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Student Health Sciences Research Journal

Hi! Welcome to the Spring 2025 issue of the INSPIRE Student Health Sciences Research Journal.

This issue has been written and peer-reviewed by students throughout 2024/2025, with the editorial board being made up of students from the universities of Bristol, Cardiff, Exeter and Plymouth, the journal's founding institutes. The journal was created as part of the INSPIRE scheme, which aims to provide students in medical dental and veterinary schools across the UK with the opportunity to participate in research and encourage them to incorporate it into their future careers.

This is a bonus issue on top of Autumn 2024 and Winter 2024/2025 thanks to the wealth of outstanding submissions we received over the last year. We hope you enjoy reading it. See all our past issues at **www.inspirestudentjournal.co.uk**. Find out more news, events, case studies and opportunities related to the INSPIRE programme at **gw4inspire.co.uk**.

Submissions for our Autumn 2025 issue are open until the end of June 2025. We are interested in research papers, features, reviews, reports, opinion, poetry and art – find out how to submit on our website. If you would like to be a peer reviewer, please email us with your course details and areas of expertise.

Best wishes,

INSPIRE Student Health Sciences Research Journal Senior Editors

Front Cover

Cover image by **Sauvit S Patil**, MSc Molecular Neuroscience, University of Bristol

"A man stares directly at the viewer. His gaze is filled with calm contemplation, as if stuck in the middle of a drowning thought. Behind him, a skeletal figure broods, personifying brain itself and playing a violin with its bony fingers while whispering a tune into the man's ear. This skeletal figure represents the neural processing involved in action initiation. This contemporary expressionist style digital illustration is inspired by Death Playing the Fiddle, a self-portrait by Arnold Böcklin (1872) [in public domain].

"Neuroscience, in its bloom, has uncovered the mechanisms that shape decisions long before they reach conscious awareness. The piece evokes the question: if the will itself is determined, who holds responsibility for the actions it drives? echoing Schopenhauer's insight—'you will to do, but not will to will' As brain researcher John-Dylan Haynes also asks, 'How can I call a will 'mine' if I don't even know when it occurred and what it has decided to do?'"

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At the mercy of two crises: displacement and the surge of zoonoses in refugee camps

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Abstract

Our world faces the worst refugee crisis in modern history.[1,2] Such statements are often repeated but seldom fully understood. This piece aims to explore the global refugee crisis through the lens of literature examining its connection with zoonotic diseases. It will also address future strategies, their limitations and the role of the One Health approach. By analysing research and journals, this work seeks to evaluate solutions to zoonoses while safeguarding vulnerable populations and addressing the complexities of implementation.

Abbreviations

HCV – hepatitis C virus
IVM – Integrated Vector Management
MSF – Médecins Sans Frontières
SWOT – Safe Water Optimization Tool
UNHCR – United Nations High Commissioner for Refugees
UNICEF – United Nations Children's Fund
WHO – World Health Organization
ZD – zoonotic disease

Introduction

Zoonotic disease and the refugee crisis

IIn 2022, 108.4 million people were forcibly displaced due to persecution, violence and human violations.[1,2] While statistics can capture the lives lost, they fail to convey the full extent of the additional issues faced by the refugee population. One often overlooked consequence is the burden of zoonotic diseases. These diseases frequently go unaddressed, highlighting the pressing need for this evaluation to explore potential solutions and mitigate their impact.

This discussion begins by examining existing literature on the transmission mechanisms of zoonoses, followed by an exploration of how these mechanisms intersect with refugee populations, particularly in relation to their living conditions. By exploring different demographics, it will assess the real-life impacts of zoonoses on displaced populations and vice versa. Finally, it will evaluate potential future strategies for addressing zoonotic disease risks, emphasising the critical role of the One Health approach in tackling these challenges and its importance in contemporary medicine, particularly for refugee populations.

Methodology

This study uses a narrative approach, synthesising findings from sources on zoonotic disease (ZD) and their impact on refugee health. While much research exists on ZD, there is limited focus on refugee populations, making this an important area to explore. Populations and sources were selected for their relevance to the global refugee crisis, availability of data and geographical diversity. The populations discussed include both recently displaced and longer-settled groups, offering a varied context for understanding ZD's impact.

Disease transmission

Zoonoses can spread through direct contact, contaminated food/water, insect bites, inhalation and environmental exposure.[3] Pathogens are often transmitted from animals to humans, with

60% of emerging infections zoonotic, 70% of which from wildlife.[3,4] Population growth and environmental exploitation have increased the likelihood of such spill-over events.[5] The underestimation of zoonotic disease has also contributed to their persistence, as unrecognised cases go unaddressed.[6,7]

ZDs are infections transmissible between animals and humans (over 200 known types), posing public health challenges worldwide. The close relationship between humans and animals, whether in agriculture, as companions, or in shared environments, creates transmission pathways. Symptoms vary depending on the specific illness but commonly include fever, fatigue and body aches. Understanding zoonotic transmission and the conditions that facilitate their spread is crucial in addressing this global health issue.[8,9]

Discussion

Exploration of refugee demographics implicated by zoonotic disease

Refugees are individuals displaced from their country due to persecution, violence or other factors requiring international protection.[10]

With 10.8+ million people internally displaced and a struggling economy, Sudan faces severe hardship. There is a critical shortage of healthcare workers, with only four doctors for every 10,000 people. The healthcare system has now nearly collapsed, leaving the Sudanese people vulnerable to preventable diseases, inadequate medical care and deteriorating health outcomes. Limited access to healthcare, coupled with insufficient aid, heightens their exposure to ZDs as gaps in prevention and treatment fosters conditions that facilitate the spread of these diseases.[11]

With over 140 million livestock in 2009 alone, Sudan has been said to be facing threats on two fronts: both from endemic and transboundary animal disease. These threats harm animal health and livelihoods whilst increasing human ZD risk through close animal contact. The displacement and mixing of animals and humans contribute significantly to ZD transmission[12] with conditions such as yellow fever and Crimean–Congo haemorrhagic fever having a particularly great impact.[13]

The destruction of key laboratories/equipment of Sudan's veterinary serves could also be a critical factor in the increased spread of ZD.[12] The violence has had a ripple effect on veterinary services. Veterinary services have been severely disrupted, with the movement and access of personnel and resources left in ruins – making disease control far more challenging. Coupled with poor sanitation, studies show that ZD from rabies to tuberculosis spread more readily during times of conflict.[11] This emphasises the importance of adopting a multisectoral approach, reinforcing the critical role of the One Health framework, promoting collaboration between human, animal and environmental health sectors to effectively manage ZD.

The challenges faced by Sudan are similarly reflected in Syria. Even after a change in leadership, Syria faces a massive task of rebuilding, with the destruction of infrastructure, including hospitals and veterinary services, severely disrupting disease control measures.[17,18]

As of June 2024, Syria remained at the heart of the world's largest displacement crisis, with 13.8 million people forcibly displaced.[14] Civilians face immense hardship, worsened by the February 2023 earthquake affecting Türkiye and Syria.[15] Between March 2011 to March 2020, 595 attacks targeted 350 medical facilities, 90% by the government and allied forces.[16] These attacks devastate medical infrastructure, leaving illnesses untreated and worsening malnutrition in already vulnerable communities. By 2015, 25% of Aleppo's 1.2 million residents remained, with approximately 95% of its doctors displaced or killed.[17] Despite the challenges, Aleppo stands as a testament to the courage of its healthcare workers, who continued providing care despite constant danger and resource shortages. In violation of international humanitarian law,[17] hospitals and medical personnel were deliberately targeted, highlighting the need for stronger enforcement of humanitarian protections and a revaluation of strategies aimed at safeguarding healthcare workers and facilities in conflict zones.

Syrians have endured some of the worst atrocities of this century, marked with immense hardship with 23 million+ internally displaced and refugees across Syria and neighbouring countries requiring aid.[18] Many livelihoods in this region rely on agriculture, facilitating trade between refugees and host countries. However, ownership and registration restrictions for non-Jordanians create institutional and political barriers to health and veterinary services, compounding the risk of ZD outbreaks.[19] Both of these reasons act as reminders of how legislation can both mitigate or exacerbate health risks. In this context, policies on livestock ownership and trade may not only hinder economic stability but also could undermine efforts to control ZD.

Moreover, the collapse of veterinary services may lead to the re-emergence of brucellosis in cattle and sheep,[18] while rising rabies circulation in animals in Syria increases the risk of human transmission.[19] Hence part of this reconstruction management of infectious disease is paramount across all stages of life, from prenatal care to geriatrics, in order to provide comprehensive health coverage and reduce long-term public health risks.

Syria's long-standing conflict and Myanmar's recent circumstance presents contrast as while Syria's crisis highlights the protracted effects of war on public health, Myanmar's more recent upheaval shows how swiftly healthcare services can deteriorate.[17,20]

From February 2021–24, Myanmar saw 75,000 homes destroyed and 4600 civilians and activists killed. Since 2021, Myanmar has endured 1257+ attacks on health infrastructure with 104 healthcare workers being killed.[20] This huge impact on the healthcare system severely hinders healthcare capacity and medical care for many, potentially obstructing future efforts to improve public health.[20]

In 1982, the Rohingya were stripped of their citizenship,[21] with Rohingya children continuing to be excluded from immunisation campaigns, heightening their vulnerability to zoonoses such as rabies and leptospirosis. This exclusion creates pathogen reservoirs, aiding their spread in displaced and host communities. Fearing deportation, many refugees avoid seeking help. As of December 2023, 971,904 Rohingya refugees were issued identification through the Bangladesh government and the United Nations High Commissioner for Refugees (UNHCR), with 52% being children.[22] This complicates disease surveillance, as children are less likely to report symptoms, requiring additional resources for detection and management.[22] An estimated 40% of children in camps suffer from diarrheal diseases, with significant gaps in antenatal and postnatal care.[23] These challenges underline the importance of prioritising antenatal and postnatal care and highlight the difficulty of conducting disease surveillance in refugee camps.

In Cox's Bazar, 20% of Rohingya adults have active HCV (hepatitis C) infections, reflecting inadequate healthcare.[24] This worsens vulnerability to zoonoses, as poor sanitation, overcrowding and weakened immune systems increase disease risks. Rohingya areas have shown high rates of tuberculosis and brucellosis, and in 2009 Bangladesh reported 2000 rabies deaths, the highest per capita rate globally.[25] The death toll among animals likely exceeds human cases, emphasising the need for better animal vaccination programmes[25] with Bangladesh aiming for zero dog-mediated rabies deaths by 2030.[26] Additionally, cases of dengue rise during the monsoon season, and poor slaughterhouse inspections increase foodborne illness risks.[25] This dangerous combination threatens to turn the region into a disease outbreak epicentre.[27] These factors increase the likelihood of ZD but also hinders containment efforts.

Similar challenges are evident in Gaza, where restricted access to medical care heightens the risk of zoonotic disease outbreaks.[29] The destruction of healthcare infrastructure, overcrowding in shelters, and limited access to clean water and sanitation create conditions that facilitate disease spread. By 29 February 2024, the UN estimated 35% of Gaza's buildings had been destroyed, with thousands of lives lost beneath the rubble,[28] representing both a profound human tragedy and a further strain on healthcare and disease surveillance. On 26 January, 2024, the International Court of Justice ruled that Israel must allow humanitarian aid into Gaza, emphasising the urgent need for medical and public health interventions.[27] Researchers estimate the death toll could reach 186,000 (8% of the population), highlighting the severe humanitarian crisis and the long-term impact on public health.[28] Coupled with the destruction of critical infrastructure, the risk of ZD transmission worsens as the breakdown of sanitation, healthcare, and disease control measures leaves populations more vulnerable. In the face of such human rights violations, there is a moral imperative to protect civilians, humanitarians, and health workers from military harm.[29] The #NotATarget campaign seeks to ensure their safety by emphasising the need for their protection in conflict zones.[30] This conveys how even when situated away from areas of active violence, raising awareness for the protection of healthcare workers and facilities may help combat ZD indirectly.

Following a confirmed case of paralytic polio in a child in Gaza, a vaccination campaign for children under 10 began on 16 September 2024.[31] However, low vaccination rates continue to fuel concerns about the resurgence of preventable diseases like measles.[31] Similarly, in Palestine, brucellosis remains a public health concern, with the Palestinian Brucellosis Control Program working to reduce its prevalence through animal vaccination.[32] These efforts highlight the crucial role of immunisation in controlling both human and zoonotic diseases. Meanwhile, in neighbouring Jordan, long a refuge for displaced populations from Palestine and Iraq, limited resources, water shortages, and underdevelopment pose further challenges to disease control.[33] Strengthening public health infrastructure and ZD prevention in both Palestine and Jordan could help mitigate health risks, reduce strain on vulnerable communities, and promote broader stability in the region.[33]

Limitations

A major limitation in ZD research for refugees is the lack of studies linking these diseases to displacement-related challenges. While ZDs are well-studied, little is known about their spread in refugee settings. Factors like overcrowding and limited healthcare is often overlooked, hindering tailored interventions. Additionally, challenges in data collection, lack of formal documentation, and destroyed healthcare infrastructure complicates accurate disease monitoring. Political barriers and fear of persecution also discourages refugees from seeking care, leaving ZD transmission unreported. Focused studies and improved surveillance can help address these gaps and reduce ZD risks.

Future steps

This section explores future steps that can be taken to enhance disease prevention and improve health outcomes in these communities.

Vector control

Vector-borne diseases cause 17% of the global burden of infectious diseases, with increased movement of people and livestock raising the risk of transmission.[34] Integrated Vector Management (IVM), using methods like insecticidal nets, larvicides and environmental management, can combat diseases like malaria and dengue.[35] Challenges include resource delivery and funding however if it is rolled out the promise is great. E.g. from 2001–2015, insecticide-treated bed nets and indoor spraying prevented an estimated 663 million malaria cases in sub-Saharan Africa[36] Maintaining political commitment is essential for prioritising vector control.[35,36] Insecticide-treated nets have notably reduced Plasmodium falciparum incidence (RR 0·55 [95% CI 0·37–0·79]; high certainty), reinforcing WHO's recommendation for their use in humanitarian crises.[37]

Vaccinations

Since 1974, vaccinations have prevented over 154 million deaths, showcasing their efficacy.[38] Vaccines reduce individual risk and community transmission.[38] Various vaccines, such as inactivated pathogen, subunit and live attenuated vaccines, are used or in development, each requiring selective application.[39] UNHCR–UNICEF (United Nations Children's Fund) guidelines stress equal vaccine access regardless of legal status for refugees, however, engagement remains low due to barriers like fear, language, finances and discrimination.[40]

In low- and middle-income countries and humanitarian settings, vaccine availability can be scarce. A 2019 study across 16 countries found conflict, damaged infrastructure and resource shortages have caused low coverage and outbreaks.[40] In Syria, prolonged disruption since 2014 have left many children under 5 under-immunised, leaving potential long-term ramifications for future generations.[40,41,42]

Clean water

Contaminated water spreads diseases like cholera and typhoid, causing 505,000 deaths annually from diarrhoeal diseases.[43] Fleeing refugees often lack access to clean water and sanitation, exposing them to these diseases.[44] Water, sanitation and hygiene services are essential to safeguarding health. UNHCR provides these during emergencies to protect dignity, prevent disease and reduce gender-based violence.[45] This places the onus on aid agencies to manage trauma, disease and the rebuild. Safe water, waste disposal and clean food have become vital components of said rebuild. Tools like Safe Water Optimization Tool (SWOT) (a low-bandwidth web platform) used in Cox's Bazar is an example whereby screening has improved the quality of water safety compared to standard chlorination guidelines, reducing the public health risks.[46]

One Health

The One Health approach emphasises the interconnectedness of human, animal and environmental health.[47] By integrating expertise from the veterinary, medical and environmental sectors, it strengthens disease surveillance, prevention and response efforts.[47] Successful examples such as rabies vaccinations have significantly reduced human fatalities.[48] Zoonoses emerge faster due to globalisation and population movement, with unhealthy practices and limited healthcare access contributing to epidemics.[49] Anthropogenic changes increasingly drive animal pathogens into human populations. While efforts focus on detecting and containing emerging diseases, prevention to reduce pathogen spillover risk are often disregarded.[50] Around 60% of emerging infectious diseases and the major pandemics, originate from zoonotic spillover, primarily from wildlife reservoirs.[51] Thus, to prevent future pandemics these factors need to be addressed upstream.

The G7 Carbis Bay Health Declaration acknowledged the upstream drivers of ZD but lacked clear prevention strategies or funding plans.50 Prevention protects vulnerable populations, while detection often shields more privileged groups. Jordan's use of the "One Health zoonotic disease prioritisation" tool demonstrated the value of a One Health approach by prioritising rabies, brucellosis and zoonotic tuberculosis, enabling targeted mitigation efforts such as animal vaccination and public awareness campaigns to reduce rabies transmission.[52,53]

Conclusion

Refugees are a vulnerable community within our society, often

overlooked and bearing the brunt of systemic crises. This article has explored the impact of zoonotic diseases on refugee populations, highlighted some challenges faced, and observed preventative measures to better protect them. It underlines the importance of targeted research and a One Health approach in addressing these issues. As future doctors, it is not just our medical knowledge, but our ability to respond to such challenges that will define our practice.

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News and Opinion

A review and critique of the Bristol Medical School long case as a clinical assessment tool with suggested modifi ations

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Abstract

Introduction The Bristol long case is a high stakes clinical assessment which medical students must pass to move into their final year. It is crucial that we constantly review our assessment methods to increase their validity and reliability.

Methods I will review classical and contemporary validity concepts and reliability definitions. I will review and critique the evidence for and against each inference in relation to the Bristol long case, before suggesting modifications to strengthen aspects of the generalisation and scoring inferences.

Conclusion Patient standardisation will reduce content specificity and strengthen the generalisation inference. However, this would drastically reduce authenticity, a unique long case feature. Therefore, to maintain authenticity, we will instead increase the number of long cases. We will increase assessor numbers to two per long case which will allow for collection of statistical data on interrater reliability and reduce the effect of singular assessor bias.

