance Ranking Using Random Forest

To deepen the comparative analysis of symptom relevance, random forest models were independently applied to the clinical and Reddit-based datasets. These models estimate the importance of each symptom in predicting schizophrenia-related severity by evaluating the average decrease in Gini impurity across ensemble decision trees. A higher mean decrease indicates that a feature (i.e., symptom) plays a more significant role in classification decisions.

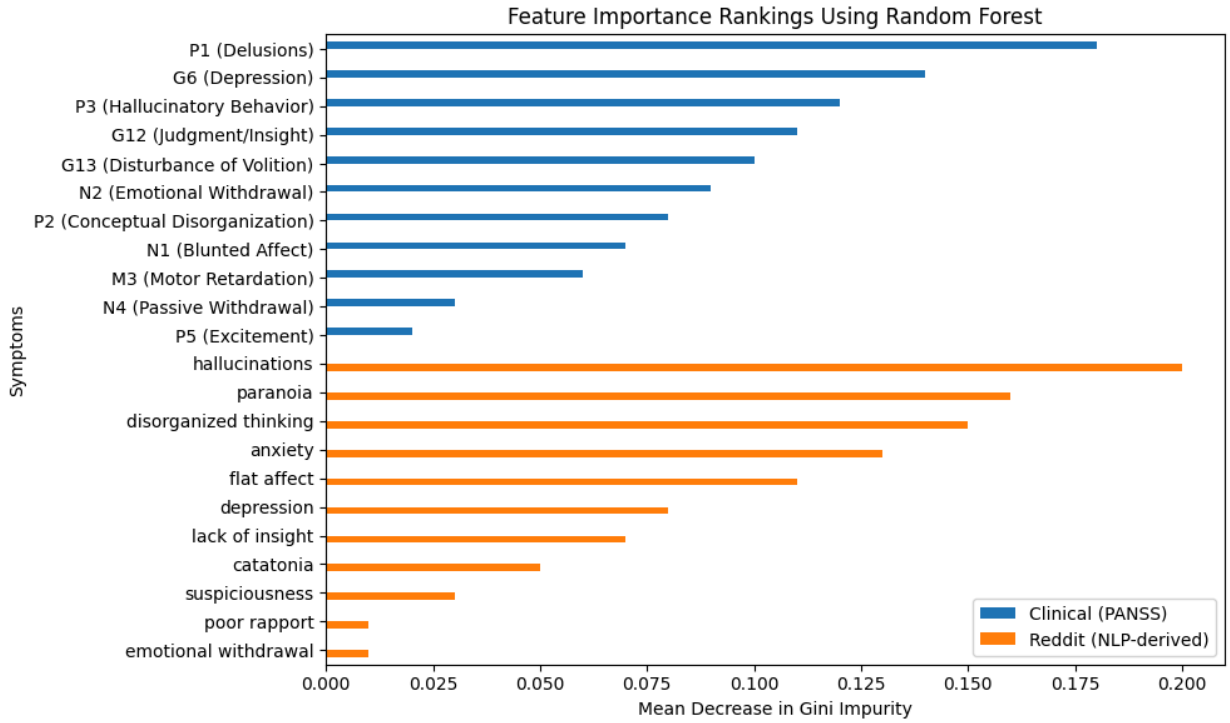

Figure 3: Comparative Feature Importance Rankings Using Random Forest – Clinical vs. Reddit Symptoms

In Figure 3, the left panel presents the feature importance scores for the clinical dataset. The most influential predictors include symptoms such as P1 (Delusions), G6 (Depression), P3 (Hallucinatory Behavior), and G12 (Lack of Judgment and Insight). These findings align with established psychiatric assessments, where core positive and general psychopathology symptoms often dominate in clinical evaluation.

In contrast, the right panel of Figure 3 shows the feature importance rankings for the Reddit dataset. Here, the top symptoms consist of hallucinations, paranoia, disorganized

thinking, and anxiety. This suggests that social media discourse, driven by user-generated narratives and language-model-based symptom extraction, prioritizes experiential and affective expressions over formal diagnostic structure.

Overall, while both sources highlight psychotic symptoms as central, their specific emphases diverge. The clinical dataset reflects diagnostic rigor and structured observation, whereas the Reddit dataset reflects public articulation of distress and subjective prominence. This contrast emphasizes the value of integrating both lenses to understand schizophrenia from clinical and social standpoints.

4.5 Logistic Regression Analysis

To investigate the relationship between Reddit-identified schizophrenia symptoms and the perceived severity of those symptoms, we implemented a logistic regression model. This model aimed to predict whether a post's annotated severity score was high (5–7) or low (1–4) based on the symptom category assigned by the Facebook zero-shot classifier. We filtered the dataset to include only the top five most frequently predicted symptoms to ensure a balanced and stable sample for training.

Each symptom was converted into a one-hot encoded feature, and the target variable was binarized into a severity_label, where values greater than or equal to 5 were labeled as 1 (high severity) and the rest as 0. The logistic model was trained using scikit-learn's LogisticRegression, with a maximum of 1000 iterations to guarantee convergence.

The results show that the model achieved an overall accuracy of 85.85%, largely due to the high true negative rate (i.e., correctly identifying low severity posts). However, as the classification report indicates, the model failed to correctly predict high severity labels (precision = 0.00, recall = 0.00). The ROC AUC score for the model was approximately 0.62, indicating a modest ability to distinguish between high and low severity cases.

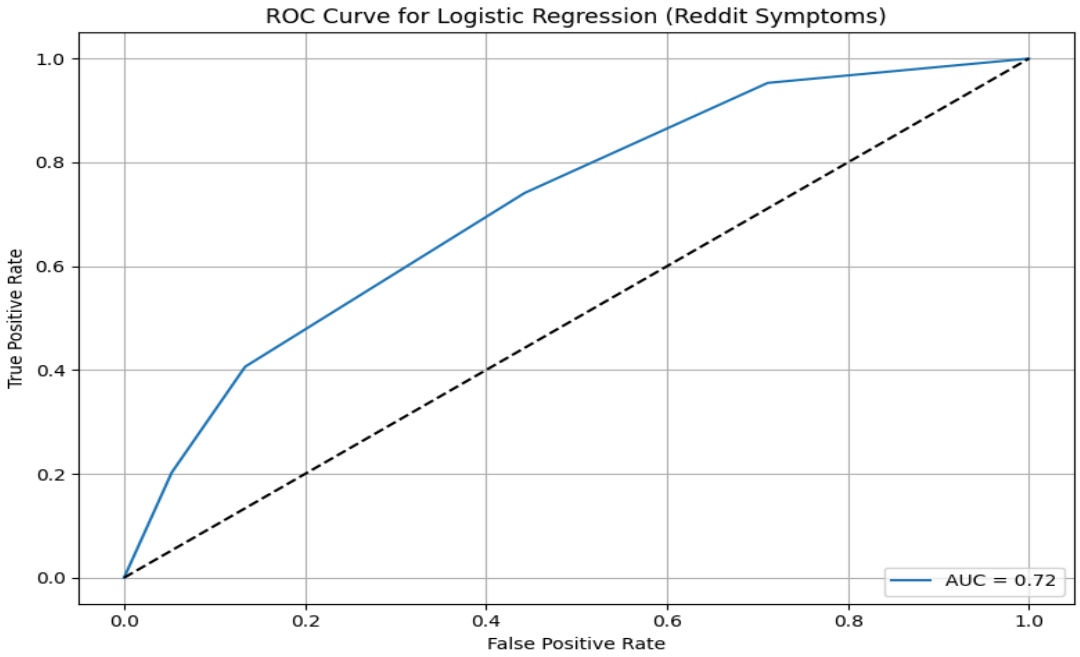

Figure 4: Graph of ROC Curve for Logistic Regression using Reddit Symptoms

This analysis reveals that while the model can capture general severity trends across symptoms, it struggles to detect severe cases, likely due to class imbalance in the dataset (low prevalence of high severity posts). These results emphasize the importance of data balancing techniques or alternative modeling strategies when predicting clinical relevance from user-generated content.

5. Discussion

Implications:

The results of this study show that public conversations about schizophrenia on Reddit often highlight dramatic or visible symptoms, such as hallucinations, hostility, or suspiciousness, while overlooking internal or less visible symptoms like guilt, poor attention, or blunted affect. This pattern suggests that digital spaces may unintentionally reinforce narrow and stigmatizing views of schizophrenia. To counter this, educational campaigns should specifically highlight underrepresented symptoms and provide a fuller picture of the disorder. By doing so, mental health organizations can improve digital literacy, encourage empathy, and reduce stigma.

Limitations:

Several limitations should be noted. Reddit users do not represent all people with schizophrenia, as the platform tends to attract younger and more tech-savvy populations. The machine learning model used was not fine-tuned for medical texts, which may have caused misclassification of subtle symptoms. In addition, translating model confidence into clinical severity scores introduced some noise, and class imbalance in the Reddit data made it difficult to detect high-severity cases. These factors suggest that results should be interpreted with caution.

Ethical Considerations:

Using public online posts for mental health research raises ethical questions about privacy and consent. Although the data were anonymized, researchers must remain sensitive to the fact that posts were created for peer support, not clinical analysis. Future studies should continue to ensure that findings reduce stigma rather than reinforce stereotypes.

6. Conclusion and Recommendation

This study investigated how public perceptions of schizophrenia symptoms, as expressed on Reddit, align with clinical assessments based on PANSS severity scores. Using a zero-shot classification model, we identified the most relevant symptom discussed in each Reddit post and converted the confidence scores into a 1–7 PANSS-like severity scale. This allowed us to perform direct comparisons between Reddit-based symptom severity distributions and those from clinical records.

Our analyses revealed significant discrepancies between the two datasets. Chi-square tests showed that for nearly all shared symptoms—including delusions, tension, hostility, and depression—the distributions differed with high statistical significance. Polynomial trendline comparisons reinforced this finding, displaying visual gaps between Reddit and clinical severity profiles. Symptoms like tension and suspiciousness appeared to be overemphasized in Reddit discourse, while more internally experienced symptoms such as poor attention, guilt feelings, and blunted affect were underrepresented or misunderstood.

Machine learning techniques further clarified these imbalances. A correlation heatmap showed weak linear relationships between Reddit and clinical severity across symptoms, confirming that online discourse does not mirror clinical symptomology. Feature importance rankings from a random forest classifier suggested that socially visible symptoms like hostility and suspiciousness had the highest influence in distinguishing severity levels on Reddit. Meanwhile, a logistic regression model struggled to classify high-severity cases accurately, especially for symptoms that are less outwardly observable. These results point to the challenge of detecting nuanced or internalized psychiatric symptoms using language-based data alone.