Abbreviations

CTF – Clinical Teaching Fellow
DOCEE – Direct Observation Clinical Encounter Exam
MCQ – multiple choice questions
OSCE – Objective Structured Clinical Examination
PACES – Practical Assessment of Clinical Examination Skills

Introduction

The Bristol long case is a high stakes clinical assessment which medical students must pass to move into their final year. The long case assesses student's history taking, examination, presentation and formulation of appropriate management plans.[1] Long cases are used as critical assessments across UK medical schools, despite ongoing concerns about its validity and reliability.[2,3] There is an argument that the long case examination in undergraduate medical education is now obsolete with the dawn of the standardised OSCE-style examinations in controlled environments.[4] Whilst there has been a drive to bring assessment back to the bedside,[5] a lack of up-to-date evidence surrounding long case validity reflects this push towards OSCE style assessment.

However, I argue that including real life patient-facing assessments early on in a student's medical career is crucial to their future success, particularly, as many postgraduate medical specialty programmes continue to use patient-facing assessments as a marker for competence. Such as PACES for the Royal College of Physicians in the UK, which is internationally recognised for its validity as a method and reliability of outcomes when assessing physician competence.[6] Looking further afield, the use of "hot cases" in intensive care medicine training in New Zealand, has been rigorously reviewed through the lens of validity frameworks, and continues to be used as a highly reliable assessment of competence.[7] Both types of assessments remain relevant and competitive within postgraduate education as they undergo rigorous and cyclical evaluations to improve validity

and reliability. The aim of this work is to thoroughly evaluate the Bristol long case and suggest modifications to ensure it is still fit for purpose within undergraduate medical education.

I will review classical and contemporary validity concepts and reliability definitions before providing an evidence-based argument for the use of Messick's unified approach[8] to validity. Using Kane's Interpretation/Use argument,[9] I will critique the evidence for and against each inference in relation to the Bristol long case before suggesting modifications to strengthen aspects of the generalisation and scoring inferences. I will evaluate the use of unstandardised patients in terms of reliability and authenticity before discussing the number of long cases needed for a strong generalisation inference and therefore valid results. I will critically appraise modifications to strengthen scoring inference via increasing examiner number, minimising examiner differences and training.

Defining alidity and reliability

Validity and reliability define the worth of a test.[10] As definitions of validity are continually evolving[11] we must state the definitions/theories that we will use for effective assessment of the Bristol long case. Classical theory includes criterion, content and construct validity.[12] Criterion validity is the correlation of test results to an independent criterion of the assessed behaviour.[10,13-15] Content validity is the extent to which the test content represents the construct being assessed.[16,17] However, content validity does not focus on evidence to sustain inferences and criterion validity is not generalisable.[8] Furthermore, both focus on the validity of the test[12,18] rather than on the score interpretation.[19] Cronbach and Meehl20 suggested the concept of construct validity to fill the gap for measurement of behavioural traits (intelligence/attitude) which cannot be measured directly.[12,19]

Contemporary views suggest that construct validity is the whole of validity[8,21] unifying content and criterion within it.[12] Critics of contemporary validity state there is nothing to unify[22] and that a multifaceted approach is too segmented.[23] However, we will use a contemporary approach as Downing[24] argues that validity in medical education should be a multi-faceted unitary concept based on evidence to support or refute interpretations assigned to assessment results. Kane[9,25] suggests that Messick's unified model[8] is comprehensive but leaves an instructional gap. Kane's argument-based approach[9] addresses issues of prioritisation in Messick' work[8] by retaining the generality of the unified concept whilst bringing in a practical framework for assessment.[26-28] Its versatility allows application to a range of assessments, including competency-based assessment.[28] For these reasons, we will use an argument-based approach[9,29] to assess the validity and reliability of the Bristol long case.

Reliability is a key aspect of assessment validity.[30] As Schmidt et al[31] argues that reliability equates to consistency of measurement, we will define reliability as the reproducibility of long case scores[32] and interrater reliability as the degree to which scores are the same when obtained by different assessors.[33] Downing[34] highlights that these definitions align with the unified model,[19] in which reliability is a quality of the assessment outcome rather than the assessment itself.

Argument-based approach

We lay out the Interpretation/Use Argument for the Bristol long case score below.[9]

A student who passes the long case is deemed to have sufficient competency in history taking, examination, diagnostic reasoning and management.

In **Appendix 1**, Interpretation/Use Argument plausibility was evaluated through stating assumptions for each of Kane's four inferences[9] in respect to the Bristol long case and then highlighting evidence to support/refute these.[28] **Appendix 1** highlights the robust evidence found for the authenticity and high face validity of the long case due to its assessment of real-life patients.[3,35,36] The long case structure provides effective feedback allowing for educational progression.[3,37] Norcini[38] and Van der Vleuten[35] highlight issues with long case reliability (and therefore, validity) which include case specificity and interrater variability. Norcini's[38] third concern regarding variability of skills assessed, is less relevant for the Bristol long case as it uses a standardised mark scheme.[39] Focusing on the weakest assumptions/inferences[9,28] with the least evidenced to back them up,[27] suggested modifications will aim to strengthen the generalisation and scoring inference.

Generalisation inference

Hamdy et al[40] state that generalisability is a key component of an assessment's reliability, especially in observational assessments.[30] Kane's generalisation inference[9] deals with test-universe performance: theoretically, does the chosen patient represent all possible patients within the assessment universe?[28] The answer for this assessment is: no, as long cases use unstandardised patients which can never be equivalent across a cohort.[41] Concern for inter-case variability has been highlighted by medical students.[36] When the Bristol long case uses an unstandardised patient, it underrepresents the main target domains (construct) of the assessment.[29] Outcomes have therefore been described as "luck of the draw"[35](p 704) or content specific[42] and a key contributor to the long case's lack of reliability which affects its validity as an assessment tool.

Should we standardise patients? The effort of patient standardisation leads to relatively small gains in reliability[41] but drastically reduces test authenticity[29,35,43] as standardised patients cannot depict the range/complexity of medical problems to be assessed.[44] We will not standardise patients in the Bristol long case as it is the long case's real-life patient encounters[43] that strengthens its face validity[28,45] and separates it from other clinical assessment tools.[35,36]

The long cases' main issue is its attempts to generalise student ability across a wide range of clinical presentations with a singular patient encounter.[46,47] Firstly, Swanson et al[48] conclude that doctors do not perform tasks consistently. Secondly, estimates of the test-universe score from the observed score is poor when the conditions of observation (patient, context, complexity) vary greatly between assessments.[9] Performance in one long case does not predict the same performance in another,[44] therefore a single long case cannot distinguish between inadequate and adequate performance.[45] Wass et al[49] consider >0.8 as an acceptable reliability coefficient for medical assessments (similar to OSCE or MCQ). Meskauskas[50] concluded that one long case produces a reliability coefficient of 0.24 (24% of differences due to variability is students' aptitude and 76% due to measurement errors). Similarly, Wass and Jolly[47] concluded that a single long case gives a reliability coefficient of 0.3. To compensate for content specificity,[42] Norcini[44] asserts that assessments must have a broad sample of patients to allow for generalisation of performance scores, especially when used as a high stakes assessment.[43] Ponnamperuma et al[3] and Van der Vleuten[35] also concluded that increasing the patient sample size is the most effective modification to improve generalisability and therefore long case validity. Meskauskas[50] highlighted that increasing the number of patient encounters by one increases reproducibility by 15% regardless of the number of examiners or mark schemes used. Therefore, we will increase the number of patient encounters for the Bristol long case to improve generalisability and validity.

How many cases are needed for an effective high stakes assessment? Cook et al[28] state that the wider and more heterogeneous the test-universe is, the more observations required. Wass et al[49] concluded that 8-10 observed history taking long cases were needed to achieve a reliability coefficient of 0.8. However, Daud et al[51] state that we must consider the assessment utility when planning assessments whilst Norman[52] expresses concern about the feasibility of students seeing

10 patients consecutively within a long case. The Bristol long case lasts over an hour per case (60 minutes for history and examination, 20 minutes for write up, presentation and discussion), meaning over 10 hours of continuous assessment if aligned with the conclusion from Wass et al.[49] Shatzer et al[53] suggests decreasing the time for each case to allow for more cases in the testing period (each of the 10 cases could last 20 minutes[49]). However, this reduces authenticity as it does not match the length of time a doctor would take to see the same patient in practice.[2] This reiterates the tension between authenticity and feasibility of method.[40] Where increasing the number of long cases is impractical, a short case or OSCE style exam could be added to allow multiple patient encounters to be assessed.[44,54] However, Hardy et al[45] conclude that the long case tests unique aspects of a student's skills, reinforcing the need to keep it as a standalone assessment. Hamdy et al[40] suggests modifying the traditional long case structure to a DOCEE. During a DOCEE,[40] students encounter four unstandardised patients consecutively in a three-hour period (30 minutes for history, examination and presentation and 15 minutes for discussion). Increasing the number of patient encounters from 1 to 4, increased the reliability coefficient to 0.85. These findings align with projections that a generalisability coefficient of >0.8 can be obtained by assessments lasting between 160–240 minutes with four cases being optimal.[2,49,55] Importantly, there is confidence that the DOCEE's[40] results can be successfully extrapolated to the Bristol long case as, the assessment layout is similar. To facilitate four patient reviews within 200 minutes,[49] timings will be 40 minute clinical encounter followed by 10 minute presentation and discussion.

Scoring inference

The Bristol long case is examined using one assessor, whose grade varies between academies. Norcini[44] highlights that examiner differences contribute to reduced interrater reliability in the long case which affects score validity. As we cannot change candidate variability, and we have discussed in modification-1 why it is undesirable to standardise the patient for the Bristol long case, we will therefore aim to increase consistency of the assessor[39] by examining Norcini's[44] suggested modifications: increasing examiner number, minimising examiner differences and training.

Whilst a secondary effect of modification-1 is an increase in interrater reliability, as errors arising from raters decrease as the number of repetitions increase,[28] an assessment tool must sample many different assessors to generate reproducible results.[44] Especially as Tong et al[56] state that the more complex an assessment is, the larger an influence the number of raters has on reliability of scores. Many papers suggest using multiple examiners in each long case[37,47,57] as strong interrater agreement infers that test scores are a true indication of the student's ability.[58] Furthermore, Nikto and Brookhart,[59] Wass et al[2] and Thornton[60] all acknowledge that multiple assessors of clinical performance reduce the effect of assessor bias, including that of student gender and ethnicity.[44,61] Wass and Jolly[47] suggest that if long case assessors show consistently high interrater reliability, one examiner could be sufficient long term. However, we would need multiple assessors per case to collect this data on interrater variation to first come to this conclusion. We should be cautious of Thornton's[60] statement that increasing assessor number itself increases interrater reliability as Wilkinson et al[32] point out that discussion between examiners inevitably leads to score modulation resulting in falsely increased interrater agreement. Faherty et al[62] therefore conclude that there is essentially no difference in reliability of scores using multiple examiners compared to a single examiner. Wilson et al[63] suggest that each assessor could mark separately prior to discussion to try and compensate for this. However, Wilkinson et al[32] argue that any discussion between assessors will result in modulation of individual assessor scoring tendency for subsequent students,[32] which will align with the more dominant assessor.[62,63] Therefore, examiners in the Bristol long case would need to examine independently without discussion.

How many examiners and how do we split them? A study[64] in which each long case (two in total) was marked by a different assessor, showed examiner agreement of 89%. However, Wass et al[49] concluded that if every long case was assessed by a different examiner,[10] long cases would be needed for a reliability coefficient of 0.8, which as we have previously discussed is not feasible.[51] Wass and Jolly[47] suggest two examiners to observe history taking and a different two examiners for the presentation. Changing examiners halfway through an assessment may mitigate for subjectivity and bias such as the halo effect/prejudice of students' performance so far.[65] However, examiners then cannot use the observed history taking to inform discussion or adjust for case difficulty. Whilst Medley et al[66] suggests that the task of recording objective behaviour accurately is all an observer can handle successfully, Roberson[67] highlights that subjectivity gives the assessor the flexibility to interpret interplays in complex settings, a concept which Price and Byrne[68] concluded still allows for satisfactory interrater reliability scores. This is especially important in the Bristol long case due to use of unstandardised patients and assessment of complex interactions between context and construct.[47] Therefore, the Bristol long case will follow Hamdy et al,[40] who suggested two pairs of examiners from different specialties, with each pair assessing two entire long cases (four long cases in total). This structure has been deemed highly effective by Newble[37] as evidenced by student/staff feedback and importantly aligns with the increase in long case number discussed in modification-1.

In the Bristol long case, examiners vary between academies: from CTFs to consultants, a concept which Norcini[44] states contributes to lack of long case validity through variability in scoring tendency. Newble[37] suggests that long case examiners should be consultants, however, Wilson et al[63] found no evidence that seniority decreases observer variation. Furthermore, experienced educators can score the same long case differently,[69] due to variations in experiences, knowledge, standards, emphasis and values.[44,69] This is backed by the results from a student survey,[57] which highlighted the excessive variability in questioning by consultants and overrepresentation of the assessors' area of expertise during long cases. This bias is known as scoring tendency, which is skewed by lived experience.[67] The halo effect could also affect the Bristol long case e.g. a CTF may judge a student as very engaged in class and therefore is more lenient in their long case.[65,67] However, despite these concerns, Newble et al[70] conclude that raters are either consistent (who do not need training) or non-consistent (who cannot be trained). This theory suggests that we merely need to find the means to identify able examiners, Newble et al[70] suggest prospective examiners mark a videotaped long case. However, all examiners are volunteers and may not want to undergo assessment themselves, reducing its feasibility.

Alternatively, we could argue that unless examiner bias is extreme (e.g. examiner giving all students identical scores) behaviours can be changed statistically[71] or by training.[72] Gleeson[39] pushes for identical examiner type; however, adequate assessor training was seen to have greater effect on interrater reliability than assessor similarity,[1,73,74] together with the use of standardised mark schemes.[39] As training is essential to the production of valid assessment systems,[75] this must be incorporated into the Bristol long case. Whilst it has been suggested that one off training is not enough to teach the accuracy needed for valid scoring,[69] Des Marchais et al[72] concluded that 2–3-hour training sessions improved the taxonomic quality of examiner clinical questioning significantly. Norcini[38] suggests examiner standardisation should involve examiner provision and familiarisation of standardised mark scheme, with examples of pass/fail outcomes, a concept that will be part of modification-2.

Conclusion

Undergraduate high stakes assessment requires continuous evaluation and modification to ensure it is fit for purpose. Therefore, the long case can still have an important educational impact if it continues to evolve in synchrony with the evolution of the medical curriculum. Its authenticity encourages students to spend time speaking to real patients, rather than rote-learning an examination

technique behind closed doors. This gives medical students a unique opportunity to experience holistic medical care and complex communication in realistic situations. This is especially important as medical education continues to distance itself from the patient's bedside, despite the increasing complex needs of the UK patient cohort.

I have defined the concepts of classical and contemporary validity[12] before using Messick's unitary approach[8] due to its alignment with validity assessment within medical education.[24] The Bristol long case was examined using Kane's argument-based approach,[9] giving a practical structure to Messick's theory.[8,26] Kane's four inferences[9] were reviewed and critiqued in relation to the Bristol long case (**Appendix 1**) and modifications suggested.

To reduce content specificity[42] and strengthen the generalisation inference, we could standardise patients. However, I feel that this would drastically reduce authenticity,[29,36,41,43] a unique long case feature. Therefore, to maintain authenticity, I suggest an increase in the number of long cases assessed. Modification-1 will be increasing the number of long cases[3] from 1 to 4, which Hamdy et al[40] concluded a satisfactory generalisability score. However, I realise that this change may cause an increase in workload for examiners and patients, reducing its practicability. Therefore, I suggest a reduction in case timings to facilitate this change and show consideration for utility[51] whilst also keeping timings authentic to a real patient review[2].

For modification-2, I suggest increasing assessor number to two per long case, with examiners changing every two long cases so that each student is assessed by four examiners in total.[37,40] Multiple examiners will allow for collection of statistical data on interrater reliability[47] and reduce the effect of singular assessor bias,[2,59,60] which will further increase interrater reliability and therefore validity of the assessment.[44,56] Examiners will score separately, reducing the effect of scoring modulation by a dominant examiner.[32,62,63] I can conclude that only recruiting examiners of consultant grade does not reduce scoring variation[63] due to examiner scoring tendency being affected by specialism and past experiences.[44,57,69] Furthermore, adequate training and mark scheme familiarisation are deemed more effective than examiner grade similarity,[1,73,74] and will allow examiners from multiple grades/specialities to be recruited,[40] keeping the increase in examiner number a feasible modification.[51]

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Appendices

Appendix 1. Kane's inferences[9] applied to the Bristol long case.