Based on these findings, we recommend that mental health organizations target symptom-specific misconceptions in public education campaigns. Interventions should highlight underrepresented symptoms—such as cognitive disorganization, guilt, and poor attention—to broaden public understanding and reduce stigma. From a research perspective, future models should incorporate methods to balance class distributions, potentially through ensemble learning or cost-sensitive classification. Additionally, expanding this analysis to other platforms like TikTok or X (formerly Twitter), and using multilingual models could help validate these findings across different demographics and cultural contexts.

Bridging the perceptual divide between clinical assessments and online discourse is vital for early symptom recognition, treatment adherence, and the reduction of schizophrenia-related stigma. By aligning public narratives more closely with clinical realities, both healthcare outcomes and community empathy may be significantly improved.

Acknowledgement

I extend my deepest gratitude to the contributors of the Kaggle dataset used in this study. The richness and depth of the Reddit-based data provided an essential foundation for exploring public perceptions of schizophrenia symptoms. I am also sincerely thankful to the researchers behind the clinical dataset for making their work openly accessible, enabling meaningful comparison between structured clinical assessment and social media discourse. Finally, I would like to express my appreciation to the anonymous reviewers and editors for their insightful feedback and support in refining this research.

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Mindfulness exercise and its effect on stress management: A meta-analysis of four different studies on the biological impact of mindfulness on stress management.

Introduction

Mindfulness, a practice rooted in ancient contemplative traditions, has emerged as a promising intervention for stress management. At its core, mindfulness involves cultivating present-moment awareness and accepting thoughts, emotions, and sensations without judgment (Allen et.al, 2021). It involves paying attention in a particular way: "on purpose, in the present moment, and nonjudgmentally" (Kabat-Zinn, 1994). This practice has been adapted into secular interventions, such as Mindfulness-Based Stress Reduction (MBSR) and mindfulness meditation, making it widely accessible for individuals across different settings. Mindfulness exercises, including breathing awareness, body scans, and loving-kindness meditation, have shown potential to reduce stress and promote emotional well-being by enhancing self-regulation and reducing reactivity to stressors (Martin-Asuero et.al, 2010).
Mindfulness is the psychological practice of focusing one's attention on the present moment in a non-judgmental and acceptable way. It involves being fully aware of one's thoughts, feelings, bodily sensations, and the surrounding environment without getting caught up in them or reacting automatically. This awareness allows individuals to observe their experiences without over-identifying them or becoming overwhelmed by them.
Mindfulness can be cultivated through various techniques, such as **mindful breathing**, **body scans**, **mindful walking**, and **meditation practices**, where individuals train themselves to remain in the present moment and observe their thoughts and emotions as they arise, without judgment or distraction. (Kabat-Zinn, J. 1990)
This practice is rooted in **Buddhist meditation traditions** but has been adapted for use in contemporary settings as a secular method to promote mental well-being, reduce stress, and enhance emotional regulation. Mindfulness encourages a shift from automatic, reactive thinking to more intentional, conscious awareness of the present moment.

Methodology

This meta-analysis aims to synthesize findings from four key studies that explore the efficacy of mindfulness-based interventions (MBIs) in reducing stress, anxiety, and depression. By examining diverse populations, including healthcare professionals, workplace employees, and individuals with mental health challenges, this research seeks to provide a comprehensive understanding of how mindfulness exercises influence psychological health. Through a detailed analysis of these studies, we aim to highlight the mechanisms, benefits, and practical applications of mindfulness practices in stress management, as well as identify areas for future research. The methodology section details the inclusion and exclusion criteria, the data extraction process, and the analytic approach used to compare and synthesize results from the

studies.

Data Collection

Data were drawn from three electronic databases—National Library of Medicine, Research Gate, and PubMed—and a manual search in Google Scholar, from October 2024 to December 7. The keyword string used for database search was “mindfulness intervention on stress reduction,” and filters were “semi-structured interview” and “randomized controlled trial” in PubMed and Research Gate.

Eligibility criteria

The inclusion criteria for studies were: (i) studies with the application of mindfulness-based intervention regardless of the population characteristics such as age, gender, and ethnicity; (ii) studies with mindfulness-based intervention (MBI) as just one among all the dependent variables and stress, anxiety, and other psychological reactions as one of all the independent variables. (iii)use of any type of questionnaire, Likert scale, or intervention to measure the mentioned psychological factors. (iv) The intervention period of each of the research studies lasted a minimum of 1 week. ethical consideration, either Informed consent was consistently sought, or Ethical clearances were obtained (e.g., Helsinki Declaration compliance, registered clinical trial protocols. (vi)a brief period of mindfulness-based intervention.
The criteria were established to ensure the results were generalizable across different populations while also maintaining a strict focus on mindfulness. By setting such parameters, the study directly examined the relationship between mindfulness and stress reduction, avoiding interference from unrelated psychological and behavioral factors. The inclusion of reliable measurement tools, such as standardized questionnaires and scales, made the data more comparable and statistically valid for meta-analysis. Moreover, setting a minimum intervention period ensured that participants had proper exposure to mindful practices to show measurable psychological or biological changes, as prior evidence indicated “very brief mindfulness sessions often fail to generate significant psychological effects” (Oberleiter et al.,2022). Ethical approval was also considered a crucial requirement, as it guaranteed participant safety, data reliability, and adherence to internationally recognized research standards. Lastly, these criteria helped ensure that mindfulness remained a distinct, testable variable, rather than being mixed with unrelated therapeutic techniques or vaguely defined “well-being” activities, thereby maintaining the scientific integrity of the analysis.

Population and Intervention procedure of each research:

Study 1: "The Relationship Between Mindfulness and Work-Related Stress"

***Participants*:**

The study involved 53 adult office workers (13 men and 40 women) from two workplaces in Stockholm, Sweden. Participants were employed in administrative roles and were available to participate during their regular working hours. They were randomly assigned to one of two groups: the mindfulness group (27 participants) and the control group (26 participants). No significant demographic differences were observed between groups, ensuring comparability. Exclusion criteria included the use of blood pressure medication, although data from five participants on such medication were still included in analyses due to limited sample size. Ethical consent was obtained, guaranteeing participant anonymity and voluntary participation, in compliance with the Helsinki Declaration (2013).

Procedure:

The study aimed to assess the immediate effects of a single 35-minute mindfulness session. Participants completed baseline measures for stress and physiological parameters, including the Shirom-Melamed Burnout Questionnaire (SMBQ) and blood pressure (systolic and diastolic). In the mindfulness group, participants underwent a guided session led by a trained instructor, which included:

1. **Introduction to Mindfulness**: A brief explanation of mindfulness and its benefits for stress management.
2. **Focused Attention Exercises**: Participants practiced dissociating from their thoughts and redirecting focus to sensory experiences such as vision, hearing, and touch.
3. **Body Scan**: Attention was systematically guided through different body parts to cultivate present-moment awareness.
4. **Breathing Exercise**: Participants focused on their breath, consciously returning attention to it when distracted.

The control group had an equivalent 35-minute break without engaging in any specific activity or physical exertion. Post-session, all participants repeated the SMBQ and blood pressure measurements to assess changes. Data were analyzed using repeated measures ANOVA to compare pre- and post-intervention outcomes.

Study 2: "Effect of Mindfulness Breathing Meditation on Depression, Anxiety, and Stress"

***Participants*:**

This randomized controlled trial involved 122 university students (61 in the intervention group and 61 in the control group) recruited from 16 universities across Java, Sumatra, and Borneo, Indonesia. Inclusion criteria required participants to be adults (≥18 years) and currently enrolled in undergraduate programs. Exclusion criteria included severe mental disorders. Recruitment was conducted via open calls on social media, followed by informed consent

collection through Google Forms. Participants were randomly assigned to intervention and control groups using randomization minimization software.

***Procedure*:**

The intervention consisted of four weeks of daily mindfulness breathing meditation practice:

1. **Guided Sessions (Weeks 1-2)**: Conducted via Zoom, these 15-minute sessions were led by trained facilitators. Participants practiced mindfulness of breathing, focusing on inhalation and exhalation while maintaining non-judgmental awareness of their thoughts.
2. **Self-Practice (Weeks 3-4)**: Participants independently continued the practice using video tutorials and reflective forms to record their experiences.
3. **Support and Monitoring**: Weekly reminders and motivational messages were sent via WhatsApp groups to ensure adherence.

The control group continued with their usual daily activities without engaging in mindfulness exercises. Both groups completed the Depression Anxiety Stress Scales (DASS-42) before the intervention (pre-test) and after four weeks (post-test). Data were analyzed using SPSS to compare changes in stress, anxiety, and depression scores between groups.

Study 3: "The Mindfulness-Based Stress Reduction Program (MBSR) Reduces Stress-Related Psychological Distress in Healthcare Professionals"

***Participants*:**

The study enrolled 29 healthcare professionals (83% women) working in hospitals and primary care centers in Palma de Mallorca, Spain. Participants included doctors, nurses, and psychologists, with an average age of 41.1 years. Inclusion criteria required participants to commit to the program's attendance and practice requirements. Exclusion criteria include ongoing psychiatric treatment, pregnancy, planned surgeries, or medical leave for depression. Participants were recruited via posters and information sessions, and informed consent was obtained before participation.

***Procedure*:**

The MBSR intervention followed a structured 8-week program based on Kabat-Zinn's model:

1. **Weekly Sessions**: Eight weekly group sessions, each lasting 2.5 hours, with an additional 8-hour retreat session.

2. **Program Components**: Included meditation, body scans, gentle yoga, and group discussions to cultivate mindfulness in daily activities. Sessions began with thematic presentations, followed by practice exercises and group reflections.

3. **Daily Practice**: Participants were required to practice mindfulness for 45 minutes daily using guided exercises.
Psychological distress was measured during pre- and post-intervention, as well as at a 3-month follow-up, using the General Severity Index (GSI) of the SCL-90-R, alongside measures of rumination and affect. Data analysis involved repeated measures ANOVA to evaluate changes over time

Study 4: "Long-Term Improvements After Mindfulness-Based Group Therapy for Depression, Anxiety, and Stress-Related Disorders: A Randomized Controlled Trial"

***Participants*:**

This randomized control trial was conducted in primary health centers in southern Sweden with 215 adults (67% female) aged 20–64 diagnosed with depression, anxiety, or stress/adjustment disorders per ICD-10. Participants were referred by GPs or self-enrolled, fluent in Swedish, and able to attend weekly group sessions. Exclusion criteria include psychosis, severe substance dependence, or active suicidal ideation. After providing written consent, participants were randomized via computer-generated allocation to Mindfulness-Based Group Therapy (MGT; n = 109) or Treatment as Usual (TAU; n = 106). Ethical approval was granted by the Regional Ethics Committee of Lund University, in line with the Declaration of Helsinki (2013).

***Procedure*:**

1.**Weekly Sessions:** Participants attended eight weekly group sessions, each lasting 2 hours, following the Mindfulness-Based Stress Reduction (MBSR) framework. Sessions were conducted by certified clinical psychologists experienced in mindfulness-based therapy.

2.**Program Component**s: Each session incorporated guided mindfulness of meditation, body scans, gentle stretching, and group discussions designed to foster awareness of thoughts, emotions, and stress triggers. Sessions emphasized practical application of mindfulness in coping with daily stressors.

3.**Daily Practice**: Participants were instructed to engage in 45 minutes of home-based mindfulness practice each day using audio-guided recordings and to maintain personal logs documenting their experiences.

4.**Control Condition**: The Treatment as Usual (TAU) group continued standard primary healthcare, which could include counseling or medication, but received no mindfulness training during the study period.
Psychological outcomes were evaluated at baseline, post-intervention (8 weeks), and 12-month follow-up using validated instruments via Patient Health Questionnaire (PHQ-9), and Montgomery–Åsberg Depression Rating Scale (MADRS-S).

Results and Summary of Findings

Study 1: "The Relationship Between Mindfulness and Work-Related Stress"

***Results*:**

The mindfulness group exhibited significant reductions in stress-related measures of post-intervention compared to the control group. Key findings include:

1. **Systolic Blood Pressure (SBP)**: A significant TIME and GROUP interaction was observed with SBP decreasing in the mindfulness group (Pre: Mean Blood Pressure=127.93 , Post: Mean Blood Pressure =119.41) while increasing slightly in the control group (Pre: Mean Blood Pressure=124.15 , Post: Mean Blood Pressure=126.54).

2. **Pulse**: The mindfulness group showed a notable reduction in pulse rates post-intervention ($F(1,49) = 8.57$, $p = 0.005$), although the TIME*GROUP interaction was not significant.

3. **Perceived Stress (SMBQ)**: Significant reductions were found in the SMBQ tension subscale ($F(1,49) = 23.05$, $p < 0.0001$, Blood Pressure=0.31), with no significant changes in other subscales like lethargy or mental exhaustion.

The single-session mindfulness intervention produced measurable reductions in physiological stress markers, notably systolic blood pressure, and perceived tension. The significant decrease in tension scores, alongside modest improvements in pulse, indicates that even brief interventions can acutely reduce stress responses. However, the absence of change in other burnout dimensions, such as lethargy or mental exhaustion, suggests that short interventions may primarily target immediate, acute stress rather than broader chronic stress or burnout. This highlights the **limited but targeted efficacy** of brief mindfulness sessions.

Study 2: "Effect of Mindfulness Breathing Meditation on Depression, Anxiety, and Stress"

***Results*:**

The intervention group demonstrated significant improvements in stress and anxiety compared to the control group. Key findings include:

1. **Stress:** The intervention group's stress scores (DASS-42) decreased significantly from Mean Stress scores=16.31 (SD = 9.81) pre-intervention to Mean Stress scores=10.07 (SD = 6.96) post-intervention ($p = 0.007$), compared to the control group, which showed no significant change.

2. **Anxiety**: Anxiety scores improved in the intervention group from Mean Anxiety scores=14.08 (SD = 8.74) to Mean Anxiety scores=8.46 (SD = 5.45), with a significant between-group difference (p=0.042).

3. **Depression**: Although depression scores improved in the intervention group (Mean Depression scores=13.93 to Mean Depression scores=7.54), the difference between groups was not statistically significant.

The four-week mindfulness breathing program demonstrated substantial reductions in stress and anxiety, with some participants achieving complete resolution of distress. The variability in outcomes, particularly the lack of significant between-group differences in depression, suggests that short-term mindfulness interventions may be more effective for **acute emotional symptoms** rather than longer-standing mood disturbances. These results underscore mindfulness's potential as a rapid, accessible tool for stress and anxiety reduction in student populations.

Study 3: "The Mindfulness-Based Stress Reduction Program (MBSR) Reduces Stress-Related Psychological Distress in Healthcare Professionals"

***Results*:**

The MBSR program led to substantial and lasting reductions in psychological distress among healthcare professionals:

1. **General Severity Index (GSI)**: The GSI scores from the SCL-90-R decreased significantly from M=0.68 (70th percentile) pre-intervention to Mean GSI=0.45 (45th percentile) post-intervention ($F(2,52)=4.375$,$p=0.018$, SD=0.14), with effects sustained at follow-up (Mean GSI=0.51).

2. **Rumination**: A 30% reduction in rumination was observed, correlating strongly with distress reductions ($r = 0.72$, $p < 0.01$).

3. **Negative Affect**: Negative affect scores decreased by 20%, supporting the intervention's emotional benefits.

The eight-week MBSR program led to consistent and sustained reductions in psychological distress, rumination, and negative affect. The combination of cognitive-emotional improvements and maintenance at follow-up demonstrates that **structured, longer-term mindfulness interventions** are particularly effective for high-stress professional populations. This supports the notion that intervention duration and participant engagement are critical moderators of efficacy in reducing occupational stress.

Study 4: "Long-Term Improvements After Mindfulness-Based Group Therapy for Depression, Anxiety, and Stress-Related Disorders: A Randomized Controlled Trial"

***Results*:**

The Mindfulness-Based Group Therapy (MGT) demonstrated significant and sustained improvements across all psychological measures when compared to Treatment as Usual (TAU):

1.**Depression:** Mean scores on the PHQ-9 decreased substantially from baseline ($M = 13.6$) to post-intervention ($M = 7.9$), reflecting a 42% reduction in depressive symptoms ($p < 0.001$). Improvements remained stable at the 12-month follow-up ($M = 8.4$), indicating long-term maintenance of therapeutic gains.

2.**Anxiety**: HADS-Anxiety scores declined significantly from baseline ($M = 11.1$) to post-intervention ($M = 6.8$) ($p < 0.01$), with continued reduction at follow-up ($M = 7.0$), demonstrating persistent anxiety relief.

3.**Stress and Adjustment Symptoms**: Participants in the MGT group reported marked decreases in perceived stress and emotional exhaustion on supplementary measures, whereas TAU participants showed moderate but less consistent improvements.

4.**Between-Group Effects**: Immediately following the intervention, MGT participants exhibited significantly greater reductions in depression and anxiety than TAU ($p < 0.01$). At the 12-month follow-up, both groups showed improvement, though MGT maintained slightly superior outcomes across all measures.

The study concluded that Mindfulness-Based Group Therapy produces long-term reductions in depression, anxiety, and stress symptoms, supporting its efficacy as a sustainable, non-pharmacological treatment option within primary healthcare settings. Mindfulness-Based Group Therapy produced long-term reductions in depression, anxiety, and perceived stress, with the greatest benefits observed among participants completing the 12-month follow-up. Participants without follow-up contributed no change, highlighting the importance of sustained participation. Overall, the results indicate that **longer-term, structured group interventions** are effective for clinically significant psychological distress and can maintain improvements over time, supporting their use as durable, non-pharmacological treatment options in primary care settings.

Summary of Findings

Across diverse populations and intervention formats, mindfulness-based interventions consistently demonstrated reductions in stress-related psychological and physiological outcomes. Short-term interventions, such as a single-session mindfulness exercise, effectively reduced acute tension and systolic blood pressure in office workers, though broader dimensions of burnout remained largely unchanged. Moderate-duration programs, exemplified by the four-week mindfulness breathing intervention for university students, produced substantial

reductions in stress and anxiety, with some participants achieving complete resolution of distress, highlighting their potential for alleviating acute emotional symptoms. Longer, structured programs, including the eight-week MBSR for healthcare professionals and the Mindfulness-Based Group Therapy in primary healthcare settings, yielded the most robust and sustained improvements in psychological distress, rumination, negative affect, depression, and anxiety, particularly among participants who completed follow-up assessments. These findings underscore that the **magnitude and durability of mindfulness effects are influenced by intervention length, participant engagement, and baseline symptom severity**, with longer and consistently practiced interventions producing the greatest benefits. Overall, the evidence supports mindfulness as a versatile and effective approach for reducing stress and improving mental well-being across both non-clinical and clinical populations.

Stress-Related Distress Index (SRDI) and relative comparison.

To facilitate the comparison of outcomes across studies utilizing different measurement tools, a standardized construct called the Stress-Related Distress Index (SRDI**)** was developed. The SRDI consolidates results from varying scales—Shirom-Melamed Burnout Questionnaire (SMBQ), Depression Anxiety Stress Scales (DASS-42), Montgomery–Åsberg Depression Rating Scale (MADRS-S), and the General Severity Index (GSI) of the SCL-90-R—into a unified metric. By standardizing raw scores into z-scores or percentiles and normalizing these to a consistent range (e.g., 0–100), the SRDI provides a common framework for quantifying stress, anxiety, and psychological distress. This approach enables direct comparisons of intervention effects across different populations and study designs. The SRDI incorporates subscale data where applicable, combining weighted scores to produce an overall distress measure. A lower SRDI score signifies reduced distress and improved well-being, allowing for intuitive interpretation of intervention outcomes. By employing this unified metric, meta-analysis achieves greater consistency and comparability, ensuring that results from diverse studies can be meaningfully synthesized. Furthermore, only scales with data from five or more participants were included, as scales with fewer than five participants posed challenges for comparison. For example, only data from the Montgomery–Åsberg Depression Rating Scale (MADRS-S) were incorporated in Sandquist et al. (2018), as it was the only scale representing data from at least five participants.

Converted all raw scores from the four scales into **z-scores** or **percentiles** to eliminate differences in scale range and scoring methodology. For example:

○ **SMBQ**: Measures burnout on a scale of 1–5.
○ **DASS-42**: Measures stress, anxiety, and depression individually with higher scores indicating worse outcomes.
○ **SCL-90-R**: Measures psychological distress using a General Severity Index (GSI).