Inference	Assumption	Evidence
Scoring	Long case outcomes are correct and repeatable	**Standardised mark scheme**[38,39] **Inter-rater reliability**[35,38,44]
Generalisation	The long case is representative of all possible cases the student could be given	**Content specifici y**[35,36,38,44]
Extrapolation	Long case performance is comparable to real-world clinical competence	**Authenticity and face validity**[1,3,32,35]
Implication	The long case has good educational consequences for the learner	**Remedial action and feedback**[3,37,60]

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Opinion

The current and potential future roles of artificial i telligence in ophthalmology

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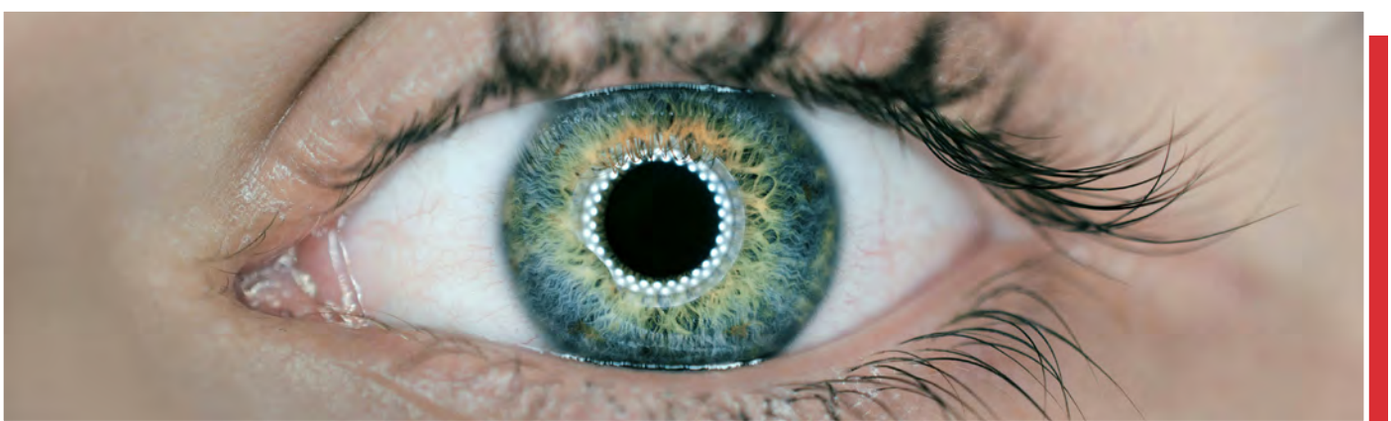

Abstract

Artificial Intelligence (AI), initially conceptualised through Alan Turing's Turing Test in 1950, has since evolved into a transformative technology. AI encompasses a broad range of computational methods that mimic human intelligence, with Machine Learning (ML) as a subfield focused on pattern detection in structured datasets. Deep Learning (DL), a further subset of ML, utilises neural networks modelled after the human brain to solve complex data-driven problems. As computer processing power advances, AI's role in fields such as ophthalmology has expanded. Current applications include AI-powered diagnostic systems, such as IDx-DR for diabetic retinopathy, and DeepSeeNet for age-related macular degeneration (AMD), which have demonstrated high accuracy, sensitivity and specificity. These advancements promise reduced diagnostic costs and improved disease management. While challenges such as algorithmic bias and ethical concerns persist, the potential of AI to revolutionise patient care and medical education remains substantial as AI tools continue to evolve.

Abbreviations

AI – artificial intelligence
AMD – age-related macular degeneration
ML – machine learning
DL – deep learning
DR – diabetic retinopathy
VR – vitreoretinal

Introduction

When Alan Turing introduced the Turing Test in 1950, he could not have anticipated how his idea would lay the groundwork for artificial intelligence (AI), which is described by some as the 'fourth revolution of mankind'.[1] AI integrates datasets with computer science to mimic human intelligence in solving problems. Within AI, machine learning (ML) identifies patterns and models results from structured datasets, while deep learning (DL), a subset of ML, utilises neural networks to process data and solve complex problems[2] **(Figure 1)**. As a result of its potential, there had been an increasing amount of excitement in the research in the application of AI in the medical field. This article explores the current applications of AI in ophthalmology and its untapped potential.

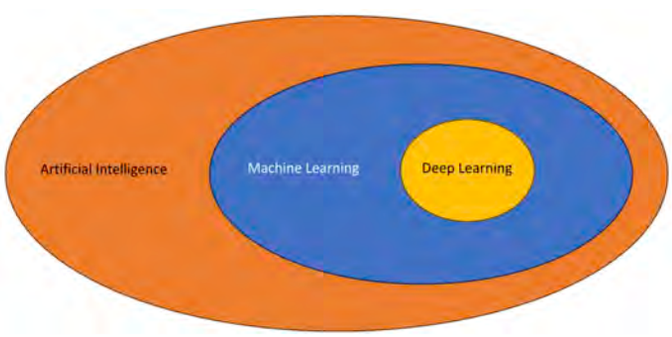

Figure 1. Diagram explaining the terms of Artificial Intelligence (AI), Machine Learning (ML), and Deep Learning (DL)

AI as a diagnostic tool

A good diagnostic tool is characterised by high sensitivity and specificity, cost effectiveness and ease of deployment. Such tools enable ophthalmologists to detect and manage diseases promptly, reducing their progression and avoiding complications.

Diabetic retinopathy (DR), a complication of diabetes, affects

one-third of diabetics and can lead to neovascularisation, retinal detachment and vision loss.[3] Ophthalmology became the first medical specialty to adopt a US FDA-approved autonomous AI diagnostic system, IDx-DR.[4,5] This system achieved sensitivities and specificities of 87.2% and 90.7% respectively in detecting DR in patients with diabetes with no previous history of the condition.4 NICE's Medtech Innovation Briefing highlights how AI technologies like RetinaLyze and Retmarker could reduce screening costs from £4.79 per patient to £0.35–£0.86 and decrease reliance on staff.[6]

Age-related macular degeneration (AMD) is the leading cause of irreversible vision loss in developed nations, accounting for over 9% of global blindness.[7] DL models, such as DeepSeeNet, have demonstrated superior accuracy compared to retinal specialists in risk stratification for AMD.[8] One study reported comparable sensitivity, specificity and precision in detecting late AMD progression.[9] Furthermore, a separate system outperformed five out of six retinal experts in predicting disease progression, underscoring AI's potential in diagnostics.[10]

AI as a treatment tool

AI is particularly prominent in vitreoretinal (VR) surgery due to its complexity. AI was shown to be able to localise, classify and segment tissues and instruments during VR procedures, which can be used by surgeons to enhance precision and reduce surgical risks.[11]

AI as an educational tool

AI can be used to track and analyse surgical movements in different stages of cataract surgery and compare the movements with expert surgeons to highlight the difference in techniques.[12] Moreover, AI can also be deployed to highlight key learning points of the surgery to facilitate independent learning.[13] Cybersight, an online training and mentorship service for eye health professionals in developing countries created by Orbis, has integrated AI in the platform to enable users to utilise AI in learning, detecting and diagnosing eye conditions in fundus images.[14]

AI's limits and concerns

Despite its potential, AI has limitations. Algorithms require extensive datasets for training, making it challenging to develop accurate models for rare eye diseases due to limited data availability. Additionally, AI models are susceptible to algorithmic bias, as their effectiveness depends on the quality and diversity of their training datasets. For example, biases in datasets can lead to disparities in diagnostic outcomes across populations.[15]

Ethical concerns also pose challenges. Issues of accountability, data privacy and informed consent must be addressed to ensure AI's responsible implementation.[15] The use of dataset in training AI models presents unique risks to data security, necessitating robust measures to protect sensitive information. Establishing clear guidelines for algorithm transparency and performance evaluation is critical for building trust and ensuring ethical compliance.

Future directions

The capacity of AI as an accurate diagnostic tool will strengthen in the future as more datasets in various ophthalmic conditions are produced and models are trained on them. With the maturation of knowledge in AI diagnostic tools, it is hopeful that deploying AI models will become more cost-effective, especially in developing countries.

The primary challenge for AI is to seamlessly integrate AI research into daily clinical practice while addressing ethical concerns. Ethical concerns can be addressed by adhering to AI-research guidelines such as Consort-AI and Spirit-AI, which aim to improve transparency and completeness of clinical trial protocols involving AI as well as other future guidelines and frameworks.[16]

Conclusion

It is evident that the application of AI in ophthalmology will continue to expand as datasets become more robust and extensive, with more AI algorithms being developed and trained. Coupled with the increasing processing power of computer chips, the potential of AI in enhancing patient care will continue to grow. Equally important is the need to equip future healthcare professionals with AI-related knowledge, enabling them to utilise this multifaceted tool effectively and safely, thereby unleashing its full potential.

Contribution statement

Both authors had substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work and drafting the work or revising it critically for important intellectual content and the final approval of the version to be included in Inspire. Vincent Ng is responsible for the integrity of the work as a whole.

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News & Opinion

The bridge between consciousness and unconsciousness: theoretical approaches of dream analysis in psychotherapy

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Introduction

This article explores the theoretical approaches of dream analysis in psychotherapy, incorporating both historical and contemporary perspectives.

Drawing on seminal works by Freud and Jung as well as both peer-reviewed and non-peer-reviewed articles and books from 1976 to 2024, it explores key developments in the field. No systematic methods or human participants were involved, making ethical approval and informed consent inapplicable.

Methods
A qualitative research approach was used, integrating multiple theories stemming from psychoanalysis and cognitive behavioural therapy. The research primarily explores the significance of dream analysis in psychotherapy. A comprehensive literature search was conducted using academic databases, inclusive of PubMed, PsycINFO and Google Scholar, to delve into the role of dreams in psychotherapeutic practice. The analysis was conducted via thematic content analysis, as the literature was reviewed and organised into key relevant themes, such as dreams revealing unconscious thoughts, Freudian and Jungian theories and cognitive behavioural therapy in addressing dreams. The analysis also involved comparing and contrasting different theoretical perspectives regarding supporting the use of dreams in psychotherapy.

The bridge between consciousness and unconsciousness: theoretical approaches of dream analysis in psychotherapy
Dreams can act as a cathartic function, providing insights into our subconscious by reflecting underlying psychological states. Within the realm of psychotherapy, some believe that they serve as one of many gateways for exploring the concealed corners of the mind, in turn unveiling profound revelations about our fears, desires and unresolved struggles. It is proposed that we dream for around three to six hours per night, with a staggering 95 percent of us having no recollection upon awakening.[1]

The importance of dreaming in psychotherapeutic practice
Dream analysis serves as a possible tool for investigating unconscious psychological processes, enabling therapists to work with clients in an attempt to dissect potential hidden messages, facilitating a deeper insight into self-awareness.

In New Science of Dreaming, a book published by the sleep psychotherapists Barrett and McNamara, it is suggested that the 'brain does not have to process new information' when sleeping, and hence uses its capacity to work on problems, based on experiences encountered in waking life that have evoked an emotional response – creating our dreams. This allows the brain to find solutions for problems more readily when sleeping than awake.[2]

Therefore, a lack of sleep is harmful for the consolidation of positive emotional content as the brain evaluates thoughts and memories, and in turn, influencing emotional reactivity and promoting mental health disorders.[3]

By incorporating dream analysis into psychotherapy, therapists may be able to gain a more comprehensive understanding of the client's psychological function, which can be analysed to resolve lingering issues through cognitive restructuring ultimately enhancing overall mental health.[4]

Interpreting dreams: symbolism and analysis

Dreams can be interpreted through cognitive behavioural therapy sessions and via two main theories: Freudian and Jungian.[5] Therapists can help clients explore the symbolism and meaning of dreams, which may help them receive an insight into their unconscious emotions, using this to ameliorate their conscious life.[6]

Dream symbolism involves the use of symbols and metaphorical imagery to convey unconscious wishes, conflicts and desires. These symbols can take miscellaneous forms, such as objects, animals, people and locations, and can then be decoded to represent themes such as transformation, emotional turmoil, freedom and vulnerability, which could reflect an individual's mental state.[7]

Evidence of dream analysis linking to psychotherapy

The use of dream analysis as a source of internal thoughts in psychotherapy has been heavily studied. Psychotherapists Luborksy and Crits-Christoph found that both therapy narratives and dreams were underlying the same unconscious relationship patterns, which allowed a thorough analysis and solution to their mental conflicts.[8]

In addition, Hall and Van de Castle developed a coding system for the content of dreams, where they concluded that it is possible to "draw personality profiles" and "predict future actions" solely from a dream.[9] This information can then be analysed in therapy, providing the support required to the client. Moreover, therapist Palombo proclaims that dreams change when a person goes through psychotherapy, as not only do dreams predict their future actions, synonymous with De Castle's opinion, but it also changes their mentality.[10] For example, in subsequent dreams that carry a storyline, dreamt over a few nights, clients may reprocess the contents from their last analytical psychotherapy session hence in their next dream their actions change, combatting their internal conflict.[11]

In a study on the dreams of a 28-year-old female with multiple personality disorder, carried out by psychotherapist Barrett, it was demonstrated that the split-off parts of her personality appeared personified in their dreams during a psychotherapy session.[11] This case study suggests that we cannot conceal our inner personalities when we dream and that our true conscious thoughts are revealed beyond our control.

Greenberg and Pearlman compared the content of dreams from the client to the content of their therapy sessions that coincided with the time of the dream and found a strong connection between the themes in the dreams and their psychotherapy.[12]

Freudian perspectives on psychoanalysis and its link to psychotherapy

Sigmund Freud asserted that dreams are the "royal road to the unconscious" – essentially providing direct access to the deepest layers of the mind.

In his seminal work, The Interpretation of Dreams, published in 1899, he proposed that dreams represent the disguised fulfilment of unconscious wishes, stemming from childhood experiences and repressed desires. In addition, he defined that dreams contain two different types of content – manifest and latent. Freudian theory states that latent content is not immediately apparent to the dreamer as it is comprised of underlying, unconscious feelings and thoughts experienced, which need to be explored to be fully understood. Whereas manifest content is made up of a combination of the latent thoughts and the images directly seen in the dream. Freud believed that a process called "Dreamwork" would unravel dreams of disguised unfulfilled wishes and allow unconscious thoughts to be transferred into conscious ones – to study the manifest content of the dream.[13]
Latent content also covers the more hidden symbolic meanings within dreams, which can be deciphered through techniques such as free association. Free association involves the spontaneous expression of thoughts, feelings and associations triggered by dream imagery or symbols, essentially saying whatever comes to mind initially, allowing the therapist to explore the underlying meanings of the dream. Freud claims that free association provides a release valve for pent-up emotions accumulated during waking life, as a form of emotional discharge. It can be interpreted via 'loose free association' or 'broad free association', the first indicating that the client talks in the absence of prompts from their therapist, thus producing a "stream of words with no association to each other" which can be pieced together. The latter refers to the therapist asking the client to close their eyes and state the first thing that comes to their mind.[14]

Jungian perspectives on psychoanalysis and its link to psychotherapy

psychiatrist Carl Jung believed that dreams provide insights into the collective unconscious, a universal repository of archetypes shared by all humanity, as they reflect personal experiences as well as deeper transpersonal aspects of the psyche. He claims that the figure in the dream psychoanalytically represents your ego consciousness, which is our awareness of ourselves as humans. Moreover, he believed the process of individualisation is the central goal of psychological development, where individuals strive to integrate both conscious and unconscious aspects of the psyche to enhance self-realisation, ultimately improving themselves from the therapy session.[15]

In Jungian dream analysis, dream symbols and images are expanded upon by associating them with cultural, mythological, religious and historical references. By drawing connections between dream content and broader cultural symbols and motifs, individuals can uncover the deeper layers of meaning within their dreams. Jung recognised that dreams contain both personal and collective meanings, reflecting the individual's unique life experiences as well as broader cultural and universal themes. Dreams are ultimately an instrument for the diagnosis, research and treatment of mental disturbances in a clinical setting.[16]

Cognitive behavioural therapy in dream analysis

Cognitive behavioural therapists assist clients in identifying and challenging beliefs and schemas manifested in their dreams, fostering cognitive restructuring and emotional healing. Practical techniques employed in cognitive behavioural dream work, such as maintaining dream journals and exploring alternative interpretations, facilitate meaningful exploration in psychotherapy. This in turn aids the process of transforming their mental framework by promoting greater emotional resilience and psychological wellbeing.[17]

These beliefs often stem from past experiences, traumas or negative self-perceptions and can contribute to emotional distress. Once identified by examining the content of their dreams and further exploring their emotional reactions evoked by dream symbols, individuals can gain insight into underlying processes shaping dream experiences. Cognitive behavioural therapy helps clients challenge and reframe their thoughts through cognitive restructuring techniques; by slowly replacing a belief with one that is more helpful and accurate. Understanding that it is normal to feel such emotions and trying to think positively about them aids the recovery process significantly within psychotherapy.

Therapists' challenges with dream interpretation

Although dreams can be incredibly valuable in psychoanalysis, certain evidence suggests that it is not the best form of extracting information during psychoanalytic sessions. Many therapists feel unprepared to attend to their client's dreams, as the results from one empirical study revealed that most clinicians work with dreams only occasionally as they are "meaningless".[18] This highlights that although dreams are a source of unconscious thoughts, in the realm of psychotherapy, dream analysis may not always be the strongest choice compared to verbal therapy sessions such as CBT, as it is not as accurate. Moreover, the sessions constitute clients retrospectively recalling their dreams, perhaps reflecting their interpretation rather than the actual occurrence of the dream. This is reinforced by a study conducted in Taiwan in 2006, where 177 students agreed that they were more likely to discuss the positive connotations of their dreams rather than the potentially deeper, more upsetting connotations.[19] This accentuates the biases involved in dream analysis as there is not

always an accurate depiction of the dream, nor do some clients find pleasant engagement during the session, reducing the amount of information they are willing to share with their therapist. This study had a large sample size; however, it was produced 18 years ago and therefore is not very up-to-date. Many advancements could still occur in the future using dream analysis, for example by supporting individuals with mental health issues, such as schizophrenia, by using psychotherapy.[20]

The therapeutic value of dream analysis in psychoanalysis and cognitive behavioural approaches

In essence, dream analysis, whether through traditional psychoanalytic methods or contemporary cognitive behavioural approaches, continues to serve as a potential avenue for self-discovery, healing and personal growth within the realm of psychotherapy. Freud viewed dreams as the 'royal road to the unconscious'[13], using techniques such as free association, whereas Jung states that dreams are often collective, as many humans experience the same dreams representing different themes such as emotional turmoil. Both theories can be used in dream analysis as an additional therapeutic tool within psychotherapy treatment. It is increasingly advised to document such dreams in journals and diaries to allow a more accurate reflection of their mental and emotional states,[21] which can then be broken down in psychotherapy.

The potential capacity of dreams to tap into the subconscious and unearth underlying psychological processes remains an asset in therapeutic practices, fostering a deeper client-therapist relationship, which in turn would enhance overall treatment efficacy.

In the future, longitudinal studies could be used to advance research in this field by providing insights into how dreaming patterns evolve over time. This could further support the idea that waking states and concerns are reflected in dreams.[22] Additionally, data analysed in psychotherapy could be integrated with neuroscience research to enhance our understanding of dreaming and its cerebral correlates.[23]

The author affirms their responsibility and accountability for the published work, having made substantial contributions to its conception or design, or to the acquisition, analysis, or interpretation of data. They have also actively participated in drafting the work or critically reviewing it for significant intellectual content and have granted final approval for its publication. Furthermore, the author agrees to be fully accountable for all aspects of the work, ensuring that any questions regarding its accuracy or integrity are thoroughly investigated and appropriately resolved.

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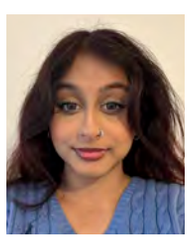

Sienna-indiya Patidar

I am a second-year medical student at the University of Plymouth. This article was written as part of a cross-cutting themes-based student-selected component, which I completed in my first year. Having this opportunity allowed me to further explore my passion for neurology and delve into the profound impact dreaming has on the deep subconscious, including the methods by which this can be analysed. Along this journey, I have also discovered my strong passion for research, and I am excited to explore this further in the future!

Review

A systematic review on reduction of bacterial load in root canals of single-canalled teeth through use of sodium hypochlorite and chlorhexidine as endodontic irrigants

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Abstract

To avoid failure of endodontic therapy, thorough disinfection of the root canals is paramount. Sodium hypochlorite has been used by dentists for decades but, due to its toxicity and irritative nature, there has been a recent increase in chlorhexidine use. This review has been conducted to determine whether sodium hypochlorite or chlorhexidine causes the greater reduction in bacterial load in mature permanent teeth undergoing root canal treatment.

OVIDMedline, Cochrane Central Trials Database and Cochrane Database of Systematic Reviews were searched on 16 December 2022. Included papers were required to be in-vivo studies using sodium hypochlorite and chlorhexidine as endodontic irrigants independently of each other, on permanent teeth.

The search yielded 182 papers, narrowed to seven by removing irrelevant, inaccessible and duplicate papers, and those that did not fulfil the inclusion criteria. Every included study was a randomised controlled trial, seeing a decrease in bacterial load of root canals between 59.4% and 100.0% through the irrigation in the intervention groups. Four papers reported a difference of less than 5.0% bacterial reduction between the two irrigants. The other three reported chlorhexidine bacteria reductions between 10.6% and 19.0% more than sodium hypochlorite.

There is evidence to suggest that chlorhexidine and sodium hypochlorite reduce bacterial load during endodontic therapy. However, inconsistency of findings makes it difficult to conclude whether chlorhexidine has greater antimicrobial effectiveness than sodium hypochlorite. More high-quality studies are needed to form a judgement regarding which irrigant is preferable to use in standard practice.

Abbreviations

CASP – Critical Appraisal Skills Programme
CFU – Colony Forming Units
CHX – Chlorhexidine
NaOCl – Sodium Hypochlorite
PCR – Polymerisation Chain Reaction
PICO – Population Intervention Comparison Outcome
RCT – Root Canal Therapy

Introduction

The rationale behind endodontic treatment is removal of necrosed pulpal tissue and associated bacteria will ensure that the periapical tissues remain healthy,[1] thereby allowing retention of a non-vital tooth in the mouth. Bacteria associated with pulpal necrosis spread through the pulp and causes damage to the periradicular

tissues, inducing inflammatory processes and leading to apical periodontitis.[2] Therefore, thorough disinfection of the root canal system during endodontic therapy is crucial to prevent development of this inflammation.

The eradication of bacteria occurs using a combination of mechanical and chemical methods.[3] Mechanical instrumentation produces debris, consisting of mineralised collagen matrix, pulpal tissue and bacteria,[4] which covers the surface of canals undergoing preparation and obstructs the exposed dentinal tubules, allowing accumulation of bacteria to occur. Whilst most bacteria, and their by-products, can be removed with good mechanical instrumentation,[5] this smear layer formation and anatomical complexities of the canal system make complete disinfection unachievable[4] without addition of an antibacterial endodontic irrigant.

Sodium hypochlorite (NaOCl) has been a popular choice of irrigant by dentists for decades due to its antibacterial effect and ability to dissolve organic material.[6] However, NaOCl is toxic to periapical tissues and can cause irritation,[6] leading researchers to investigate alternative irrigants and their properties, with a focus on improved biocompatibility whilst retaining antibacterial function. Despite its lack of organic tissue dissolving properties, use of chlorhexidine (CHX) as an endodontic irrigant has grown in recent years due to its biocompatibility and substantivity, non-toxic nature and being less irritating to periapical tissues[7] than NaOCl. However, there is uncertainty amongst researchers and dental professionals as to which irrigant is most effective.

Despite the various attributes and drawbacks of each irrigant, a firm conclusion on their antimicrobial efficacies is yet to be made, mainly due to the inconsistency of results of existing studies. Hence, a review of the evidence comparing the antibacterial effectiveness of NaOCl and CHX endodontic irrigation, in patients with mature permanent teeth needing root canal therapy, is required.

A systematic review was published in 2012,[8] which included 11 papers dated between 1978 and 2010. Only four trials directly compared NaOCl and CHX as irrigants. In these papers, no primary outcomes, and only one secondary outcome (bacterial growth cultures), were stated.

Another systematic review was published in 2022,[9] which included seven papers dated between 2009 and 2020. Only two of these trials compared the antimicrobial efficacy of NaOCl and CHX, concluding that there was a significant reduction in bacterial load with use of either irrigant (between 56.0% and 99.8%), but differences of less than 4.0% between the two irrigants. The validity of this conclusion is questionable as it was based on only two studies. Hence a comprehensive review based on the PICO provided in **Table 1** is warranted.

Methods

Search strategy

A search of OVIDMedline, the Cochrane Central Trials Database and the Cochrane Database of Systematic Reviews was conducted on 16 December 2022, using the search strategy detailed in **Figure 1**.

Paper screening and eligibility evaluation

The inclusion criteria led to acceptance of papers that are in-vivo studies, randomised controlled trials, have quantitative methodology and/or results, included permanent/mature teeth, used any concentration of irrigant, and included both irrigants that are being evaluated.

The exclusion criteria led to omission of papers that have qualitative methodology and/or results, no full text available, are in a language other than English, included deciduous/immature teeth, included endodontic retreatment, included only one or neither of the irrigants being evaluated, only used the irrigants as a final rinse, and when the irrigants are only used in combination with others.

All paper processing was completed independently by the two authors. First, duplicate papers were removed. The titles and abstracts of each remaining paper were read, leading to omissions due to fulfilling the exclusion criteria. Several full texts were inaccessible, again leading to omission. The full texts of the remaining papers were read, further being excluded. Differences in exclusion by the two authors were discussed and settled, producing a list of seven studies[10,11,12,13,14,15,16] to be included in this review.

Outcome variables and analysis

The primary outcome investigated was reduction in bacterial load. No secondary outcomes were investigated. Only one study[14] contained a full data set. Another[10], contained discrete data. None of the included studies stated standard deviations or confidence intervals. Due to these factors, a meta-analysis was not performed. Therefore, integration of the studies relied upon p-values and mean percentage reduction of bacterial load.

Paper evaluation

The Critical Appraisal Skills Programme (CASP)[17] checklist for randomised controlled trials was used by both authors independently to examine the quality of the papers included in the review to ensure they were of a sufficient calibre. This was used in conjunction with Cochrane Review Group risk of bias 2 tool[18] to produce a risk of bias analysis.

Results

Search outcomes

As shown in **Figure 2**, 182 records were obtained from the literature searches. After removing eight duplicates, 174 papers had their titles and abstracts screened, of which 150 were then excluded. The remaining 24 papers underwent full-text screening, of which seven could not be retrieved. Ten were excluded because they either only used NaOCl and CHX in conjunction, only tested one irrigant, were ex-vivo studies or involved teeth that had been previously treated. Hence seven studies[10,11,12,13,14,15,16] were included in this review.

Characteristics of papers

Prior to inclusion, each study was quality assessed using the CASP tool for randomised controlled trials. Certain parameters were selected to act as indicators of sufficient quality: a targeted PICO question, equal quality of provided care, magnitudes of bacterial reduction stated (as raw data or percentage), and sufficient applicability to general practice dentistry. Every included paper fulfilled each of these conditions, thereby being deemed appropriate to be included in this review. This type of screening also highlighted certain biases and shortcomings of the papers, which are explored further in the Discussion section and **Figure 3**.

All studies included were randomised controlled trials and investigated single canalled teeth that were non-vital or had primary endodontic infection. Sample sizes varied between the studies, with 10,[11,12,13] 15,[10] 16,[14] 20,[15] and 25[16] teeth per intervention being tested. Across the seven papers, a total of 212 teeth underwent endodontic therapy.

Two papers[10,11] used 5.25% NaOCl at 2ml volume, one[15] used 5ml 1% NaOCl. All other papers[12,13,14,16] compared 2.5% NaOCl with volumes of 3ml,[12,13] 5ml[14] and 15ml.[16] Other than the study which used 0.2%,[12] every study used 2% CHX solution (with one[14] using a gel form) with the volume used ranging from 1ml to 15ml.

Two of the studies,[11,14] qualified the exposure time as 20 minutes, during which the chemomechanical preparation of the canal occurred; the five other studies did not present these data. Only one paper[12] collected data for the irrigant use independently, the other six studies concentrating on treatment where chemomechanical preparation was undertaken.

Characteristics of outcome measures

As seen in **Table 2**, three papers[10,12,14] supplied mean values of CFU/mL (colony forming units) pre- and post-irrigation. One of these[10] also recorded the percentage distributions of specific growing and non-growing bacteria. Three studies[11,14,15] recorded average values for CFU/mL pre- and post-irrigation, as well as recording incidence of positive bacterial presence using a PCR (polymerase chain reaction) technique. The final study[16] measured the incidence of positive microbial presence using 16s rRNA gene-based primers, a type of PCR technique, pre- and post-irrigation.

Summary of findings

Through the irrigative process, every study saw a decrease in bacterial load of between 59.4% and 100.0%.

Based on statistical evidence only, four papers[11,12,15,16] reported no differences between the bacterial reduction with NaOCl, compared with CHX (no p-values stated, $p>0.05$, $p>0.05$, $p>0.05$, respectively). The remaining three studies[10,13,14] all found greater reductions in bacteria for CHX compared to NaOCl, with $p=0.09$,[10] $p<0.05$,[13] and $p<0.01$.[14]

Four of the papers[11,12,15,16] showed less than 5.0% difference between the percentage bacterial reduction of the two irrigants. The other three[10,13,14] concluded that CHX is more effective than NaOCl, causing between 10.6% and 19.0% more reduction in bacterial load of root canals. However, none of the studies include confidence intervals, or contain a complete enough data set to calculate them, thereby calling into question the precision of the published results.

More information about the characteristics, irrigation protocols and results of each study have been outlined in **Table 2**. A graphical comparison of data can be found in **Figure 4**.

Discussion

Current literature

Previous systematic reviews[8,9] concluded that there was insufficient evidence to suggest a difference between the antibacterial effectiveness of NaOCl and CHX. This review aimed to address shortcomings in the published reviews but found inconsistency in the findings of the seven included papers. While three papers[10,13,14] found CHX had greater antibacterial efficacy than NaOCl regarding root canal treatment, the other four studies[11,12,15,16] did not find a difference.

Review of included studies

CASP was used to quality assess the included papers prior to results collation. Whilst each study was deemed acceptable to be included in the summary, more high-quality research into this area should be conducted.

The studies that were used were broadly compatible as they all measured the bacterial load and showed reductions in presence of bacteria with intervention/control group, despite using three different methods to do so. One paper[12] is, perhaps, less applicable than the others due to the lack of mechanical preparation of the root canals; this was something that was not accounted for in the exclusion criteria.

Every study randomly sorted their participants into two groups, testing either NaOCl or CHX, however, five[10,12,13,14,15] of these studies failed to declare how the randomisation was undertaken. This lack of information calls into question the soundness of their approach as it could generate randomisation bias. One paper[11] asked the participants to choose between groups of envelopes, randomly assigning them to an intervention group depending on what was in their envelope. Another study[16] obtained randomisation by drawing lots.

The only paper[16] to include power calculations, to justify the sample size used, was notably the study with the greatest number of participants – 25% more than the next largest study.[15] The limited number of participants included in each of the studies, and lack of power calculations, casts doubt upon their ability to detect the intended clinical effects. There is also no information in any study about the demographics of each of the treatment groups post-allocation. This may indicate a lack of relevancy of results to a real-world application depending on spread of different social factors. There was no mention of blinding participants or investigators in six of the studies.[10,11,12,13,14,15] One study[16] stated that it was not feasible to blind the patient or treatment provider because of the recognisable odour of NaOCl. Whilst patient blinding would not be necessary, due to the nature of the study, blinding of the dentist would have eradicated opportunity for performance bias.

Each study only looked at the irrigant effects in single canalled teeth, limiting relevance of the summary as endodontic therapy is not only conducted on single canalled teeth. Further research, into whether the outcomes of irrigant use are different when all canals of multi-rooted teeth are treated, should be undertaken to remove this limitation.

None of the papers compared irrigants of the same concentration as each other within the individual studies and failed to provide rationale of concentration selection, calling into question the real-life application of their results. The concentrations of the irrigants are not consistent between the studies either, with two papers[10,11] comparing 5.25% NaOCl and 2% CHX, three papers[13,14,16] comparing 2.5% NaOCl and 2% CHX, and the remaining two[12,14] comparing 2.5% NaOCl with 0.2% CHX and 1% NaOCl with 2% CHX respectively. This provides a challenge when evaluating whether the papers' conclusions are capable of integration. Studies testing multiple concentrations of NaOCl and CHX under the same clinical method would be useful to overcome this uncertainty.

Only two studies[11,14] measured the irrigant exposure time. Ambiguity regarding this begs the question of how easily integrated the results of the studies can be, as the antimicrobial effect of irrigants may be dependent on the period they are within the canal and, therefore, in contact with bacteria. Every study collected bacterial samples directly after irrigation. By doing so, the substantivity of CHX, one of its main advantageous properties, was not considered. Further research investigating antibacterial reduction over time, perhaps a year post-op, would be useful to assess whether substantivity influences the bacterial load within the canals. This was something that was considered as a possible outcome to be measured but was discarded due to the limited literature available.

Whilst deeming bacterial reduction statistically significant or not would appear to make integration of the papers more straightforward, P-values are a very arbitrary way to assess this. The discrepancy between papers that consider bacterial reduction statistically significant and those which have sizeable reduction in terms of magnitude, make conclusion consolidation difficult, therefore, affecting real-world application of the studies.

Despite not directly investigating this, measurements of success of the endodontic treatments would have been interesting to see; potentially giving an indication of a threshold value for bacterial load, beyond which, treatment is successful. It may also have exposed

alternative properties of the irrigants or side effects that increase likelihood of failure.

Although being deemed of high enough quality to be included in this summary, the included papers have issues regarding potential biases and are difficult to integrate due to the variability of clinical method. Only one paper[14] included full datasets that could be used for statistical analysis, making meta-analysis, sensitivity testing and formal integration of the papers impossible. Standardisation of investigative protocol – primarily exposure time, volume and concentration of irrigants used – and data collection could be instrumental in refining our understanding of the effectiveness of endodontic irrigation. More high-quality studies are needed to allow a decision to be made regarding optimisation of technique of this therapy.

Conclusion

Through the selected studies, this summary concludes that use of NaOCl and CHX as endodontic irrigants decrease the bacterial load of root canals in need of root canal therapy, highlighting their importance. However, due to inconsistency of results of the included literature, a firm judgement regarding which irrigant has a greater antibacterial effect cannot be made.

Further to this, more research needs to be conducted into the different properties, as well as side effects, of sodium hypochlorite and chlorhexidine to establish which irrigant should be of standard use by dental practitioners.

Contribution statement

The authors of this review both made substantial contributions to the acquisition, analysis, and interpretation of data for the work; drafting and revising it critically for important intellectual content; and have both approved the final version for inclusion in INSPIRE.
Poppy Daly is the guarantor of this work.

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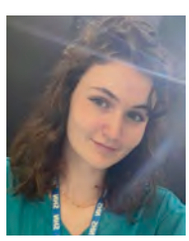

Poppy Daly

Hello, I'm Poppy. I graduated from University of Bristol in 2024 and am now working as a foundation dentist in Devon. This paper was written when we were in fourth year of university. I am enjoying growing my experience in general practice and getting used to working life! In the future, I plan to specialise in endodontics. In my spare time, I love exploring new places with my

Lily Lester

Hi! I am Lily, I have recently graduated from University of Bristol and am currently doing a two-year DFT/DCT scheme in North Central London. I am thoroughly enjoying my first year working as a dentist and would consider specialising or further training in the future. I love spending my spare time outdoors, especially at the beach in my hometown Swansea.

Search conducted 16/12/2022:
Ovid MEDLINE(R) <1946 to present>
Yielded 57 results.