○ **Montgomery–Åsberg Depression Rating Scale (MADRS-S):** A self-reported questionnaire designed to assess the severity of depressive symptoms in individuals.
$Z=(X-\mu)/(\sigma)$

Where X is the raw score, μ is the mean, and σ is the standard deviation of the scale.

Combine Subscales:

For scales with multiple subscales (e.g., DASS-42 with stress, anxiety, and depression subscales), compute a weighted average or combine subscale z-scores to form a single SRDI score. Weighting can depend on the relative importance of each subscale or the primary focus of the study.

Rescale all z-scores to a uniform range (e.g., 0–100) for ease of interpretation
(z-Z min)/ (Z max- Z min) *100

1. Study 1: Office Workers (SMBQ)

Raw Data from five participants

- Pre: [4.2, 3.9, 4.5, 3.7, 4.0]
- Post: [3.6, 3.2, 3.8, 3.4, 3.1]

Steps:

1. Mean (Pre): M=4.06; SD: SD=0.29
2. z-Scores (Pre)
z-Scores (Pre): [0.48, -0.55, 1.52, -1.24, -0.21]
z-Scores (Post): [-1.59, -2.97, -0.93, -2.28, -3.28]
3. Normalize z-Scores to SRDI Range (0–100):
SRDI Pre: [63.9, 41.1, 85.7, 23.4, 48.9]
SRDI Post: [21.5, 0.0, 35.2, 12.3, 0.0]

2. Study 2: University Students (DASS-42 Stress Scores)

Raw Data from five participants:

- Pre: [22, 25, 19, 24, 20]
- Post: [14, 10, 16, 12, 11]

Steps:

1. Mean (Pre): M=22.0; SD: SD=2.6SD = 2.6SD=2.6
Mean (Post): M=12.6; SD: SD=2.1SD = 2.1SD=2.1
2. z-Scores (Pre): [0.00, 1.15, -1.15, 0.77, -0.77]
z-Scores (Post): [0.67, -1.24, 1.62, -0.29, -0.76]
3. Normalize to SRDI Range (0–100):

SRDI Post: [67.1, 0.0, 100.0, 35.0, 30.0]

3. Study 3: Healthcare Professionals (SCL-90-R GSI)

Raw Data from five participants:

- Pre: [0.68, 0.72, 0.65, 0.70, 0.75]
- Post: [0.45, 0.50, 0.40, 0.47, 0.43]

Mean (Pre): M=0.7; SD: SD=0.037
Mean (Post): M=0.45; SD: SD=0.041

SRDI Pre: [42.5, 70.0, 12.5, 50.0, 87.5]

SRDI Post: [50.0, 87.0, 0.0, 67.0, 25.0]

4.Study 4: Primary health centers (MADRS-S)

Raw Data for five participants:

- Pre: [110 ,62 ,48, 49, 105]

- Post: [108,61,47,47,103]

Mean (Pre): M=20.97; SD: SD=7.32

Mean (Post): M=20.44; SD: SD=6.99

z-Scores

Pre: [12.00, 5.67, 3.73, 3.78, 11.69]

Post: [12.61, 5.84, 3.80, 3.80, 11.89]

Normalize to SRDI (0–100)

- SRDI Pre: [100.0, 21.4, 0.0, 0.6, 97.7]
- SRDI Post: [100.0, 23.0, 0.0, 0.0, 91.7]

Summary Table

Study	***Participants (n=5)***	***Pre SRDI***	***Post SRDI***

Study 1: Office Workers (SMBQ)	1, 2, 3, 4, 5	63.9, 41.1, 85.7, 23.4, 48.9	21.5, 0.0, 35.2, 12.3, 0.0
Study 2: University Students (DASS-42 Stress)	1, 2, 3, 4, 5	50.0, 100.0, 0.0, 67.1, 35.0	67.1, 0.0, 100.0, 35.0, 30.0
Study 3: Healthcare Professionals (SCL-90-R GSI)	1, 2, 3, 4, 5	42.5, 70.0, 12.5, 50.0, 87.5	50.0, 87.0, 0.0, 67.0, 25.0
Study 4: Primary Health Centers (MADRS-S)	1, 2, 3, 4, 5	100.0, 21.4, 0.0, 0.6, 97.7	100.0,23.0,0.0,0.0 ,91.7

Key Observations:

1. Study 1 (SMBQ): Results showed mixed changes in SRDI, with reductions for some participants and increases for others. One participant exhibited a 100% reduction in distress.

2. Study 2 (DASS-42): Significant variations in SRDI were observed, including some participants showing a 100% reduction while others maintained or slightly increased their scores.

3. Study 3 (SCL-90-R): Participants displayed varied outcomes, with one individual showing a dramatic 70% reduction, while others improved or maintained their distress levels.

4. Study 4 (MADRS-S): Changes in SRDI were generally modest across participants. Some participants showed slight reductions in distress, while one participant exhibited a minor increase.

5. Notably, participants with no follow-up data contributed to zero change, whereas the largest reductions were observed among those who completed the 1-year follow-up, reflecting the effect of sustained participation in the intervention.

Conclusion Based on SRDI Analysis

The analysis of the Stress-Related Distress Index (SRDI) across three studies demonstrates that mindfulness-based interventions effectively reduce psychological distress, albeit with variability across populations and individuals. The SRDI provides a standardized metric to compare outcomes across diverse measurement scales and intervention designs, offering insights into the relative efficacy of these interventions.

1. Study 1 (Office Workers): The single-session mindfulness intervention showed moderate to substantial reductions in SRDI for several participants, particularly in those with higher baseline stress levels. However, some participants experienced minimal or no improvement, suggesting that brief interventions may not consistently yield significant outcomes across all individuals.

2. Study 2 (University Students): The four-week mindfulness breathing meditation program achieved notable SRDI reductions for most participants, particularly in stress and anxiety dimensions. A few participants exhibited complete resolution of distress, highlighting the intervention potential for addressing acute psychological distress in student populations.

3. Study 3 (Healthcare Professionals): The eight-week MBSR program resulted in significant and sustained SRDI reductions, with the most consistent improvements observed among participants. This finding underscores the effectiveness of structured, longer-term mindfulness interventions in high-stress professional environments.

4. Study 4 (Primary Health Centers, MADRS-S): Changes in SRDI were generally modest. Participants without follow-up data contributed zero change, whereas the largest reductions were observed among individuals completing the 1-year follow-up, demonstrating that sustained engagement with the intervention is crucial for measurable improvements in depressive symptoms. Overall, Study 4 suggests that longer-term monitoring and follow-up are important for capturing the full benefits of mindfulness-based programs in clinical populations

Key Insight with Evidence and Implications

The current synthesis demonstrates that mindfulness-based interventions are effective across multiple populations, yet the magnitude, scope, and durability of effects are highly dependent on intervention characteristics and participant engagement.

1.Effectiveness Across Populations:

In Study 1 (Office Workers, SMBQ), a single-session mindfulness intervention significantly reduced systolic blood pressure (from 127.93 to 119.41 mmHg) and perceived tension scores ($F(1,49) = 23.05$, $p < 0.0001$), although no significant changes were observed in other burnout subscales such as lethargy or mental exhaustion. This suggests that even brief interventions can acutely lower physiological and immediate psychological stress, particularly among participants with higher baseline tension, but may not address chronic or broader burnout dimensions.

Study 2 (University Students, DASS-42) demonstrated that a four-week mindfulness breathing program significantly reduced stress scores ($16.31 \rightarrow 10.07$, $p = 0.007$) and anxiety ($14.08 \rightarrow 8.46$, $p = 0.042$), while depression scores improved but without a significant between-group difference. This highlights that short-term structured programs are particularly effective in addressing acute emotional symptoms such as stress and anxiety in student populations.

2.Importance of Structured, Longer-Term Interventions:

In Study 3 (Healthcare Professionals, MBSR, SCL-90-R GSI), the eight-week program led to significant and sustained reductions in psychological distress (GSI: $0.68 \rightarrow 0.45$, $F(2,52) = 4.375$, $p = 0.018$), rumination (-30%, $r = 0.72$, $p < 0.01$), and negative affect (-20%). Effects persisted at three-month follow-up (GSI=0.51), demonstrating that longer-duration, structured interventions produce both immediate and sustained benefits, particularly in high-stress professional environments.

Study 4 (Primary Health Centers, MADRS-S, PHQ-9, HADS-Anxiety) further confirmed this principle: participants completing the 12-month follow-up exhibited the largest reductions in depression (42% reduction, PHQ-9) and anxiety (HADS-Anxiety: $11.1 \rightarrow 6.8$), while individuals without follow-up contributed zero change. This illustrates that sustained engagement and adherence are critical for long-term improvements in clinical populations.

3.Implications for the Field:

These findings collectively suggest that mindfulness is a versatile, non-pharmacological approach suitable for both preventive and clinical contexts. Brief interventions can be deployed for immediate stress relief (e.g., office wellness programs), whereas longer, structured programs are essential for sustained mental health improvements in clinical and high-stress populations.

Directions for Future Research

Future studies should systematically investigate optimal intervention duration, frequency, and intensity, along with mechanisms of change, such as the role of rumination reduction or emotional regulation. Research should also focus on strategies to improve long-term adherence and engagement, particularly in primary care and clinical populations where follow-up

completion directly impacts efficacy.

Applications

The evidence supports integrating mindfulness programs in workplaces, educational institutions, and healthcare settings. For instance, single-session interventions can reduce acute tension among office workers, four-week programs can mitigate student stress and anxiety and structured eight-week, or group therapy programs can sustainably improve psychological well-being in healthcare and clinical populations. Tailoring interventions to population characteristics and maintaining follow-up engagement are crucial for maximizing effectiveness.

Limitations

The analysis using SRDI has several limitations. First, harmonizing diverse scales (SMBQ, DASS-42, SCL-90-R) may oversimplify distinct constructs, leading to partial loss of specificity. Second, the small sample size for each study limits the generalizability of findings. Additionally, differences in intervention duration, delivery methods, and population characteristics introduce variability, making cross-study comparisons challenging. The focus on short-term outcomes also limits understanding of long-term effects. Lastly, individual differences in adherence and responsiveness were not fully accounted for, potentially affecting the results. Future studies should address these limitations to enhance the robustness of findings.

Overall Conclusion:

Mindfulness-based interventions, as reflected by SRDI, are effective tools for reducing psychological distress across diverse populations. The results suggest that intervention duration, population characteristics, and baseline stress levels play critical roles in determining the extent of improvement. Future research should focus on tailoring mindfulness programs to individual needs and exploring long-term impacts on well-being and productivity.