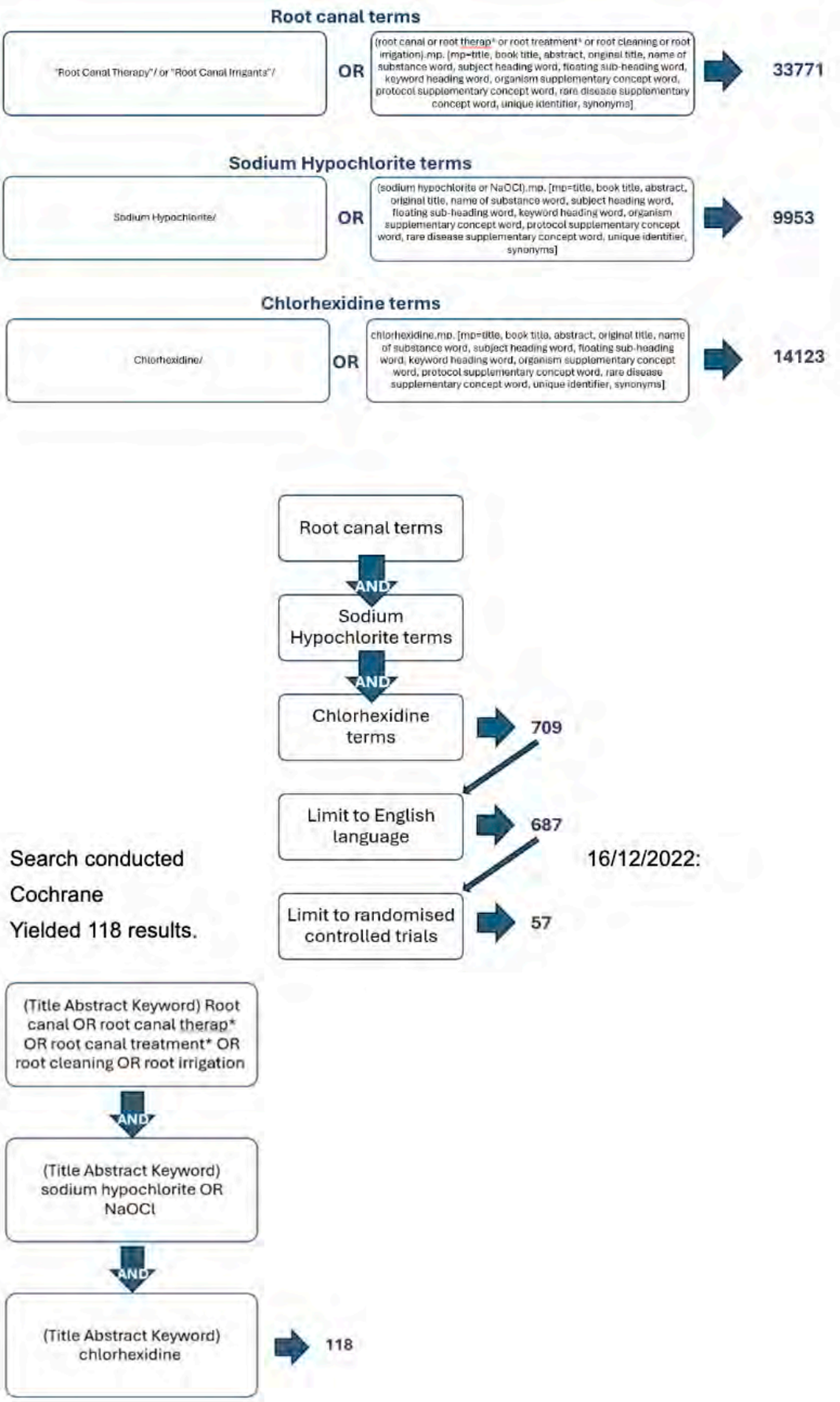

Figure 1. Search strategy depicted with flowcharts.

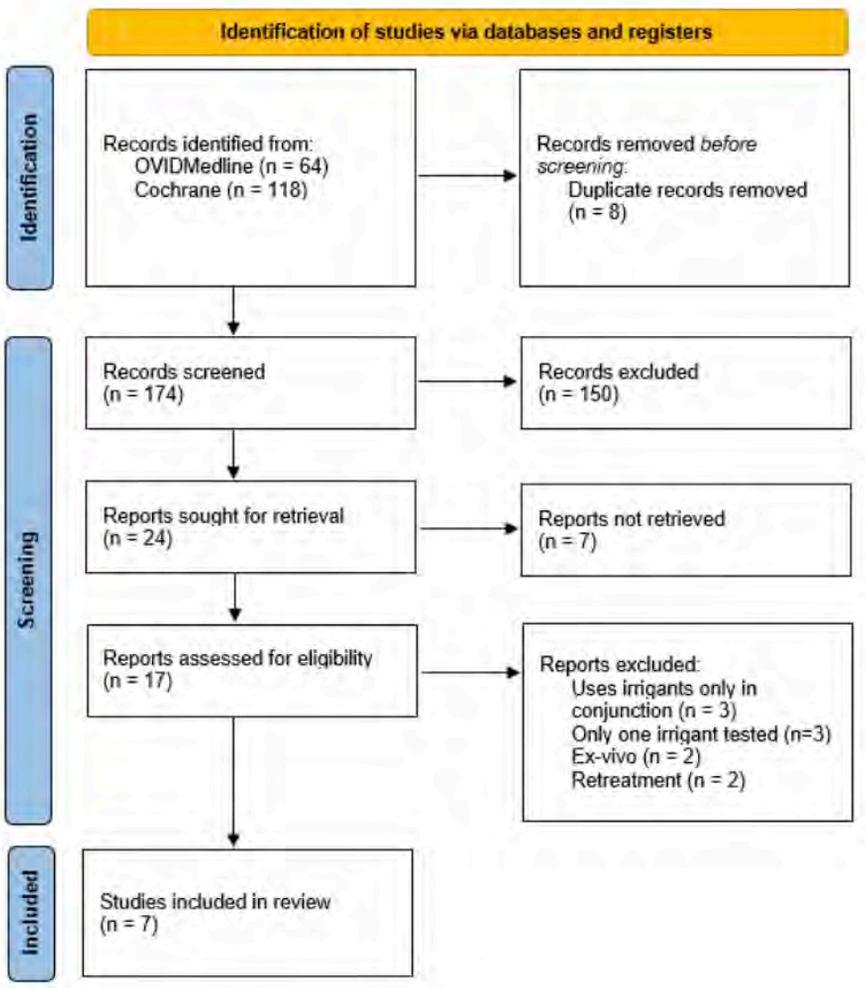

Figure 2. PRISMA flow diagram depicting the search strategy.

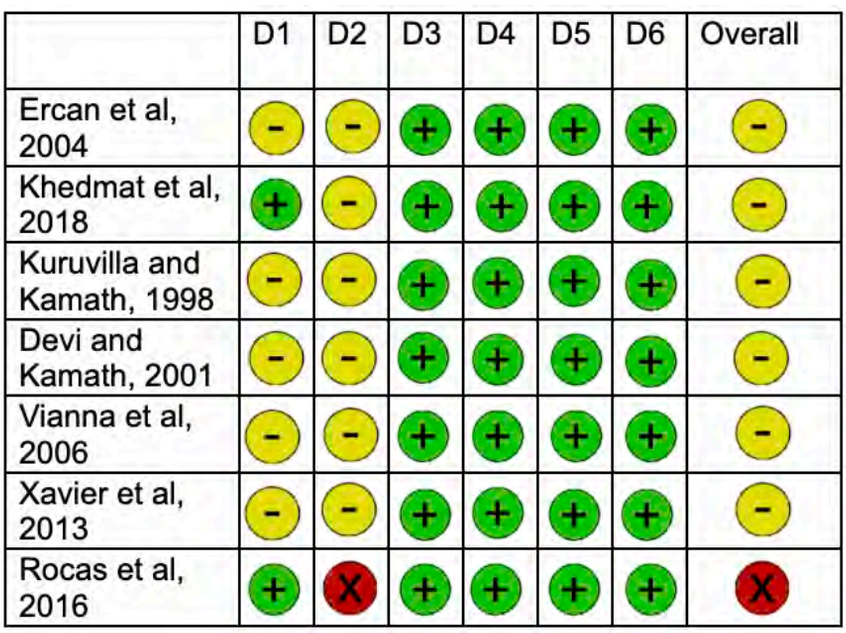

Figure 3. Risk of bias assessment of included studies.

D1 – Bias arising from randomisation process
D2 – Bias arising from blinding
D3 – Bias due to deviations from intended intervention
D4 – Bias arising from incomplete outcome data
D5 – Bias in measurement of outcome
D6 – Bias in selection of reported result

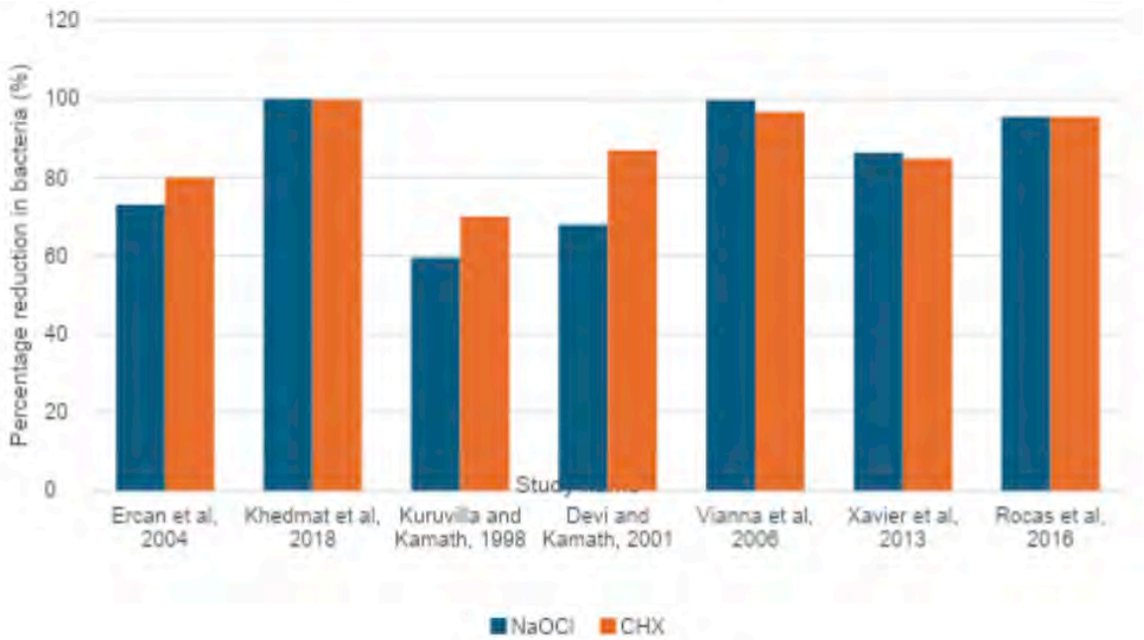

Figure 4. Chart to show percentage reduction in bacteria in canals under NaOCl and CHX irrigation

Table 1. PICO question to be explored in this review

Patient/population/problem	Patients needing root canal treatment
Intervention/exposure	Chlorhexidine irrigation (CHX)
Comparison	Sodium hypochlorite irrigation (NaOCl)
Outcome	Reduction in bacterial load

Table 2. Summary table of the findings f om the included studies

Main outcomes	Difference in reduction	CHX was more effective than NaOCl for both sampling periods (p<0.001) No confidence e intervals stated	No evidence to suggest a superior irrigant No p-values stated No confidence intervals stated	No evidence to suggest a significant difference between groups (p > 0.05) No confidence intervals stated	Evidence to suggest CHX provided greater (p < 0.05) bacterial reduction than NaOCl No confidence intervals stated	Evidence suggests that NaOCl reduced bacterial load more than CHX (P<0.01). No confidence intervals stated	No evidence of a significant difference between the median percentage values of bacterial reduction found in NaOCl and CHX (P > 0.05) No confidence intervals stated	No evidence to suggest a significant difference in reduction between the groups (p > 0.05) No confidence intervals stated
	Reduction in CHX	CHX saw 10/15 to 0.75/15 (80.0%)	CHX from $5.2x10^5$ CFU/ml to 80CFU/ml (99.8%)	Reduction of bacteria with CHX – 70%.	CHX from 5.04 CFU/ml to 0.46 CFU/ml (86.9%)	CHX from $2.3x10^8$ to $6.2x10^4$ (96.6%) (SYBR) and $3.0x10^8$ to $4.3x10^4$ (96.6%) (TaqMan)	CHX from 146 EU/ml to 19.76 EU/ml (84.8%)	CHX from $8.77x10^4$ to $2.81x10^3$ (95.4%)
	Reduction in NaOCl	NaOCl reduction from a mean of 11.25/15 canals containing bacteria to 1.75/15 (73.0%)	NaOCl levels were reduced from $5.5x10^5$ CFU/ml to 70CFU/ml (99.9%)	Reduction of bacteria with NaOCl – 59.4%	NaOCl levels were reduced from 4.96 CFU/ml to 1.67 CFU/ml (67.9%)	NaOCl saw reduction from $2.8x10^8$ to $2.0x10^2$ RNA copy numbers (99.99%) (SYBR) and $7.6x10^8$ to $1.6x10^4$ (99.6%) (TaqMan)	NaOCl levels reduced from 114.5 EU/ml to 15.65 EU/ml (86.3%)	NaOCl levels reduced from $3.70x10^5$ to $5.49x10^2$ (95.5%)
Irrigation protocol	Incubation periods (37° c)	5-7 days	7 days	72 hours	72 hours	7 days	Up to 14 days	NS
	Exposure time	NS	20 mins	NS	NS	20 mins	NS	NS
	Type/concentration/volume	2ml 5.25% NaOCl / 2ml 2% CHX	2ml 5.25% NaOCl / 2ml 2% CHX	3ml 2.5% NaOCl / 3ml 0.2% CHX	3ml 2.5% NaOCl / 3ml 2% CHX	5ml 2.5% NaOCl / 1ml 2% CHX gel	5ml 1% NaOCl / 1ml 2% CHX	15ml 2.5% NaOCl / 15ml 2% CHX
Tooth	Infection status	Pulpal necrosis; apical pathosis; both	Necrotic pulp	Non-vital; definite apical radiolucency	Non-vital; definite apical radiolucency	Non-symptomatic; no response to sensitivity testing	Primary endodontic infection	Necrotic pulp; asymptomatic apical periodontitis
	Type	Incisor and premolar teeth with single canal	Single rooted premolars	Single rooted anterior teeth	Single rooted teeth	Single rooted teeth	Single rooted teeth	Single rooted and single canal teeth
	Sample characteristics	30 (NaOCl n=15; CHX n=15) Age: 20-52 years	20 (NaOCl n=10; CHX n=10) Age: NS	20 NaOCl n=10; CHX n=10) Age: NS	20 (NaOCl n=10; CHX n=10) Age: NS	32 (NaOCl n=16; CHX n=16) Age: 19-63 years	40 (NaOCl n=20; CHX n=20) Age: NS	50 (NaOCl n=25; CHX n=25) Age: 13-52 years (mean 29 years)
	Country of study	NS	NS	NS	NS	Brazil	Brazil	Brazil
	Randomised controlled trial	Ercan et al, 2004	Khedmat et al, 2018	Kuruvilla and Kamath, 1998	Kamath and Devi, 2001	Vianna et al, 2006	Xavier et al, 2013	Rôças et al, 2016

NaOCl – sodium hypochlorite; CHX – chlorhexidine; n – number; NS – not stated

Review

Evaluation of updated NG51 guidelines on early recognition and sepsis outcomes in elderly patients

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Abstract

On 31 January 2024, NICE updated NG51, following recommendations from the Academy of Medical Royal Colleges in 2022. After years of stalling progress for sepsis outcomes, particularly in the elderly population, this guideline update seeks to address sepsis mortality rates by introducing new recommendations surrounding early administration of antibiotics, and, most significantly, encouraging universal use of NEWS2 to identify deterioration, aiding identification of patients with early sepsis. This review critically examines the evidence and arguments regarding the impacts of the updated NG51 guidelines on future sepsis identification, diagnosis and outcomes. Drawing on personal observations of sepsis management in the emergency department, this review also includes original recommendations for potential future updates to the NG51 guidelines.

Abbreviations

ADL – Activities of Daily Living Score
AoMRC – Academy of Medical Royal Colleges
BP – blood pressure
CFS – Clinical Frailty Score
COPD – chronic obstructive pulmonary disease
CRP – C-reactive protein
DNR – do not resuscitate
HR – heart rate
NEWS2 – National Early Warning Score[2]
NG51 – NICE Guideline 51
NICE – National Institute for Health and Care Excellence
ReSPECT – Recommended Summary Plan for Emergency Care and Treatment
RR – respiratory rate
SaO_2 – peripheral capillary oxygen saturation
SIRS – systemic inflammatory response syndrome

Introduction

Sepsis is defined as life-threatening organ dysfunction due to an unregulated host response to infection. The Lancet Journal of Respiratory Medicine reported 245,000 sepsis cases annually in England, with a 20.3% mortality rate, responsible for more deaths than leukaemia, breast, bowel and prostate cancer combined.[1,2] In 2016, the National Institute for Health and Care Excellence published NICE Guidelines 51 (NG51), a protocol for recognition, early diagnosis and management of sepsis. On 31 January 2024, NICE updated NG51, following recommendations from the Academy of Medical Royal Colleges in 2022. Specifically, the elderly population typically suffer the least favourable sepsis outcomes, with mortality in 75- to 79-year-olds in England increasing by 351 annual deaths from 2015 to 2022.[3,4] Therefore, this update aims to address the challenges surrounding diagnosis and sepsis treatment, given early intervention has proven to significantly mitigate mortality.

This academic review aims to critically evaluate the updated NG51 guidelines on early recognition and sepsis outcomes in elderly patients, analysing the impact in this vulnerable patient demographic. The 2024 NG51 update holds positive implications

for sepsis outcomes, however, some limitations remain unresolved since its original publication in 2016. Given limited progress to improve outcomes in recent years, this review will propose original recommendations for research and updates for future guideline amendments.

Methodology

The purpose of this methodology section is to detail the approach used to ensure the reliability and validity of the findings regarding the NG51 guidelines presented in this review. The research was conducted across several databases, including PubMed, Google Scholar and articles published by the UK Sepsis Trust, Academy of Medical Royal Colleges and NHS England. To ensure research bias was minimised, relevant keywords were developed related to the themes of this review and were consistently used, including 'elderly sepsis', 'NICE guidelines', 'detecting sepsis' and 'sepsis outcomes'. Titles and abstracts were screened first, prior to review of the full text. Moreover, a combination of research articles, reports, news articles and quotes were used to provide further context on current perspectives and challenges in sepsis management from leading experts.

Studies that did not directly address the research question regarding sepsis detection and outcomes in the elderly patient demographic (adults aged 65 years or older) were excluded from this review. Furthermore, whilst international studies were included in this review, providing particularly valuable insights for future iterations to NICE guidelines, UK-based studies on sepsis management and outcomes were prioritised due to the intention to focus specifically on the implementation and impact of NICE guidelines within the UK healthcare context.

Limitations of this review include the limitations of the included studies and the potential for publication bias, as studies with inconclusive results may be underrepresented in the literature included.

Positive implications of NG51 updates

The 2024 NG51 update amends important considerations involving recognising sepsis early. Firstly, whilst sepsis is typically suspected in individuals recording a temperature >39°C or <36°C, some people with sepsis will record normal body temperature, previously including patients who are elderly, infants, have cancer and severe sepsis. The 2024 update includes patients with spinal cord injuries, thus increasing vigilance for potential hidden cases of sepsis.

NG51 includes further details informing early antibiotic treatment. Evidence highlights prescribing antibiotics within the first hour of suspecting sepsis is crucial for successful recovery. From 2024, ambulance staff should administer antibiotics if the hospital transfer time exceeds one hour and if the patient meets any high-risk criteria, minimising delayed treatment. Outlined are the high-risk criteria for patients aged >12 years: new altered mental state, respiratory rate >25bpm, requiring >40% oxygen delivery to maintain SaO_2>92% (SaO_2>88% in COPD), systolic BP <90mmHg (alternatively >40mmHg below their normal systolic pressure), heart rate >130bpm, no urine output in previous 18 hours, cyanosis, mottled/ashen skin.

Prior to the 2024 update, research at James Paget University Hospital discovered the significance of early antibiotic administration. The trust increased the number of patients receiving antibiotics within one hour of suspecting sepsis from 63% to 87%. Subsequently, sepsis mortality decreased by 2.4% and admission length decreased by 3.3 days.[5] Thus, promoting early antibiotic treatment in the updated NG51 guidelines aims to reduce mortality rates and hospitalisation, enhancing patient reintegration into society and improving outcomes.

The most significant update is introducing the National Early Warning Score (NEWS2) for use in hospital, mental health and ambulance settings. Early warning scores assess patient deterioration, monitoring: temperature, heart rate, respiratory rate, oxygen saturation, blood pressure and consciousness level.[6]

A normal parameter scores 0, whilst the maximum score of 3 for a single parameter indicates increased risk of organ dysfunction.[7] NEWS2 facilitates regular vital sign monitoring, providing a visible trajectory of deterioration. Following recommendations by the Academy of Medical Royal Colleges in 2022, proposing "NEWS2 should be used to supplement clinical judgement to identify adult patients with suspected sepsis", using NEWS2 allows stratification of patients into risk categories, shown in **Table 1**.

Table 1. Data adapted from the Academy of Medical Royal Colleges (AoMRC) 'Statement on the initial antimicrobial treatment of sepsis: synthesis and recommendations'.[8]

Risk Category	Time of Sepsis Six Treatment Activation
High	Within one hour of suspecting sepsis
Moderate	Deferred for up to 3 hours to gather more specific diagnosis
Low	Deferred for up to 6 hours to gather more specific diagnosis

This intervention supports clinical decision-making by providing additional time for information gathering for a more precise diagnosis. This simultaneously benefits clinicians with clear frameworks to plan the most appropriate treatment pathway, and enhances patient outcomes by promoting antimicrobial stewardship, limiting excessive antibiotics, thus reducing antibiotic resistance.

Currently, 100% of ambulance trusts use NEWS2 for initial assessment, contrasting 76% of acute trusts using NEWS2 in England, with remaining trusts opting for alternative early warning scores.[9] Mandating NEWS2 use in NG51 targets universal application, aiming to reduce current confusion caused by nationwide variations in early warning scores, thus minimising compromising patient safety. NHS England argue national standardisation of NEWS2 in acute hospitals could prevent 1800 deaths annually, further stressing the significance of standardising NEWS2, proposed in NG51.[10]

Limitations of updates

Despite NG51 addressing some concerns, sepsis remains challenging to detect and treat accordingly, with new guidance still leaving ambiguity for healthcare professionals. NG51 urges clinicians to consider every sepsis diagnosis unique and to recognise nuances in history-taking, negatively encouraging hyper-vigilance. Nuances in history-taking are seen as common early sepsis markers, including heart rate, blood pressure, oxygen saturation, altered mental state and body temperature, could all remain normal despite underlying sepsis present, causing potential for more confusion than coherence for clinicians. Therefore, the headline "UK Sepsis Trust welcomes NICE sepsis guideline updates which herald end of confusing period for health professionals" arguably inflates the impact of NG51.[11]

Furthermore, a lack of guidance for sepsis over-diagnosis limits the value of NG51. Dr Paul Morgan, Sepsis Lead at Cardiff and Vale University Health Board, proposed, "Could this pressure to improve sepsis management be counterproductive and lead to over-diagnosis of sepsis?", suggesting hyper-vigilance, fuelled by new guidance, can generate over-diagnosis in non-septic patients.[12] The published NG51 'Recommendations for research' suggests: "The consequences of getting the decision-making wrong can be catastrophic and therefore many patients are potentially over-investigated and admitted inappropriately," further implying the consequence of over-diagnosis from NG51.[26]

A further limitation arises from the subjectivity in interpreting clinical guidelines, especially regarding antibiotic prescription. Given concerns regarding antibiotic resistance, this can create challenges in sepsis management. Specifically, the need for careful evaluation before initiating antibiotics introduces the potential for discrepancies amongst clinicians in determining appropriate treatment regimens based off differing interpretations of clinical guidelines and patient markers.[13] These disagreements can lead to delayed antibiotic administration, a critical factor in sepsis survival, and, subsequently, may contribute to workplace conflict.

Whilst over-diagnosis is favoured over risking consequences of misdiagnosis, treating patients without sepsis with Sepsis Six results in unnecessary invasive procedures and antibiotic misuse, contributing towards antibiotic resistance. Given antibiotics are the most effective sepsis treatment, inappropriate use risks affecting effectiveness of future treatments, worsening sepsis mortality.[14]

Regarding NG51 recommendations, a recent Netherlands-based trial suggested limited evidence behind the effectiveness of pre-hospital antibiotics. Despite administering antibiotic treatment (median 26 minutes) prior to hospital arrival, the study found no signs of prognosis improvement, questioning NG51 recommendations.[15]

Challenges in elderly patients

Recognising and managing sepsis is challenging for clinicians; this task becomes increasingly complicated involving elderly patients, dominating sepsis prevalence, given the mean sepsis patient age in 2021–22 being 71 years old. Additionally, elderly patient outcomes are significantly worse, with 77% of sepsis-related deaths in England in people aged 75 years or older, therefore NG51 should aim to improve these outcomes given years of stalling progress.[16]

Complex histories often seen in elderly patients complicates early sepsis detection. Upon initial assessment, elderly patients with sepsis often present with non-specific symptoms, including confusion, immobility and incontinence, easily discouraging clinicians from diagnosing sepsis. Alternatively, many elderly patients suffer comorbidities and exacerbation can cause organ dysfunction, mirroring sepsis, misleading clinicians into a false sepsis diagnosis; this bears potentially fatal consequences. Moreover, some comorbidities can cause an individual's blood variables to deviate outside the 'normal range,' potentially leading clinicians to over-diagnose sepsis due to misinterpreting these variables, which may be normal for the patient's comorbidity. Thus, NG51 should further emphasise the importance of considering the individual's medical history to reduce over-diagnosis.[17] Subsequently, patients receive inappropriate or delayed treatments for sepsis, elevating mortality rates.

Furthermore, ethical considerations should be appropriately discussed when treating elderly patients with sepsis. Treatments must respect patient autonomy and dignity, and clinicians must consider legal and ethical frameworks to guide treatment accordingly. Many elderly patients clarify their 'ceilings of treatment,' commonly including DNR and ReSPECT; these can impose significant limitations on sepsis treatment, which involves invasive interventions, notably lumbar punctures and administering intravenous antibiotics and fluids. These treatments must be evaluated alongside the individual's best interests, given many older patients argue quality of life supersedes intensive treatments that potentially lengthen life.[18]

Moreover, whilst evidence regarding over-treating sepsis is limited, a 2020 study assessing elderly cancer patients highlighted "vulnerable older patients treated with intensive therapy may actually have higher all-cause mortality as a result of treatment toxicity", indicating the complications treating sepsis in elderly patients, as urgent clinical decisions require an understanding of complex physiology, twinned with patient beliefs and ethical considerations.[19]

Considerations for future updates

Whilst NEWS2 should be encouraged to aid identifying suspected sepsis, the increasing emphasis fuelled by NG51 poses a serious risk of NEWS2 over-reliance, highlighted by the Health and Safety Investigation Branch: "NEWS2 is not intended to be a stand-alone tool."[20]

Patient age is a common leading determinant for treatment, however, future NG51 amendments should encourage using patient scoring systems, promoting holistic decision-making. The Clinical Frailty Score (CFS) could partner alongside NEWS2; a 2022 study discovered those classified as 'frail' (CFS 5-9) had a 10% increased sepsis mortality risk than 'non-frail' patients (CFS 1-4).[21] During the COVID-19 pandemic, CFS was endorsed by NICE to identify at-risk patients, discovering for every one-point score increase, mortality rose by 12%.[22,23] CFS has only been validated in patients over the age of 65 years, but the Clinical Frailty Score offers a practical advantage in emergency settings: its rapid assessment by healthcare staff, combined with evidence from a 2023 study suggesting it is both relevant and easy to use, provides clinicians with additional support for informed clinical decision-making in sepsis.[24]

Furthermore, the Katz Index of Independence in Activities of Daily Living can be utilised to aid sepsis prognosis and outcomes in hospitalised patients. The score assesses six Activities of Daily Living (ADL): bathing, dressing, toilet use, transferring, continence and eating. A 2023 study found approximately 79% of elderly patients with sepsis developed brain volume reduction, with a strong positive correlation to poor ADL function. Reduced ADL function significantly increases the risk of post-intensive care syndrome, decreasing the likelihood of successful reintegration into society for elderly patients.[25] Implementing the Katz Index to assess an individual's functional ability will assist clinicians in planning appropriate re-integrative care for elderly patients with sepsis. This highlights the importance of encouraging the use of alternative scoring systems in future NG51 updates, supporting sepsis diagnosis and improving post-sepsis outcomes.

The original 2016 NG51 guidelines recommended research into developing "a set of clinical decision rules or a predictive tool to rule out sepsis". Using NEWS2 initially, followed by a blood test confirming systemic infection, is essential for clarifying a sepsis diagnosis.[26] However, since obtaining blood test results typically takes hours, individuals are prescribed antibiotics prior to receiving a confirmed diagnosis. Elevated biomarkers, including white blood cell count (indicating active immune response), C-reactive protein (suggesting inflammation), and lactate (produced in hypoxic conditions, such as infection) are key indicators of sepsis in a blood test.[27] Bedside biomarker tests could therefore enhance early sepsis detection and limit over-diagnosis. Currently, tests are available, such as Actim CRP, a skin-prick blood test which records CRP levels within 5 minutes, contrasting hours awaiting blood test results.[28] Experts from a 2024 study analysing various biomarkers for sepsis diagnosis recommended "The combination of biomarkers allows for a more holistic assessment of the pathophysiology of sepsis, leading to a more accurate diagnosis and monitoring of the disease", thus enabling clinicians to "customise treatment plans based on the individual patient's response to therapy and disease progression".[29] Future research should therefore investigate the association between bedside biomarker monitoring in suspected sepsis cases and the risk of severe illness or death.

Current NICE guidance states NEWS2 use is not mandatory in primary care. In secondary care settings, NEWS2 has a clear 'tracking' value, as patients are monitored at regular time intervals. This poses a significant challenge in primary care due to impracticalities surrounding regular patient monitoring. Despite this, there is an argument to encourage NEWS2 use in primary care, supported by recent recommendations by the Royal College of General Practitioners "for GPs to use NEWS2 scores as part of their clinical

assessment of acutely deteriorating patients".[30] A 2021 study found in a sample of 206 GPs, overwhelmingly 98.1% concluded 'gut feeling' was their most used diagnostic method for suspecting sepsis. Only 1.5% of participants used the UK Sepsis Trust criteria as their main method for identifying sepsis.[31]

Given a considerable proportion of primary care consultations involve elderly patients who may present with infection, using NEWS2 and other scoring systems for clinical decision-making, rather than reliance on 'gut feeling', could prompt earlier identification of sepsis in community settings, thus improving outcomes. Dr Ron Daniels, CEO of UK Sepsis Trust, argued involving GPs in sepsis detection "is increasingly relevant as transit times increases and could be potentially transformational in terms of patient outcomes".[32] Thus, investigating a correlation between NEWS2 use in primary care for infectious patients and sepsis incidence in the community is important for future research in identifying sepsis, particularly involving hidden cases amongst elderly patients.

Detecting early signs of sepsis in care homes could be enhanced by proposing NEWS2 use to track deterioration. Andy Platt, Project Manager at Kent Community Health NHS Foundation Trust, argued care home residents "aren't monitored very closely and usually only receive care once the care home staff notice that the patient's health has visibly deteriorated", yet introduction of the NEWS2 scoring system could aid premature detection and treatment for resident deterioration, preventing severe complications of sepsis.[33] Implementing NEWS2 use in care homes has proven popular, supporting care staff to make decisions regarding escalating health concerns in addition to improving clearer communication between care and healthcare staff.[34] Therefore, updating NG51 to encourage GP and care staff to use NEWS2 for elderly patients presenting with infection could minimise current misdiagnosis, thus being hugely impactful.

Conclusion and refle tions

In conclusion, the 2024 NG51 update aims to advance sepsis outcomes in England by addressing key improvements in identifying and treating suspected sepsis cases. Recognising sepsis is a subjective challenge for clinicians daily, and by standardising NEWS2 use to detect patient deterioration and early sepsis, healthcare staff will be capable of administering antibiotic treatment promptly. Moreover, NG51 is coherent and thorough, with important clinical decision-making supported by the outlined NEWS2 risk categories.

Upon reflection, diagnosing sepsis in elderly patients will remain challenging for the foreseeable future, and whilst NG51 will continue supporting clinicians with new tools, such as NEWS2, this alone is unlikely to transform sepsis management. Ultimately, whilst future iterations of NG51 have potential to enhance primary care guidance by targeting the clinical characteristics of the elderly patient cohort specifically with additional diagnostic support, its application in emergency settings reinforces the synergy between clear guidelines and informed clinical decision-making to improve sepsis outcomes in elderly patients.

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I am a second-year medical student at the University of Bristol. Within medicine, I'm motivated to leverage insights from guidance and policies to create real-world, practical, impactful solutions and frameworks that equip healthcare professionals to deliver optimal patient care. My current interests in medicine include emergency care and oncology, which I am keen to explore further.

Review

Unmasking the dangers of society's idealisation of sleep deprivation

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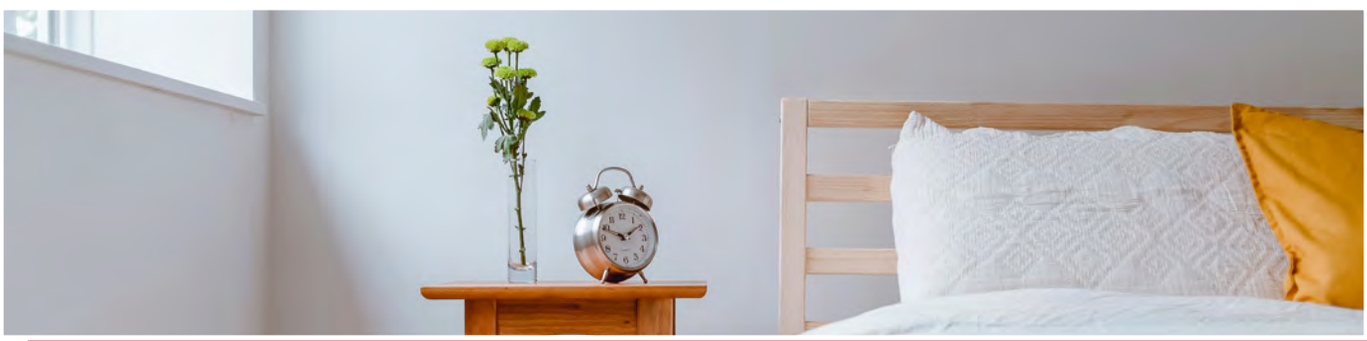

Abstract

This review explores the prevalence of sleep deprivation and the societal norms that perpetuate it, as well as the subsequent health consequences. A review of existing literature from databases such as PubMed, Science Direct and Google Scholar was conducted. This paper finds that factors such as social influences around perceived attainment from reduced sleep, socioeconomic disparities and urbanisation contribute to widespread sleep deprivation, disproportionately affecting individuals from lower-income and minority backgrounds. The glorification of reduced sleep, particularly in high-pressure professions, further exacerbates this trend. Findings highlight the urgent need to challenge societal perceptions of sleep and implement public health initiatives. Addressing sleep deprivation requires a cultural shift that prioritises health over the relentless pursuit of productivity.

Abbreviations

CRP – C-Reactive Protein
HPA – Hypothalamic-Pituitary-Adrenal Axis
IL-6 – Interleukin-6

Introduction

Sleep is a crucial physiological process for both mental and physical well-being. Insufficient sleep significantly elevates the risk of long-term health complications, such as an increased risk for cardiovascular disease, depression and cancer.[1] Nevertheless, modern society venerates sleep deprivation and boasts about heightened productivity and achievement resulting from reduced sleep duration. Since embracing a 24/7-hour work culture in our modern society, our focus has shifted toward career advancement at the expense of prioritising health, when, in fact, sleep deprivation undermines productivity and well-being.[2] The societal idealisation of sleep deprivation refers to the way in which society promotes overworking and functioning on minimal sleep as a sign of dedication, productivity and success. The recommended sleep duration for adults stands at 7–9 hours per night.[1] However, a substantial portion of adults fail to meet this recommendation. A study analysing the average sleep duration among American adults from 2010 to 2018 revealed that 33.6% reported sleeping 6 hours or less, with this figure escalating to 35.6% when looking solely at the data from 2018.[3] This presents an increasingly substantial challenge, influenced in part by demographic factors such as culture and socioeconomic status.