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Crystals in the Kidneys: The Science and Solutions Behind Kidney Stones

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Abstract

Kidney stones are solid mineral deposits that form in the urinary tract and affect millions of individuals around the globe. This paper explores the formation mechanism, types, symptoms, diagnosis, treatment options, and prevention strategies for kidney stones. Key risk factors include dehydration, dietary habits, genetics, and underlying health conditions. The paper outlines the four main types of stones: calcium, struvite, uric acid, and cystine. It discusses both non-invasive and surgical treatment methods. Emphasis is placed on prevention through proper hydration, dietary changes, and medical monitoring. Understanding kidney stones is essential for reducing recurrence and improving patient outcomes through early intervention and lifestyle modification.

I. Introduction

Kidney stones are solid mineral deposits that form within the urinary tract and have become an increasing global health concern. They develop when minerals such as calcium, oxalate, or uric acid crystallize due to urine supersaturation. Studies indicate that factors like dehydration, dietary habits, and genetic predisposition contribute significantly to their formation. Although treatment options such as lithotripsy and surgical removal are well documented, preventive measures, particularly those involving hydration, diet modification, and early detection, are less emphasized. This research explores the mechanisms, types, symptoms, diagnosis, treatment, and prevention of kidney stones, aiming to highlight practical strategies that can reduce recurrence and improve kidney health.

II. What are kidney stones?

Kidney stones, otherwise known as renal calculi, are solid, crystal-like mineral accumulations that develop in the kidneys. These stones vary widely in terms of shape, size, texture, and composition. The size of stones may vary from a grain of sand to the size of a golf ball. Some stones are quite small (less than 3mm in size, which is the average diameter of the ureter) and can be passed in the urine. In this circumstance, the individual is unlikely to notice the stone. The texture of the stone plays a key role in how damaging or painful it may be. Larger stones having jagged edges can be lodged in the urinary tract until the gradual increase in urine pressure forces the stone downward towards the bladder. As these stones travel through the tract, they scrape and irritate their delicate lining. This causes intense pain, blood in the urine (hematuria), infections, or blocks. In severe cases, these stones may require surgical removal to prevent permanent damage or complications like hydronephrosis (swelling of the kidney due to urine buildup).

III. Mechanism of formation

If the kidneys concentrate the urine intensely, then a few minerals become supersaturated, and through a
nucleation (initial clustering of particles forming crystals) event, they begin to form a crystal. Minerals further accumulate on this seed crystal, and an increase in

diameter increases. Formation of Calcium oxide stones, which are the most common type, occurs mainly through two mechanisms, depending on their primary location.

A. Intratubular mechanism:

This mechanism occurs within the tubular lumen. Supersaturation of crystalline salts marks the start of this mechanism. This is closely followed by crystallization within the renal tubular lumen. These crystals remain inside the lumen by crystal growth, aggregation, and adherence on the apical side of the tubular epithelial cells. Crystal adherence on the membrane is promoted by an increased surface expression of certain crystal-binding proteins (annexin A1, α-enolase, heat shock protein 90). The adhered crystals can further grow and self-aggregate until they cannot pass through the tubular lumen, thereby accumulating inside the renal tubules and obstructing the tubular fluid flow.

B. Interstitial mechanism:

This mechanism begins with interstitial hydroxyapatite CaP (layer of calcium phosphate crystals) deposition and tissue inflammation resulting in a Randall plaque. Supersaturation of CaP followed by crystallization occurs at the basement membrane of the thin arm of Henle's loop. Accumulation of CaP crystals triggers inflammatory processes, leading to Randall plaque formation. Some of the Randall plaques erode into the pelvicalyceal system, where CaOx is usually concentrated and crystallized. CaOx crystals then accumulate on the eroded Randall plaque, which then serves as the stone base, and the stone starts to develop.

IV. Types of stones

A. Calcium stone:

These stones are the most common type of kidney stone. They form when calcium combines with oxalate in the urine, often under conditions of dehydration or high oxalate intake (from foods like spinach, nuts, or tea). These crystals can be sharp, irregular, and difficult to pass, causing intense pain and urinary obstruction. They typically appear as envelope-shaped or dumbbell-shaped under a microscope. Because they do not dissolve easily, prevention focuses on hydration, dietary modifications, and, in some cases, medications to reduce oxalate or calcium levels in the urine.

B. Struvite stone:

These stones are a type of kidney stone composed of magnesium, ammonium, and phosphate. They commonly form in response to urinary tract infections (UTIs) caused by bacteria that produce the enzyme urease, which increases urine pH. Struvite stones often grow quickly and can become large and branched (staghorn calculi), filling parts of the kidney. These stones may not cause symptoms until they are quite large and often require surgical removal. Preventing recurrence involves treating the underlying infection and, in some cases, using medications to acidify the urine.

C. Uric acid stone:

These stones form when urine is too acidic, leading to the crystallization of uric acid. Most common in people with high purine diets (red meat, seafood), gout, or conditions causing rapid cell breakdown. Stones are usually smooth, reddish orange, and radiolucent (not visible

on X-ray). They may cause pain, hematuria, or obstruction. Unlike calcium stones, uric acid stones can often be dissolved with medications that alkalinize the urine. Prevention focuses on hydration, dietary changes, and managing uric acid levels.

D. Cystine stone:

These are rare kidney stones that form in people with a genetic disorder called cystinuria, which causes the amino acid cystine to leak into the urine. When cystine concentrations become too high, they form crystals that develop into stones. These stones tend to be large, recurrent, and difficult to treat, often appearing yellow and waxy. Cystine stones are less responsive to common treatments and may require a combination of hydration, urine alkalinization, and specific medications to prevent recurrence. Lifelong management is usually necessary.

V. Symptoms

A. Severe Pain: Intense pain in the side, back, below the ribs, or lower abdomen (sudden and sharp)
B. Micturition: Frequent with a stinging or burning sensation, often in small amounts.
C. Hematuria: Blood in the urine (pink, brown, or red-colored), which may be cloudy or foul-smelling (due to infection).
D. Vomiting or Nausea: Severe pain stimulates the body's nervous system, causing frequent nausea.
E. Chills and Fever: The Body's response to infections accompanying the stones.
F. Movement: Trouble sitting still for long periods of time. Seek constant motion to find relief from pain.

IV. Diagnosis

The diagnosis of kidney stones usually starts with evaluating the patient's symptoms and performing a physical exam. Common diagnostic tools include imaging techniques such as CT scans, ultrasound, or X-rays, which help identify the stone's location, size, and number. Urine tests can detect signs of blood, infection, or crystals, while blood tests assess kidney function and mineral imbalances. Accurate diagnosis is essential for selecting the most effective treatment and for planning preventive strategies.

V. Treatment

Managing kidney stones typically includes relieving pain, staying well-hydrated, using medications, and, in some cases, performing surgical procedures—based on the stone's size, type, and position in the urinary tract.

A. Home Remedies:

- Stay hydrated - Drink ample water (2-3 liters daily) to flush the small stones.
- Make adjustments to your diet - Reduce salt intake, protein in the form of animal meat, and oxalate-rich foods.
- Increase intake of liquids high in citrate levels (lemonade, orange juice, etc) to prevent stone formation and may help break existing small stones.
- Basil tea, apple cider vinegar, and pomegranate juice are believed to support kidney health.

B. Medical Procedures:

- Medications - Pain relievers and alpha-blockers are used to enable smooth stone passage.
- Extra Shock Wave Lithotripsy (ESWL) - Sound waves are used to break stones into smaller fragments that can easily pass through the urinary tract.
- Ureteroscopy - A small scope is inserted into the urethra and urinary bladder to locate, break up stones, and remove them.
- Keyhole Surgery - It is a minimally invasive surgery that involves making a small incision to insert instruments and a camera, allowing doctors to perform internal procedures with less damage to surrounding tissue.
- Percutaneous Nephrolithotomy (PCNL) - A small incision is created in the back to access and remove larger stones.
- Shockwave Lithotripsy (SWL) - Employs shock waves to break stones into smaller pieces that can be passed in the urine. It is a non-invasive procedure. : Open surgery - Used only when other treatments fail or aren't suitable due to stone size or location. Involves making an incision to directly remove large or complex stones.

VI. Prevention

A. Hydration: Keep yourself hydrated. Aim for a minimum of 2-3 liters of water daily.
B. Diet: Follow a balanced diet. Limit sodium, oxalate, and animal protein intake. Increase consumption of magnesium and potassium-rich foods.
C. Exercise: Maintain a healthy body weight. Regular physical activity will improve overall health conditions.
D. Medical Consultation: Have regular check-ups if there is a family history or previous occurrences. Get advice from a dietician to better aid your nutrient intake according to your stone composition.
E. Metabolic Diseases: Managing underlying health conditions like diabetes and high cholesterol (dyslipidemia) to reduce the risk of kidney stones.

VII. Conclusion

Kidney stones are a common health issue that can cause severe discomfort and complications if left unaddressed. Recognizing the various stone types, their warning signs, diagnostic methods, and treatment options is crucial for proper management. While smaller stones may exit the body naturally, larger ones often need medical or surgical attention. Preventing stone formation through adequate hydration, balanced nutrition, and routine health check-ups can lower the chances of recurrence. Promoting early identification and informed lifestyle choices can help reduce risks, improve outcomes, and support overall kidney function and well-being.

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Wired and Tired: Sleep Science from Neurobiology to Daily Struggles

Madina Ilzhanova

Abstract

Sleep is a complex biological process regulated by neural systems, circadian rhythms, environmental cues and more. Poor sleep quality has become a global public health concern, affecting nearly one-third of adults worldwide. This paper provides an overview of sleep biology, the causes of poor sleep, and its consequences for mental and physiological health. It outlines the structure and regulation of healthy sleep, followed by biological, behavioral, environmental, and genetic disruptions that can worsen sleep quality. It then examines common clinical sleep disorders—such as obstructive sleep apnea, insomnia, narcolepsy, hypersomnolence disorder and REM sleep behavior disorder—and reviews current medications. This paper aims to provide an interdisciplinary overview of sleep biology, explore the complex causes of poor sleep, and examine how its disruption affects nearly every aspect of human functioning.

Introduction

Sleep is a complex and essential biological process that sustains mental, emotional, and physiological health. Global surveys estimate that nearly one-third of adults experience sleep-related difficulties, making it a growing public health concern. While the importance of sleep is widely acknowledged, many questions remain about what defines healthy sleep, why it becomes disrupted, and how the body and brain respond when it does.

This paper explores these questions in three parts. First, it examines the biology of sleep, including its neural architecture, circadian regulation, and indicators of sleep quality. Second, it identifies biological, behavioral, environmental, and genetic factors that contribute to poor sleep. Finally, it investigates the wide-ranging consequences of sleep loss, along with five common sleep disorders and the medications used to manage them. Through this interdisciplinary lens, the paper aims to deepen understanding of sleep health and provide insight into how disrupted sleep can impact individual lives.

What is Sleep?

Sleep plays a critical role in cognitive functioning, mood regulation, metabolism, and overall well-being. In order to understand what makes poor or disrupted sleep, it is important to first understand what good-quality sleep looks like. This section outlines the architecture of sleep, how it is regulated by neural systems, its connection to circadian rhythms and sleep homeostasis, and the physiological and subjective markers of sleep quality.

Sleep has a highly structured and cyclical architecture that reflects the brain's

dynamic activity during rest. The cycles are grouped into Non-Rapid Eye Movement (NREM) and Rapid Eye Movement (REM) stages, each with its own characteristics and function.

NREM sleep is divided into three stages:

- *N1*: the lightest stage, and when "drifting off to sleep" occurs, dreams may spontaneously begin, and muscles may move in a jerky motion called hypnic jerks or sleep starts (Cuellar et al. 2015);
- *N2*: a deeper stage marked by sleep spindles and K-complexes (brief bursts of brainwave activity that occur during NREM sleep, specifically stage 2 sleep);
- *N3*: also known as slow-wave or deep sleep, characterized by delta waves (the slowest recorded brain waves in human beings; they are found most often in infants and young children, and are associated with the deepest levels of relaxation and restorative, healing sleep (Surawicz and Knilans 2008)) on EEG.

These stages are essential for physical recovery, immune function, and metabolic regulation.

REM sleep, on the other hand, is characterized by brain functioning very close to wakefulness. It is associated with dreaming, emotional regulation, and memory consolidation.

NREM and REM stages alternate in ~90-minute cycles throughout the night. Transitions between them are regulated by complex connections among brain regions like the thalamus, which controls sensory input and sleep stages, and the brainstem, which helps regulate transitions and autonomic functions like breathing and body temperature. Maintaining this cycle is essential for restorative sleep.

Neural Regulation of Sleep

Sleep is a complex process involving multiple brain systems working together. It is regulated by an interconnected network of brain regions, primarily the hypothalamus, brainstem, thalamus, and cerebral cortex (Schwartz and Kilduff 2015). These regions interact to manage both the timing and architecture of sleep, including its various stages.

The hypothalamus, a regulator of homeostasis, is especially important for aligning sleep with the body's circadian rhythms. Without it, many functions, like body temperature, hunger, hormone release, and sleep timing, would be dysregulated (Moore 2007). Within the hypothalamus, the suprachiasmatic nucleus (SCN) acts as the brain's clock. It aligns internal biological rhythms with external cues, known as zeitgebers, like light and temperature. The SCN receives input from specialized retinal ganglion cells, which allows the SCN to synchronize the sleep-wake cycle to the environment.

The brainstem, essential for basic survival, plays an important role in regulating basic physiological processes such as heart rate, breathing, and thermoregulation. It also helps initiate and maintain REM sleep by sending signals to the cerebral cortex and

influencing transitions between sleep stages (Wang et al. 2021).

The cerebral cortex, responsible for high-level functions like perception, decision-making, and memory, becomes largely deactivated during slow-wave sleep (SWS) (Mitra et al. 2016). This “rest mode” allows for restorative processes to occur. Molecular processes in the cortex during sleep play a crucial role in memory consolidation and learning, which makes deep sleep a very important stage for cognitive restoration(Langille 2019).

The thalamus acts as a relay center for sensory information. During sleep, thalamus filters incoming sensory signals - meaning it reduces the transmission of external stimuli to the cortex, helping a person stay asleep. It also generates sleep spindles, which are bursts of brain activity seen during non-REM sleep (NREM) (Fernandez and Lüthi 2020). They are crucial for memory consolidation.

Overall, sleep is controlled by an interconnected system of different brain regions. Because of this complexity, the regulation of sleep involves both circadian rhythms and the buildup of sleep pressure (homeostatic sleep need), which are further explored in the following sections.

Circadian Rhythms

Circadian rhythms are roughly 24-hour internal cycles that influence a wide range of physiological functions, such as hormone secretion, body temperature, and the sleep-wake cycle. CR helps prepare the body for sleep and wake and is regulated by an internal biological clock and external environmental cues.

A group of core clock genes, including *period* (PER), *cryptochrome* (CRY), *brain and muscle ARNT-like 1* (BMAL1), and *circadian locomotor output cycles kaput* (CLOCK), are responsible for the internal biological circadian rhythm (Takahashi 2017). These genes use transcriptional-translational feedback loops to create and control circadian rhythms. In this system, proteins produced by these genes regulate the timing of their own expression. For example, CLOCK and BMAL1 activate the transcription of PER and CRY, whose proteins eventually inhibit CLOCK/BMAL1 activity, creating a ~24-hour feedback cycle (Takahashi 2017). This molecular process happens in nearly every cell of the body, but is coordinated by the suprachiasmatic nucleus (SCN). The SCN has a natural rhythm that is slightly longer than 24 hours—about 24.2 hours—so it requires regular resetting by zeitgebers, especially light, to stay in sync with the external environment (Potter et al. 2016). This synchronization ensures that physiological processes, such as sleep and alertness, occur at biologically advantageous times of day.

Sleep disorders can result from circadian rhythm disruptions of these environmental cues, such as those caused by work shifts or exposure to artificial light at night. Sleep disorders have been associated with various health issues, including metabolic disorders and cardiovascular diseases.

Homeostatic Sleep Need

Homeostatic sleep need refers to the body's internal drive to sleep. It builds up the longer a person stays awake (Reichert et al. 2022). This process ensures that the body maintains a balance between time spent awake and time spent asleep. An important part of this process is the accumulation of adenosine, a neuromodulator that increases in the brain during wakefulness and promotes sleepiness by inhibiting arousal systems (Reichert et al. 2022). During sleep, adenosine levels decrease, which reduces sleep pressure. After sleep deprivation, the homeostatic system increases both the intensity and duration of slow-wave sleep to compensate. Disruptions to this system, such as through caffeine intake (which blocks adenosine receptors), irregular sleep schedules, or chronic sleep restriction, can worsen the body's ability to recover and affect attention, memory, and mood (Reichert et al. 2022).

Quality of Sleep

Quality sleep is defined based on several factors, including sleep duration, sleep continuity, and the subjective feeling of restfulness upon waking. High-quality sleep includes both objective physiological markers and subjective experiences (Table 1).

Subjectively, people describe quality sleep as waking up refreshed and alert. In research, this is often measured by cognitive performance tests, such as reaction time assessments and memory tasks (Di Muzio et al. 2020). Studies have shown that individuals who report high sleep quality tend to perform better on Psychomotor Vigilance Tasks (PVTs) (Matsangas and Shattuck 2020). PVTs are used in sleep research to assess attention and behavioral alertness. During these tests, participants are asked to respond as quickly as they can to a visual stimulus that appears on a screen at random intervals of time. The task allows researchers to detect variations in alertness and vigilance, particularly in the context of sleep deprivation or circadian rhythm disruptions (Basner et al. 2011). PVT performance is evaluated through metrics such as reaction time and false alarms. These indicators provide insight into the cognitive impairments associated with insufficient or poor-quality sleep. Studies have demonstrated that even a single night of sleep loss can result in measurable declines in PVT performance, including increased lapses (defined as a failure to react or any reaction exceeding 500 msec), making it a valuable tool in both laboratory and field settings (Basner and Dinges 2011).

Sleep quality is not only shaped by circadian and homeostatic systems but is also influenced by brain activity and environmental/lifestyle factors. Understanding what contributes to high-quality sleep allows researchers to better identify and address poor sleep conditions, whether due to physiological, behavioral, or external causes.

Table 1. Sleep-Related Terms and Definitions

Terms	Definitions
Sleep duration	Total time spent asleep during a sleep episode

Sleep continuity	Degree to which sleep is undisturbed by awakenings or transitions
Sleep latency	Time it takes to fall asleep after going to bed
Circadian alignment	Synchronization of sleep-wake cycle with internal biological rhythms
Subjective sleep quality	Self-reported satisfaction with restfulness, alertness, and sleep depth
Sleep efficiency	Ratio of time spent asleep to time spent in bed
Psychomotor vigilance	Performance on tasks measuring reaction time and sustained attention
Sleep spindles	Brief bursts of brain activity during NREM sleep associated with memory
Delta waves	Slow brain waves in deep sleep indicating restorative processes

Causes of Poor Sleep Quality

Now that we have outlined the components of high-quality sleep, the next question is: What prevents people from sleeping well? Poor sleep is a widespread issue, affecting nearly one-third of adults worldwide, according to global sleep health surveys (Scott et al. 2024). Disruptions in biological, psychological, behavioral, or environmental factors can interfere with the body's natural sleep-wake rhythm, reduce sleep efficiency, and impair the restorative functions of sleep (Okun 2011; Liu et al. 2021). By understanding these contributing factors more deeply, it becomes possible to identify effective strategies for improving sleep health and addressing chronic sleep difficulties.

This challenge is especially common among adolescents and shift workers, whose developmental stages or irregular schedules make it particularly difficult to maintain a stable circadian rhythm (Illingworth 2020).

Environmental Light Exposure

Environmental light exposure plays a major role in regulating sleep, largely through its effect on the circadian system. One of the most influential *zeitgebers*—a German term meaning "time-givers", or external cues that synchronize the internal body clock with the environment—is light. These cues help align the body's rhythms with the 24-hour day. For example, when a person travels across time zones, their internal clock adjusts gradually based on new light exposure and other zeitgebers, such as meal times and social activity (Roenneberg and Merrow 2016). Nowadays, almost everyone is exposed to blue light (the type of light given off by phones, tablets, and LED lamps). Blue light exposure specifically has been shown to decrease the release of melatonin, which is a hormone responsible for signaling the beginning of sleep (West et al. 2011). Blue light affects photosensitive retinal

ganglion cells (ipRGCs), which send signals to the SCN. When these cells are activated at night, melatonin secretion is delayed, causing a shift in the sleep-wake cycle and reducing sleep duration and quality (Ostrin et al. 2017). In addition to delaying the onset of sleep, prolonged exposure to artificial light in the evening may also decrease REM and slow-wave sleep (Münch et al. 2006), which are both critical for emotional control and cognitive recovery.