Research indicates that individuals from lower socioeconomic backgrounds often experience shorter sleep durations due to work-related pressures and urban migration. Sleep disparities are further compounded by racial and ethnic inequalities. In the UK, for example, Black, African, Caribbean or Black British employees earned a lower median hourly wage than their White counterparts as of 2022, making it more likely for them to work overtime or multiple jobs, especially amid the current cost of living crisis, ultimately reducing their sleep duration.[4] Similar pay gaps are observed in the USA.[5] Findings from multiple studies reinforce the idea that these disparities in sleep patterns contribute to broader health inequalities.6 Ultimately, this societal shift neglects natural sleep cycles, warranting an examination of its origins and strategies for improving individuals' health outcomes concerning sleep quality and adequacy.

The idealisation of sleep deprivation

Historically, our sleep duration has significantly changed, with notable observed deviations between the mid-20th century and contemporary times. During the 1950s, the average duration of nightly sleep approximated 8 hours, markedly contrasting with prevailing trends in modern-day culture where adults typically allocate approximately 6.5 hours to sleep.[7] We are increasingly abstaining from our natural circadian rhythm, and a multitude of factors have been postulated to account for this deviation, such as urbanisation and technological advancements.[8] However, a pivotal determinant contributing to this trend lies in the societal pressure emphasised on economic attainment, coupled with the pressures of competitive working environments.[2]

An illustrative manifestation of this is seen in the widespread propagation of the '5am routine' phenomenon across various social media platforms, thereby instigating feelings of culpability among individuals who fail to adhere to these ostensibly health-oriented trends.[9] This tendency is especially pronounced in certain professions, where compromised sleep quality is revered if it translates to

heightened productivity or accomplishment. Medical students represent a pertinent example, renowned for prioritising their academic responsibilities over adequate sleep. A study conducted among a cohort of 177 medical students found that 49.7% reported poor sleep quality, with 26.5% reporting nightly sleep durations of less than 6 hours.[10] The reasons for this trend were found to be a pursuit of enhanced academic success and the persuasive influence of peer norms within the medical community. However, the findings of this study found that compromised sleep duration correlated inversely with academic attainment, as well as detrimental effects on both physical and mental health.[2,10]

Adherence to societal pressures can largely be attributed to conformity to social norms. Studies have explored the neural mechanisms underlying conformity, revealing that most individuals are highly influenced by majority opinion, particularly when it is consistent with prevailing trends.[11] People conform to the majority to avoid negative consequences or social rejection. It is human nature to seek acceptance, especially when misinformation leads us to believe that certain behaviours, such as reduced sleep, are beneficial.[11] However, it is important to acknowledge that the neural mechanisms behind social conformity are not yet fully understood.[12] Additionally, the populations studied may be more susceptible to compliance in environments where a dominant opinion is expressed. While some individuals may challenge these norms, the sharp rise in poor sleep duration across Western populations suggests that conformity plays a significant role in perpetuating this trend. Therefore, it is crucial to challenge these societal beliefs and dispel the misinformation surrounding sleep deprivation and its true impact on health and well-being.

The impact of sleep deprivation on health

Sleep deprivation not only impacts productivity but also entails significant long-term health implications, including cardiovascular disease, dementia and respiratory disorders.[1] Several hypothesised mechanisms explain how sleep deprivation affects cardiovascular health; one of the primary theories is via inflammation. Research has linked insufficient sleep with increased levels of biomarkers such as C-reactive protein (CRP) and interleukin-6 (IL-6), both of which are key inflammatory molecules. Elevated CRP is a biomarker for individuals at risk of cardiovascular disease, while IL-6 has been linked to impairments in cortisol regulation. This disruption negatively affects the cortisol awakening response and its daily decline, leading to fatigue and further difficulties with both falling asleep and waking up.[13,14]

Additionally, inflammation resulting from sleep deprivation has been found to heighten activity in the hypothalamic-pituitary-adrenal (HPA) axis. The HPA axis plays a crucial role in sleep modulation and cardiometabolic regulation through its effects on inflammatory mediators. When overactive, the HPA axis has been associated with elevated blood pressure and increased central adiposity.[15] Furthermore, its activation is theorised to contribute to inflammatory mechanisms involved in the pathogenesis of atherosclerosis. These factors collectively increase the risk of developing cardiovascular disease.[14]

Beyond cardiovascular disease, there are also correlations between sleep deprivation and depression, which is underscored in numerous studies, with this association closely linked to burnout.[16] Moreover, sufficient sleep has been identified as a crucial factor in lifespan. A meta-analysis involving 1,382,999 participants of both genders examined the relationship between sleep duration and mortality risk, with the findings indicating that shorter sleep duration was associated with an increased mortality risk.[17] As well as this, the 24/7 work culture disrupts our natural circadian rhythms, and chronic disturbances of these rhythms have been theorised to contribute to the development of cancer.[18]

Beyond its enduring health ramifications, sleep deprivation significantly compromises performance, particularly in terms of concentration and reaction time. Multiple studies have investigated the comparative effects of alcohol consumption and sleep deprivation on reaction time and alertness. One study revealed that reaction times when sleeping less than 6 hours equated to those after consuming three pints of beer, while others discerned slower response speeds in sleep-deprived individuals compared to those drinking alcohol.[19, 20] The danger posed by sleep deprivation manifests in its potential impact on driving safety and occupational performance, with ramifications extending to medical practice. Notably, it was reported that over 5 years, 29,834 fatalities were attributed to accidents involving drowsy drivers.[21] Collectively, these studies underscore the profound effects of sleep deprivation, advocating for heightened awareness of its detrimental consequences to mitigate the societal idealisation thereof.

Barriers to healthy sleep

Numerous factors impede individuals from prioritising sleep, including work demands, urbanisation and socioeconomic deprivation. The migration of individuals from rural to urban areas for employment has surged significantly, particularly in developing nations, with the urbanisation rate skyrocketing from 14% to 50% since the 20th century. This demographic shift is closely linked to disruptions in circadian rhythms, as urban environments encourage sedentary lifestyles and expose individuals to noise pollution and irregular work schedules.[22] A review of multiple studies found that individuals in urban settings are significantly more likely to develop insomnia than those in rural areas.[23] One reason for this is that urban residents are more likely to live alone or in densely populated cities with higher crime rates, making them more sensitive to potential dangers at night. Additionally, urban living may be inherently misaligned with human evolutionary adaptations, as rapid urbanisation disrupts natural sleep cycles.[23] Research has further highlighted behavioural factors contributing to poor sleep in urban areas, including reduced physical activity and increased screen time.

While the mechanisms linking exercise to sleep quality are not fully understood, physical activity has been shown to produce anti-inflammatory cytokines, improve mental health and promote brain neurogenesis, all of which benefit sleep.[24] In addition to urbanisation, socioeconomic pressures further exacerbate sleep deprivation. The prevalence of these behaviours can be attributed to the longer working hours of individuals in cities, driven by the widespread belief that reduced sleep enhances productivity. Additionally, the escalating cost of living in urban areas necessitates longer work hours, reinforcing the pervasive sleep deprivation culture. This trend is particularly pronounced among individuals of Black ethnicity, exemplified by the stark income disparity between Black and White households, where in the United States, the median Black household income is ten times less than their White counterparts.[5] Consequently, individuals of Black ethnicity frequently report nightly sleep durations of 5 hours or less compared to people of White ethnicity.[25] Socioeconomic disadvantages often compel individuals to undertake multiple jobs or night shifts, significantly disrupting their natural sleep cycle. Disparities in sleep duration across ethnicities contribute to the heightened prevalence of chronic health conditions among non-Hispanic Black, non-Hispanic Asian and non-Mexican Hispanic/Latino people, all of whom report considerably shorter sleep durations than non-Hispanic White people.[25] Due to the imperative of maintaining employment and sustaining basic living standards, individuals experiencing socioeconomic deprivation often struggle to obtain sufficient sleep as the necessity to work to support themselves and their families impedes their ability to prioritise rest.[3] Consequently, accessible support mechanisms need to be available to address the adverse impact of sleep deprivation on their well-being. These could include community programs that provide support for sleep hygiene and education, as well as workplace initiatives that promote more flexible schedules. Additionally, workplaces should offer education on the health impacts of sleep to raise awareness within the community about the importance of a good night's rest.

Challenging the sleep deprivation epidemic

To address the sleep deprivation epidemic, it is imperative to implement strategies aimed at promoting optimal sleep health and raising awareness about the dangers of inadequate sleep, commencing from childhood. While most health promotion initiatives prioritise exercise and dietary habits, the significance of adequate sleep and sleep hygiene rarely receives attention.[26] Efforts directed towards enhancing public understanding of sleep's vital role in overall well-being may facilitate the mitigation of this pervasive issue. For individuals having trouble falling asleep, numerous studies have underscored the efficacy of several methods such as relaxation techniques, mindfulness and listening to soothing music in improving sleep duration and quality.[27,28] Greater accessibility and encouragement of such methods could potentially precipitate a transformation in societal norms surrounding sleep. Promoting a balanced approach to work and personal life, coupled with educational endeavours aimed at guiding individuals towards seeking support when their lifestyle impedes adequate sleep, could yield substantial benefits.[26] While immediate changes may not be evident, reshaping societal attitudes towards recognising the health benefits of a good night's sleep represents a pivotal starting point.[28]

Conclusion

The idealisation of sleep deprivation in contemporary society poses significant threats to both individual health and societal well-being. Despite clear evidence highlighting the importance of adequate sleep, modern culture often celebrates reduced sleep duration as a symbol of productivity and success. Societal pressures, economic demands and disparities in access to resources further exacerbate the problem, putting people at risk for long-term health problems, particularly among those experiencing socioeconomic deprivation. In essence, recognising the detrimental consequences of sleep deprivation and taking proactive measures to address them is paramount for fostering a healthier and more resilient society. By implementing public health initiatives, such as introducing sleep education programmes in schools and encouraging workplaces to adopt flexible working hours into their policies, we can begin to reshape societal attitudes toward sleep. By promoting the 7–9 hours of sleep needed per night, we can begin to mitigate the adverse effects of sleep deprivation and promote overall well-being for individuals and communities alike. This harmful idealisation can be halted by spreading awareness of the importance of adequate sleep.

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Holly Kean

I am a second-year medical student at the University of Plymouth. I began this piece in my first year during a Student Selected Unit and developed a strong interest in the topic, particularly in the role of public health campaigns and education in improving health. I have thoroughly enjoyed the writing process and hope to continue conducting further research and writing projects in my current fields of interest: cardiology and neurology. In my free time, I enjoy dancing, particularly ballet, which has been a lifelong passion of mine.

Review

How effective is aducanumab at reducing beta-amyloid plaque in Alzheimer's Disease?

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Abstract

Alzheimer's Disease (AD) is a widespread fatal neurodegenerative disease. Evidence suggests toxic beta-amyloid, which is produced in the brain, aggregates into plaque unique to Alzheimer's, which causes symptoms commonly associated with AD. No cure exists, creating an urgency to design drugs targeting the disease's pathophysiology. Aducanumab shows promise in plaque reduction. This is monitored using biomarkers, functional imaging and cognition scoring. This review aims to evaluate the effectiveness of aducanumab at reducing beta-amyloid plaques, by considering change in biomarkers, position emission tomography (PET) results and cognition. When observed using amyloid biomarkers to detect plaques, studies show aducanumab is effective at reducing plaques at certain doses. This is supported by studies using PET scans to visualise and assess plaque levels. These results were statistically significant and applicable to the wider population. However, studies disagree on cognitive findings, remaining unclear about the extent of clinical benefits of aducanumab, and the link between reducing plaques and improving cognition. Long-term randomised controlled trials are needed to investigate whether there is a correlation between plaque removal and cognition, while evaluating optimal dosing strategies.

Abbreviations

AD – Alzheimer's Disease
Aβ - beta-amyloid
mAb – monoclonal antibody
IgG1 – immunoglobulin G1
FDA – food and drug administration
MCI – mild cognitive impairment
CSF – cerebrospinal fluid
PET – positron emission tomography
Aβ-PET – positron emission tomography for beta-amyloid plaques
CDR-SB – Clinical Dementia Rating Sum of Boxes
MMSE – Mini Mental State Examination
ADAS-Cog13 - Alzheimer's Disease Assessment Scale-Cognitive Subscale
RCT – randomised controlled trial
PV3 – protocol version 3
PV4 – protocol version 4
ARIA – Amyloid Related Imaging Abnormalities
ApoE – apolipoprotein E

Introduction

Alzheimer's Disease (AD) is a neurodegenerative disease destroying memory and thinking skills and, over time, the ability to perform everyday activities.[1] It is the most common form of dementia in the UK.[2] More than 6 million Americans live with AD, and by 2050 this is expected to increase to 13 million.[3] Currently there are no curative treatments, and previous treatment focuses only on reducing and managing symptoms, not modifying disease pathology,[4] which is why drug development is so important in treating and potentially reversing the disease.

Evidence supports the amyloid cascade hypothesis. This is where toxic beta-amyloid protein (Aβ) is produced in the brain in soluble monomer form, which then aggregates into larger molecules, including soluble oligomers then protofibrils, until insoluble fibrils are formed which accumulate into plaques;[5] this is one of the characteristic pathologies underlying AD.[5] These plaques reduce the ability for synaptic transmission, causing neurones to shrink and die,

which contributes to symptoms. The most neurotoxic form is Aβ42, which is most likely to form plaque.[6] This pathway can be targeted by monoclonal antibodies.[5]

As such, aducanumab is a recombinant human monoclonal antibody (mAb), so binds selectively to a specific target. Aducanumab is a humanised immunoglobulin G1 (IgG1) molecule.[7,8] It is derived from a blood lymphocyte library collected from a healthy donor population of elderly individuals who exhibit slow or absent cognitive decline.[9,10] The mechanism of action involves binding to both aggregated soluble Aβ oligomers and insoluble fibrils to cause plaque removal, since the monomers are non-neurotoxic.[11–13] Aducanumab is the first Food and Drug Administration (FDA) approved anti-amyloid mAb. It is widely tested in early stages of AD, primarily in mild to moderate cognitive impairment (MCI) due to AD or mild Alzheimer's dementia.[12]

Consequently, aducanumab's effectiveness can be measured in numerous ways, including via biomarkers. A biomarker is a measured characteristic indicating normal biological or pathogenic processes, or responses to an exposure or intervention.[14] A pharmacodynamic biomarker measures change in disease progression by assessing response to therapeutic agents.[15] The main Aβ biomarker is an Aβ isoform, Aβ42, which is present in cerebrospinal fluid (CSF) and plasma.[16] An inverse relationship exists between Aβ42 levels in CSF and plasma, and the number of amyloid plaques,[16] because there is less soluble Aβ42 as it has aggregated into fibrillar state in plaques.

However, because biomarkers alone are not enough to provide substantial evidence of plaque reduction, both biomarkers and imaging are used together to evaluate plaque reduction.[17] One imaging form used is positron emission tomography (PET) for beta-amyloid plaques (Aβ-PET). By using radioactive pharmaceuticals that bind to insoluble Aβ fibrils,[18] plaques become visible in imaging.

Although reducing plaques is useful, an important feature of drugs is clinical efficacy. This is quantified by cognitive assessment, which is achieved by multiple scoring systems to assess severity of disease and symptoms. These measure thinking abilities such as memory, language, reasoning and perception, which are some of the symptomatic areas affected in this disease.[19] The primary method is Clinical Dementia Rating Sum of Boxes (CDR-SB). Other methods include Mini Mental State Examination (MMSE), and Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog13). This review aims to evaluate the effectiveness of aducanumab through its reduction on Aβ plaques, by considering biomarkers, PET imaging and cognitive effects.

Methods

Both Medline (PubMed) and Web of Science databases were searched. The search string used was as follows: (anti-amyloid beta protein drugs) OR (amyloid beta) AND (monoclonal antibodies) OR (MAB) OR (amyloid plaque) AND (Alzheimer's) AND (Aducanumab). Randomised controlled trials (RCTs) and clinical trials were included, and papers published before 2018 were excluded, to ensure recent up-to-date research, yielding three primary studies after screening against irrelevance and incongruent endpoints. Other sources were retrieved using reputable websites, PubMed, and systematic reviews. **Figure 1** illustrates the process of primary evidence synthesis.[20]

Results and discussion

Biomarkers

A study by Ferrero et al investigating both pharmacodynamics and the effect of aducanumab on plasma biomarkers reported no significant effect on plasma Aβ levels between the minimal dosage (0.3mg/kg) and maximally tolerated dosage (30mg/kg).[21] This is consistent with aducanumab's very low affinity for binding soluble monomeric Aβ,[21] since it specifically targets oligomers and fibrils and not monomers. It also reported an increase in Aβ42 at the maximum dose given (60mg/kg). A later study by Biogen called EMERGE investigated biomarker effects as secondary and tertiary outcomes as part of a sub-study.[22] They reported statistically significant changes across the secondary endpoints of biomarkers. The biomarkers displayed dose-dependent increase in CSF $A\beta_{1-42}$ levels. The same results were observed in Biogen's identical study [22] ENGAGE. This suggests that aducanumab is binding to the soluble Aβ, leading to increased Aβ plasma concentration due to the stabilisation of circulating peptides.[23] All studies included[21,22] were randomised, double-blind, placebo-controlled trials, reducing bias in allocation and maintenance. However, a limitation is the subset of participants was not randomised, since the participants chose to opt-in to further sub-studies.[22] The study by Ferrero et al[21] had a small sample size of 53 with one participant withdrawing, however, at the maximum dosage administered, the increase in Aβ may be due to small sample size; this cohort demonstrated higher baseline values and patient variability than those with lower dosage,[21] so results may be positively skewed. However, despite the other studies[22] having a larger sample size overall, the biomarker sub-study tested 78 patients in EMERGE and 53 in ENGAGE,[22] which is a small sample size, not greatly aiding validity and reliability. Despite limitations, these outcomes provide supporting evidence for each other, suggesting aducanumab can reduce amyloid plaque levels. All three studies support each other's findings at a high dose level, however, classification of 'high dose' varies, with Ferrero et al's being higher than Biogen's. Ferrero et al show no significant effect at lower dose, but Biogen's show significant plaque reduction at their higher dose, suggesting multiple doses above 10mg/kg are most effective.