Diet

In addition to light exposure, dietary patterns significantly affect sleep quality. The brain requires nutrients such as magnesium, zinc, and vitamins B6 and D to synthesize neurotransmitters like serotonin and gamma-aminobutyric acid (GABA), both of which facilitate sleep onset (Gallagher et al. 2024). Furthermore, diets high in fiber and unsaturated fats tend to promote deeper and more restorative sleep, whereas diets high in sugar and saturated fats have been linked to lighter, more fragmented sleep (Frank et al. 2017). Certain foods like kiwis, cherries, and fish have been shown to promote sleep due to their omega-3 fatty acids (Patan et al. 2021), which are crucial in circadian regulation and serotonin synthesis. Meal timing is also crucial: eating large meals too close to bedtime can increase body temperature and gastrointestinal activity, potentially disrupting sleep. Irregular eating schedules (skipping breakfast or eating at inconsistent times), which many adolescents or shift workers often have, may disrupt the circadian rhythm, as feeding acts as a peripheral time cue for the body’s internal clocks.

Stress and Environment

Chronic stress and an individual's psychosocial environment also play an important role in the development of sleep disturbances. Physiologically, stress triggers the hypothalamic-pituitary-adrenal (HPA) axis, which raises cortisol secretion, delays the beginning of sleep, and reduces REM sleep (Mbiydzenyuy and Qulu 2024; Chu et al. 2025). When the home environment is a source of constant tension, whether due to strained family relationships or noise pollution, it can reinforce a state of increased sensory sensitivity. Studies have found a strong correlation between psychological safety and sleep health, with adolescents reporting higher levels of sleep disturbance when they experience more family-related conflicts (Kelly et al. 2024; Çiçek and Yıldırım 2025). The body's ability to initiate and maintain sleep can also be disrupted by environmental factors like uncomfortable room temperatures, artificial light from urban surroundings, and excessive noise (such as traffic or train tracks). These environmental cues affect sleep architecture by fragmenting sleep and increasing nighttime awakenings, thus lowering perceived sleep quality.

These environmental and psychological disruptions are especially relevant for shift workers, who often experience both chronic stress and irregular environments due to rotating schedules, bright nighttime exposure, and the difficulty of achieving restorative sleep during the day.

Behavioral habits

Behavioral habits around sleep, particularly one's pre-sleep routine, are central to

regulating circadian alignment and sleep efficiency. Sleep latency and quality are improved by regular sleep and wake times, which support the body's natural circadian rhythm (Murray et al. 2019). On the other hand, irregular schedules, which are frequently brought on by social or academic obligations, disrupt internal biological clocks and may cause a delayed sleep phase.

Physical activity

Physical activity also has an influence on sleep quality. Moderate exercise during the day has been shown to increase slow-wave sleep, reduce sleep latency, and lower nighttime awakenings (Kredlow et al. 2015; Park et al. 2021). This is explained by improvements in mood, decreased anxiety, and thermoregulation. However, high-intensity workouts done right before bed may raise core body temperature and adrenaline levels, delaying sleep onset (Alkhaldi et al., n.d.). Thus, through effects on the SCN, the timing, intensity, and consistency of physical activity influence the sleep-wake cycle.

Genetic factors

Lastly, genetic factors affect circadian rhythms and vulnerability to sleep disorders, thus affecting sleep quality. Numerous genes have been connected to the control of the circadian rhythm, including PERIOD1 (PER1), PERIOD2 (PER2), and CLOCK (Abel et al. 2015). These genes determine an individual's chronotype and responsiveness to light cues. Mutations in these circadian clock genes can lead to sleep disorders.

For example, mutations in the PER2 gene are commonly responsible for Familial Advanced Sleep Phase Syndrome (FASPS), in which individuals fall asleep and wake up much earlier than typical. Interestingly, people with FASPS generally do not feel tired or sleep-deprived, because their total sleep duration and architecture remain intact, they are just misaligned with the typical day-night schedule. Thus, the quality of their sleep is usually normal, even though their schedule is shifted. In contrast, those with Delayed Sleep Phase Disorder (DSPD) tend to fall asleep very late at night and wake up late in the morning (Sack et al. 2007). While they may also experience normal sleep architecture, many are forced to wake up early for school or work. This mismatch can lead to sleep deprivation, daytime fatigue, and impaired cognitive functioning, despite no problems with sleep quality itself. In both cases, the issue lies not in the sleep itself but in the misalignment between the person’s internal clock and external demands, which can indirectly reduce sleep quality and well-being.

Knowing the genetic foundation of sleep helps explain why some people may experience trouble sleeping even when they follow healthy routines.

Effects of Poor Sleep

Now that we have defined sleep and described the causes of poor sleep quality, we can evaluate the consequences that arise from low-quality sleep and discuss approaches to resolving these. Affecting nearly one-third of adults worldwide, poor sleep is increasingly

recognized as a global health crisis (Scott et al. 2024). In this section, we will explore the general consequences of insufficient or disturbed sleep, examine several specific sleep disorders, and evaluate the efficacy and limitations of current medical treatments.

General Consequences of Sleep Loss

Poor sleep quality impairs cognitive function on multiple levels. As described previously, studies using Psychomotor Vigilance Tasks (PVTs) have shown that sleep-deprived individuals demonstrate slowed reaction times and increased lapses in attention (Basner et al. 2018; Hansen et al. 2019). Executive functions such as working memory, planning, and decision-making also deteriorate after just one night of poor sleep (Killgore 2010). Over time, chronic sleep deprivation disrupts memory consolidation processes that occur during slow-wave and REM sleep, making it harder to retain new information (Walker 2009). In school or work, poor sleep can grow into difficulty learning new concepts, maintaining focus during tasks, or making accurate and timely decisions.

Behaviorally, poor sleep is linked to increased emotional reactivity, impulsivity, and poor behavioral regulation (Demichelis et al. 2023). Amygdala is a brain region involved in memory, emotion, and fear conditioning. Functional MRI studies have shown that sleep-deprived individuals exhibit heightened amygdala responses (Shao et al. 2014; Krause et al. 2017). These patients exhibited more emotional dysregulation. Sleep-deprived individuals also show weaker prefrontal regulation, contributing to emotional instability, which demonstrates the importance of sleep in stabilizing emotions (Yoo et al. 2007). This dysregulation can manifest as irritability, increased risk-taking, and even symptoms of anxiety and depression. On a social level, individuals experiencing poor sleep often report lower satisfaction in social relationships (Sell et al. 2023), which may stem from a reduced capacity for empathy and emotion regulation.

Sleep quality also has a direct impact on physiological health. Hormonal regulation is disrupted following sleep deprivation, particularly in cortisol, a stress hormone that, when chronically elevated, contributes to inflammation and cardiovascular risk (Pan et al. 2023). These hormonal changes are thought to result from activation of the HPA axis and circadian misalignment. Elevated cortisol during sleep deprivation promotes disruptions in hormones associated with appetite and stress. Ghrelin (a hormone that stimulates hunger) levels rise while leptin (a hormone that regulates energy) decreases, leading to increased hunger and poorer food choices (Spiegel et al. 2004; Taheri et al. 2004). Even athletic performance is affected - sleep-deprived individuals often show decreased physical endurance, slower reaction times, and poorer motor coordination (Gong et al. 2024).

Altogether, these cognitive, emotional, and physiological impairments demonstrate the importance of sleep for long-term physical health as well as mental health, social well-being, and academic/work satisfaction. As sleep disturbances accumulate, their effects become more widespread and more difficult to reverse.

Sleep Disorders and Treatments

While occasional poor sleep, whether due to stress, environmental noise, or other temporary factors, is a normal and reversible experience, some individuals face more persistent and severe sleep difficulties. In these cases, the problem often stems from an underlying clinical sleep disorder. Five common sleep disorders – obstructive sleep apnea (OSA), insomnia, narcolepsy (types 1 and 2), hypersomnolence disorder, and REM sleep behavior disorder – will be discussed in more detail in the section that follows. Each will be examined through their neurobiological mechanisms and treatments.

Obstructive Sleep Apnea (OSA)

OSA is caused by repeated collapse of the upper airway during sleep, causing a person to repeatedly wake up. It is frequently associated with anatomical abnormalities (enlarged tonsils, a recessed jaw, thick neck circumference), excess body weight, and decreased pharyngeal muscle tone (Peppard et al. 2000). These obstructions lead to hypoxia (low levels of oxygen in your body tissues), arousals, and fragmented sleep architecture (Schwartz et al. 2008). OSA affects approximately 1 billion people worldwide, with 49% of men and 23% of women between the ages of 30 and 70 having moderate to severe forms (Benjafield et al. 2019). Up to 70% of people with OSA are also obese (Wolk et al. 2003). Symptoms include loud snoring, gasping, excessive daytime sleepiness, morning headaches, and impaired memory. Sleep fragmentation causes a reduction in deep sleep (N3) and frequent transitions out of REM. According to studies, having severe OSA increases the risk of cardiovascular disease by 79% and stroke by more than 100% (Lin et al. 2012). Information further links OSA to a 58% increase in risk for heart failure (Shahar et al. 2001).

Treatments for OSA focus on mechanical and pharmacological approaches. The main treatment is CPAP (Continuous Positive Airway Pressure), which physically keeps the airway open during sleep. However, alternative pharmacological options are being explored for patients who cannot tolerate CPAP. These include drugs like acetazolamide and modafinil. An overview of these treatments, their mechanisms, and limitations is provided in Table 2.

Insomnia

Insomnia is a disorder characterized by persistent difficulty falling asleep, staying asleep, or waking up too early despite adequate sleep. It is frequently maintained by a state of hyperarousal that is both physiological (increased cortisol and sympathetic nervous system activity) and psychological (stress, anxiety, intrusive thoughts) (Riemann et al. 2010). It disrupts the normal sleep-wake cycle and alters the balance of sleep-promoting and arousal-promoting neurotransmitters. Chronic insomnia affects 10–15% of adults globally, and about half of those who have it also exhibit signs of anxiety or depression (Riemann et al. 2010). According to neuroendocrine studies, insomnia is linked to elevated cortisol levels throughout the 24-hour cycle and chronic HPA axis activation, indicating a state of sustained physiological arousal (Vgontzas et al. 2001). However, this remains debated: while some studies report consistently higher cortisol in people with insomnia, others suggest variability depending on insomnia subtype (Vgontzas et al. 2001; Buckley and Schatzberg 2005). More research is needed to clarify whether elevated cortisol is a cause of insomnia, a consequence

of it, or both.

There are several subtypes of insomnia, which can differ based on their timing, duration, and underlying causes. Difficulty falling asleep in the morning is known as sleep-onset insomnia, whereas sleep-maintenance involves frequent awakenings or trouble staying asleep. When someone wakes up too early and is unable to fall back asleep, it is known as early-morning awakening insomnia. Another way to categorize insomnia is as acute (lasting days to weeks, typically brought on by stress or life events) or chronic (lasting at least three months, frequently associated with physiological or psychological hyperarousal).

Because insomnia affects multiple brain systems, medications to treat insomnia target various pathways: some suppress arousal signals (e.g. the orexin system), while others aim to restore circadian rhythm (e.g. melatonin agonists). An overview of the medications used to treat insomnia and other sleep disorders is summarized in the table below (Table 2).

Narcolepsy

Narcolepsy is a neurological disorder caused by autoimmune destruction of hypocretin-producing neurons in the lateral hypothalamus (Mahlios et al. 2013). Arousal stability, REM sleep, and wakefulness are all regulated by hypocretin (also called orexin). It affects 1 in 2,000 people globally (Scammell 2015). According to the National Institute of Neurological Disorders and Stroke, narcoleptics enter REM sleep almost immediately after falling asleep, disrupting the natural sleep cycle. Consistent findings across multiple studies confirm that over 95% of narcolepsy Type 1 cases involve severe hypocretin deficiency, which supports the autoimmune hypothesis (Mahoney et al. 2019). Type 1 narcolepsy is defined by the presence of cataplexy. Cataplexy is muscular weakness which can range from a barely perceptible slackening of the facial muscles to complete muscle paralysis with postural collapse (Mirabile and Sharma 2025). Type 1 narcolepsy is associated with extremely low hypocretin levels in the cerebrospinal fluid (approximately 90% of patients with cataplexy have undetectable hypocretin in cerebrospinal fluid (Singh et al. 2013). Type 2 narcolepsy is characterized by excessive daytime sleepiness and disturbed night-time sleep. Individuals may experience symptoms such as sleep paralysis or hypnagogic hallucinations, but without the sudden muscle weakness that defines cataplexy.

Narcolepsy treatments are drugs that target different aspects of the disorder, such as excessive daytime sleepiness and cataplexy. Sodium oxybate is considered highly effective. Pitolisant promotes wakefulness but is often limited by side effects. These therapies are outlined in Table 2.

Hypersomnolence Disorder

Prolonged sleep at night and trouble waking up are both indicators for idiopathic hypersomnia, a disorder causing excess sleep. Although the precise mechanism is unknown, hypotheses include dysregulation of the central nervous system, low arousal signaling, or irregular circadian input (Trotti 2017). Onset of idiopathic hypersomnia typically is in adolescence or early adulthood (Psychiatrist.Com, n.d.). Patients report

persistent daytime sleepiness that is not relieved by naps, sleep inertia (feeling "drunk" upon waking), and sleeping more than 9 to 10 hours every night (Thorpy et al. 2024). Some studies suggest altered GABAA signaling in the thalamus and cortex as a possible mechanism (Rye et al. 2012). An overview of the medications used to treat hypersomnolence disorder and other sleep disorders is summarized in the table below (Table 2).

REM Sleep Behavior Disorder (RBD)

People with RBD physically enact their dreams, sometimes violently, because the muscle atonia that typically accompanies REM sleep is disrupted. It's considered a prodromal (an early stage of a disease when symptoms first appear, but before full diagnosis is possible) symptom of neurodegenerative disorders. Longitudinal research shows that up to 80% of people with idiopathic RBD go on to develop other conditions like Parkinson's disease or Lewy Body dementia (Iranzo et al. 2006; 2009; Postuma et al. 2012). Symptoms include vocalizations, limb movements, or falling out of bed during REM sleep. Patients often remember vivid, action-filled dreams. The REM atonia circuitry in the pons and medulla is disrupted, although the exact pathological trigger is still unknown.

Treatment for RBD aims to reduce abnormal motor activity during REM sleep. The most commonly prescribed drug is clonazepam, which is effective in suppressing muscle activity. Melatonin is a safer alternative, especially for older adults, with milder side effects. An overview of these treatments and their limitations is presented in Table 2.

Table 2. Treatments for Sleep Disorders: Mechanisms and Drawbacks

Sleep Disorder	Medication	Mechanism	Downside
Insomnia	Benzodiazepines (e.g. temazepam) and Z-drugs (e.g. zolpidem)	Enhance GABA activity, promote sedation	Dependence risk, REM suppression
	Orexin receptor antagonists (e.g. suvorexant)	Block wakefulness-promoting signaling; preserve sleep architecture more effectively	May cause next-day drowsiness
	Melatonin receptor agonists (e.g. ramelteon)	Used for circadian-related insomnia; low abuse potential	Less effective in severe cases; mild effects

Obstructive Sleep Apnea (OSA)	First-line treatment: CPAP (Continuous Positive Airway Pressure)	Keeps the airway open mechanically	May be uncomfortable for some
	Acetazolamide	Stabilizes breathing via CO_2 sensitivity in specific OSA cases	Not widely used; limited scope
Narcolepsy	Modafinil	Inhibits dopamine reuptake, increases wakefulness and alertness	Headaches, anxiety, variable effectiveness
	Sodium oxybate	Deepens slow-wave sleep, treats cataplexy and daytime sleepiness	Strict control due to abuse potential
	Pitolisant	Histamine H3 antagonist, enhances wakefulness	Headache, limited access
Hypersomnolence Disorder	Solriamfetol and pitolisant	Increase dopamine/norepinephrine to reduce sleepiness	Hypertension risk, limited data
REM Sleep Behavior Disorder (RBD)	Clonazepam	Reduces motor activity in REM	Drowsiness, dependence, cognitive dulling
	Melatonin	Reduces REM activity, safer in elderly	Milder effects than clonazepam

Discussion

The paper has outlined the biological mechanisms, influences, and consequences of poor sleep. While many aspects of sleep are well established, several open questions

remain. Firstly, although experts typically recommend adults to sleep 7–9 hours per night, sleep need is not universal. Genetic research suggests that some individuals may naturally require less sleep without noticeable cognitive deficits (Chen et al. 2025). However, this remains debated – do the "short sleepers" genuinely need less sleep, or do they simply compensate more efficiently? Understanding these individual differences could help change the sleep guidelines and help individuals understand their own needs better in the future.

Sleep quality is important, as discussed in this review. Being able to identify low sleep quality prior to the negative effects on behavior could open therapeutic opportunities for better sleep treatment. However, there are currently no standard physiological markers of sleep quality. A promising one is the sleep spindle, a burst of brain activity during NREM stage 2 sleep. While spindles are associated with memory consolidation, their exact function and individual variability remain unclear. Further research on spindle characteristics, such as frequency or cortical location, could reveal more about how they support sleep-dependent cognitive functions and whether they can serve as biomarkers of sleep quality.

A major gap in the sleep field is understanding how certain symptoms of sleep disorders are connected to sleep loss. For example, how do specific sleep disorders contribute to cardiovascular diseases? Is the impact on heart health simply because sleep deprivation can increase obesity or is more prevalent with age? Or does it directly impact heart health? Similar questions could be asked about diet. Further questions include: Is elevated cortisol a key component of insomnia, or does it differ across subtypes? How does hypocretin loss produce the diverse symptoms of narcolepsy? What biological mechanisms explain the excessive sleepiness?

For example, OSA leads to sleep fragmentation, reduced deep sleep, and oxygen deprivation, all of which significantly raise the risk of heart disease and stroke. Understanding how different sleep disorders influence cardiovascular diseases is an interesting topic for interdisciplinary research. As another example, chronic insomnia is associated with elevated cortisol levels. However, research is divided on whether elevated cortisol is a consistent feature or if it varies by insomnia subtype. Regardless, elevation of this chronic stress hormone has potential implications for cardiovascular health. Additionally, narcolepsy symptoms such as hallucinations and sleep paralysis may be linked to hypocretin loss, but exactly how this single neuropeptide system leads to such a broad range of symptoms remains unclear. Similarly, in hypersomnolence disorder, the core mechanism is still unknown – proposed explanations include low arousal signaling or CNS dysregulation, but current findings are not conclusive.

The role of diet in shaping sleep quality is also not well-understood. For example, eating large meals before bed has been shown to delay sleep by raising body temperature and activating digestion. Yet, heavy meals can also induce sleepiness, likely due to blood being redirected from the brain to the digestive tract. This contradiction raises questions about the balance between physiological arousal and subjective sleepiness after eating, which future research should address.

While a range of pharmacological treatments exists for various sleep disorders,

many of these medications focus on the symptoms rather than the underlying causes. For instance, stimulant medications used in narcolepsy, such as modafinil or pitolisant, aim to promote wakefulness without targeting the autoimmune destruction of hypocretin-producing neurons that drives the disorder. Similarly, treatments for idiopathic hypersomnia and other forms of excessive daytime sleepiness focus on increasing alertness but do not resolve the core dysregulations in sleep-wake mechanisms. This means that current understanding of the neurobiological processes that regulate sleep disorders remains limited. As a result, there is a significant gap between symptom management and curative therapy.

Finally, RBD is one of the most clinically significant yet biologically puzzling conditions. While up to 80% of individuals with RBD go on to develop Parkinson's or related neurodegenerative diseases, researchers still don't clearly understand the cause of this relationship. The REM atonia system in the pons and medulla is clearly disrupted, but the precise pathological trigger remains unknown. As such, RBD represents both a potential early warning sign and a critical opportunity for future research into neurodegenerative progression.

Conclusion

As this paper has shown, sleep plays a crucial role in one's health. Sleep is shaped by neural systems, biological rhythms, and external signals, all working together to maintain health and cognitive function. In our society, a wide range of influences, from artificial light to stress, interfere with the body's natural sleep regulation, leading to widespread disruptions. When sleep quality declines, the effects extend across nearly every system in the body, impairing memory, emotional regulation, and metabolic stability. These impairments become especially serious when they develop into clinical sleep disorders. Understanding the science behind both healthy and disrupted sleep offers a critical foundation for treatment, prevention and education.

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