PET amyloid burden

Both EMERGE and ENGAGE recruited individuals with AD with MCI due to Alzheimer's or mild AD, aged 50-85, with confirmed amyloid pathology via PET scan.[22] They tested longitudinal amyloid imaging via PET scan. Both reported dose and time-dependent reduction in the amyloid burden shown on the PET scan. For EMERGE, the mean difference from baseline between high dose and placebo was -0.278 (95% CI, -0.306 to -0.250; P<0.0001), and for ENGAGE, it was -0.232 (95% CI, -0.256 to -0.208; P<0.0001).[22] The 95% CI for both studies is negative, suggesting a definitive reduction in amyloid burden compared to placebo cohorts. The very small p-values suggest there is strong evidence that, in this study, the mean amyloid burden in the intervention arm is not the same as the control arm, after 78 weeks. The sample size in these sub-studies was larger than the biomarker sub-studies, increasing the generalisability of this data; 488 and 585 participants in EMERGE and ENGAGE, respectively.[22] This reinforces that aducanumab is effective at reducing plaques. Two statistically significant results demonstrate concordance among both studies, however, the identical nature of the studies must be taken into account when drawing conclusions. However, when used with biomarker results, results from PET imaging can confirm conclusions drawn from biomarkers.

Cognition

Ferrero et al also investigated cognition. They documented no dose-dependent response or effect observed in the change of mean ADAS-Cog13 scores from baseline, suggesting no cognitive improvement.[21] EMERGE met its primary endpoint for CDR-SB, reporting 22% reduction in decline for high dose compared to placebo. Furthermore, all cognitive endpoints showed less cognitive decline compared to placebo, reporting across MMSE and ADAS-Cog13.[22] However, data from ENGAGE contradicts these findings, with an increase in cognitive decline in CDR-SB, of 2% vs placebo. This is supported by the secondary findings for MMSE and ADAS-Cog13, being not statistically significant.[22]

The study by Ferrero et al was single dose, with the highest safe and tolerable dose being 30mg/kg.[21] EMERGE was a phase three multi-dose trial. Participants received 20 doses of either high dose 10mg/kg, low dose 6mg/kg or placebo, in a 1:1:1 ratio over 76 weeks.[22] The differences in results may be explained by the difference in dosage

and dosing intervals; EMERGE delivered a lower dose in multiple doses at regular intervals over a longer period, whereas Ferrero et al's delivered a higher single dose.[21,22] This suggests multiple lower doses are more effective at improving cognition.

Two protocol adjustments were made in both EMERGE and ENGAGE during the trials that allowed more participants to receive the maximum dose. Protocol version 3 (PV3) allowed participants who had to suspend treatment due to adverse effects of Amyloid Related Imaging Abnormalities (ARIA), to resume dosing at the same dose and continue titration to the target dose, instead of resuming at a lower dose. Protocol version 4 (PV4) targeted apolipoprotein E (ApoE) ε4 carriers. This is a variant of the ApoE gene that increases the risk of developing AD and other dementias.[24,25] This increased the dose for carriers to the same target dose as non-carriers. Since nearly two thirds of participants were ApoE4+ carriers, PV4 had the greater potential to impact more individuals.[22] However, Biogen claim these adjustments were of greater benefit to EMERGE patients since it started one month later than ENGAGE and enrolled more individuals after each amendment.[22] This may explain the differences in results between the two trials, since more EMERGE participants received a higher dosage. The differences in the cognitive results appeared to violate pre-determined futility criteria, since the two trials appeared to be displaying different results, and so both trials were ended prematurely. However, it was later determined that statistical analysis had been done incorrectly and so results up until the day before futility was declared were used. Since the results were taken still under double-blind conditions, validity remains unaffected.[22]

Biogen's studies, however, had a much larger cohort than Ferrero et al's, of 1638 and 1647 respectively. With these taking place at 348 sites in 20 countries,[22] this setting provides external validity, meaning the results are more likely to be applicable to a broader demographic. However, the mean number of participants per site was nine, which is a very small sample size so is not representative of the population surrounding each site. They[22] are also more representative of the global population than the earlier study.[21] Despite all three studies having a majority of White participants,[21,22] EMERGE and ENGAGE have 74–80% White participants in each cohort,[22] whereas Ferrero et al's study has four dosage groups at 100% White participants, and the others between 67–93%.[21] EMERGE and ENGAGE therefore had a higher proportion of non-White participants compared to the other,[21,22] therefore offering greater representation of the different populations.

Cognitive screening tests are widely used to assess Alzheimer's staging, severity and changes, however, each have their own limitations.[29] The ADAS-Cog tests, such as subtype ADAS-Cog13, has limited utility in MCI, as there may be little cognitive decline to detect. This may affect the ability of the test to detect change so early on and may be insufficiently responsive for trials with MCI.[26] Confounding variables are hugely present in the MMSE. Intellectual disability, educational level, cultural differences, physical problems, and language or speech problems can all affect the absolute score, relying upon factors other than memory.[27–29] However, since this is being used to track a trend, the influence of the test itself on the overall outcome of the study becomes largely irrelevant. The CDR-SB is obtained by interviewing both patient and care partner,[30–32] which increases reliability and provides sociocultural context and baseline function, although this is of questionable relevance when tracking trends.

The disease and symptoms of AD are not solely due to Aβ plaque deposition.[33] Plaque deposition leads to hyperphosphorylation of tau protein, causing protein misfolding and aggregation within neurons.[33] This forms neurofibrillary tangles, which is another characteristic feature of AD.[33] Theoretically, the reduction in plaques seen with aducanumab treatment should reduce hyperphosphorylation of tau, and therefore should cause downstream effects on cognition. As such, any changes in tau tangles, which are also multifactorial, could act as confounding factors for changes in cognition. Additionally, consideration needs to be given to the rates at which plaques are synthesised and deposited, their removal by aducanumab, and their net deposition. Other confounding factors include aducanumab safety considerations, such as treatment-related adverse events, like ARIA.[3] These encompass neuroinflammatory changes such as interstitial vasogenic oedema or sulcal effusion, (ARIA-E), and microhaemorrhages, and haemosiderin deposition, (ARIA-H)[34] which in turn, may alter cognition.

The studies demonstrate variation in cognitive results. The differences between Ferrero et al's study and EMERGE suggest multiple doses of 10mg/kg are more effective than a single 30mg/kg dose, however, ENGAGE data contradicts this. Nevertheless, this does not provide convincing evidence that the drug is ineffective as there is no accounting for confounding variables, differences in patient cohort or protocol adjustments impacting the trials differently.

Conclusion

Aducanumab is proven to be effective, as recognised by FDA approval. Studies show it removes Aβ plaques, demonstrated by an increase in CSF biomarkers, indicating plaque reduction. Both EMERGE and ENGAGE agree aducanumab is effective at reducing amyloid burden on PET imaging, supporting biomarker conclusions. Variation is observed in cognitive results.

Aducanumab is therefore shown to be quite effective at reducing Aβ plaques in early AD and demonstrates potential to exhibit cognitive improvements. However, there is no clear relationship between the extent of plaque removal and cognitive improvement. Longer-term RCTs should be conducted to correlate plaque removal and cognitive improvements, whilst considering regression to the mean and confounding variables. In addition, different dosing regimens should be trialled, from single to multi-dosing, low to high dose and frequency of dose, to find optimal dosing strategies for clinical outcomes in consideration with safety profile.

Since this review was conducted, Biogen have announced aducanumab will be discontinued and are reprioritising resources for further drug development.[35] This decision had nothing to do with efficacy or safety concerns.[35] Aducanumab has laid the groundwork for further research and has paved the way for a new class of drugs.[35] The principles of this drug have been refined in the form of lecanemab, a similar mAb.[36] Building upon selective Aβ targeting, lecanemab has a higher affinity for toxic protofibrils than aducanumab, the most toxic amyloid form.[36,37] Plaque removal has been honed and can now remove plaque much more quickly, and even prevent deposition of plaques.[37] Safety has also been improved, with a lower incidence of ARIA.[37] These advances would not have been possible without the foundations laid by aducanumab, and the potential it demonstrated, and so even though aducanumab is unlikely to be continued, its benefits will have long lasting impacts in future research.

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Sareena Khan

Sareena Khan is a second-year medical student at the University of Exeter. She has an avid interest in public health and global health policy, focusing particularly on health inequalities. She is very passionate about obliterating the gender inequalities that exist for women, particularly in cardiovascular health. She presented this article in poster form at the INSPIRE conference this year and also delivered an oral presentation on another poignant topic. She is a firm believer that passions outside of medicine should be explored, and so in her free time she loves to paint, play golf, and explore the Cornish coastline.

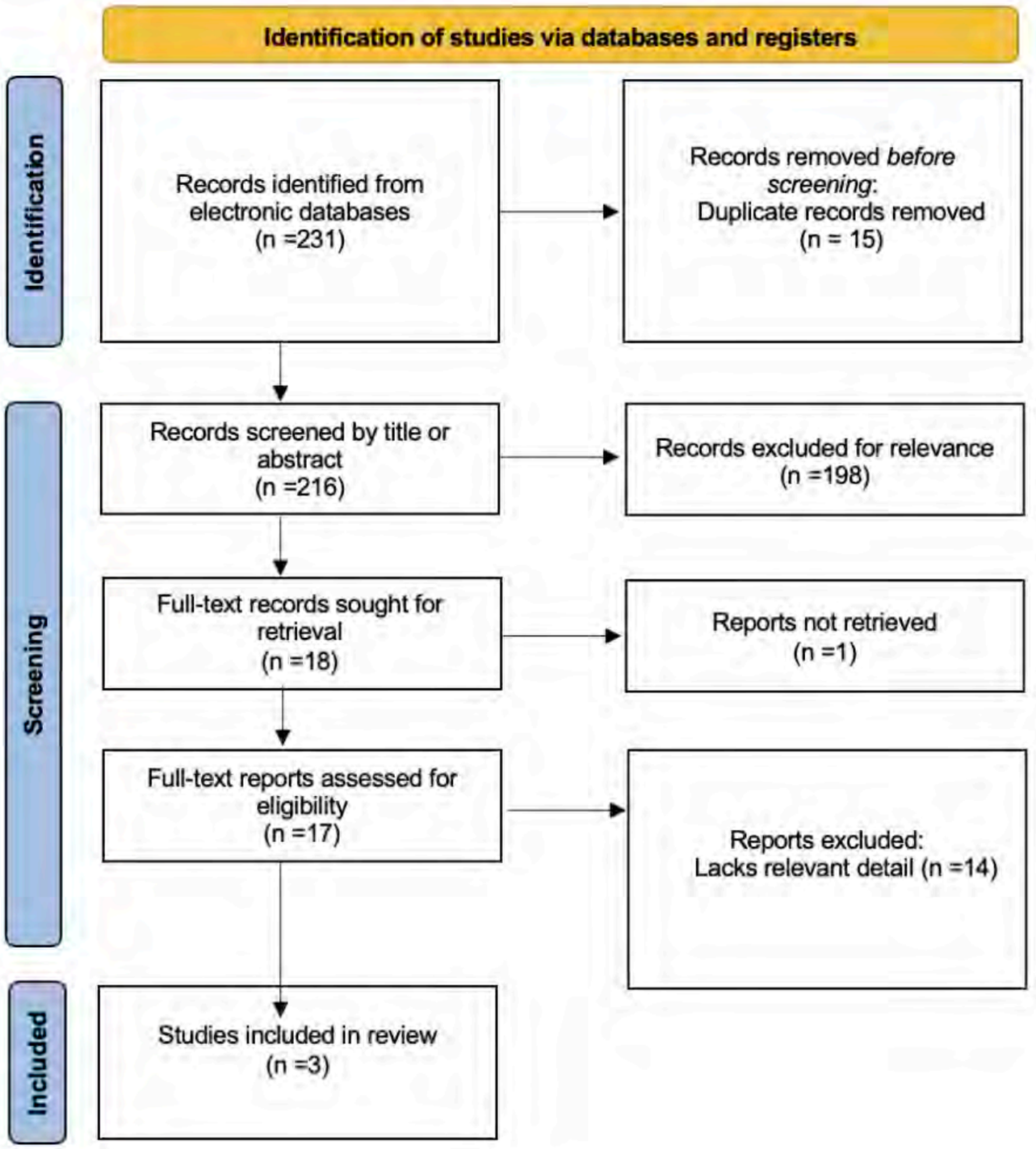

Figure 1. PRISMA diagram outlining primary evidence literature synthesis for this review. This PRISMA diagram has been adapted from the BMJ Prisma 2020 Statement.[20]

Review

To what extent do biological sex and gender affect women's symptoms and therefore mortality from acute coronary syndrome?

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Abbreviations

ACS – acute coronary syndrome
MI – myocardial infarction
UA – unstable angina
NSTEMI - non-ST-segment-elevation myocardial infarction
STEMI - ST-segment-elevation myocardial infarction
SCAD – spontaneous coronary artery dissection
ED – emergency department
RCT – randomised controlled trial
AMI – acute myocardial infarction
MAPMISS - McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey

Abstract

Acute Coronary Syndrome (ACS) is a highly prevalent fatal disease. It encompasses conditions like myocardial infarction (MI), which are due to a sudden reduction of blood flow to the heart, usually by a blood clot. Women are more likely than men to die from this, despite a lower prevalence. This disparity creates a health inequality. This review aims to investigate why there is a difference between in-hospital mortality for women hospitalised with ACS compared to men, by understanding whether there is a dimorphism between symptom presentation, and patient perception of symptoms, as two possible causes. Studies show symptom presentation differs between men and women, due to physiological differences, which are not widely recognised. In women, these differing symptoms appear to be perceived incorrectly, as 'atypical' symptoms, which in turn contributes to their statistically significant increased mortality. Studies should aim to quantify the extent of sex and gender interplay in symptomatology and mortality.

Introduction

Acute Coronary Syndrome (ACS) encompasses conditions including unstable angina (UA), non-ST-segment-elevation myocardial infarction (NSTEMI) and ST-segment-elevation myocardial infarction (STEMI), caused by sudden reduced blood flow to the heart, commonly due to a blood clot within a coronary artery.[1] Other causes include plaque rupture, coronary vasospasm and spontaneous coronary artery dissection (SCAD).[2] Currently, 2.3 million people in the UK are affected, with 66,000 deaths a year.[3–5] Although disease prevalence is higher in men, women are more than twice as likely to die from ACS.[6] This disparity creates a fundamental health inequality between men and women.

The difference exists due to many factors. There are differences in ACS pathophysiology, varying with subclassification; STEMI occurs due to a blocked coronary artery or branch of supplying the heart, causing heart muscle death. Blood flow is reduced in UA and NSTEMI, but there is no muscle death.[1] The distinguishing feature between UA and NSTEMI is elevated cardiac markers in NSTEMI, like troponin, implying myocardial damage.[7] The most frequent diagnosis among

women presenting to the emergency department (ED) with suspected ACS is NSTEMI and UA.[8]

Sex is a biological variable, determined by genetic complement and chromosomes, which influences physiology and pathophysiology.[9] Specific to cardiovascular physiology, women have smaller epicardial coronary arteries and lower plaque burden than men. These may contribute to sex-based pathophysiological differences, such as more diffuse and non-obstructive coronary artery disease, twice the prevalence of microvascular dysfunction,[10–13] and having more plaque erosion and coronary vasospasm.[13]

These pathophysiological differences in turn cause differences in symptomatology and disease presentation and affect how women experience the disease.[14] Such differences are poorly understood and not widely realised due to a fundamental problem, which is cardiovascular research bias. Most studies do not report on sex, or they have mostly male participants and extrapolate results to women.[15,16] Consequently, the disease model has been built towards male physiology.[17] This has led to disease patterns and phenotypes causing symptoms more common to women being classed as 'atypical' compared to the traditional male model.[18] One study defines typical symptoms as chest pressure/heaviness/tightness/pain, sweating, shortness of breath, arm pain, jaw/neck pain. It defines atypical symptoms as chest numbness/tingling/pricking/stabbing, palpitation, nausea/vomiting, dizziness or syncope, fatigue, and indigestion.[19] Typically, chest pain is the most common symptom of ACS, however, this is more common in men than in women.[19]

The deficiency of research and awareness surrounding these differences in women leads to incorrect symptom perception, from both patient and provider sides. Focusing on patient perception, many women are unable to recognise their symptoms, as often they are not exclusively chest pain. Patient perception is influenced by gender not sex. Gender is a social construct, affecting access to healthcare and health-seeking behaviour, as well as perception of risk.[18] The effects of gender are determined by socio-cultural factors like gender representation, education and it affects knowledge of pathologies additionally.[10] This, in addition to different pain manifestations, aggravates this sexual dimorphism.[10] Due to the possibility of different symptom presentation, it can be harder for women to interpret their symptoms correctly and seek timely and appropriate medical diagnosis and intervention.

Lack of timely intervention, in this case from delayed symptom recognition, contributes to treatment delay, infarct expansion, and worse prognosis,[20] all contributing to higher mortality in women than men. Mortality is used as an outcome, due to the definitive nature of this endpoint being objective not subjective. It relates to the number of deaths caused by the health event under investigation,[21] in this case ACS. This review aims to investigate why there is a difference in in-hospital mortality for women hospitalised with ACS compared to men, by understanding whether there is a difference between symptom presentation and perception, as two possible causes.

Methods

Medline (PubMed), Cochrane Library and Trip Database were searched, using the search string ("symptomatology" OR "symptom" OR "symptom presentation") AND ("gender" OR "sex") AND ("diagnosis") AND ("mortality") AND ("women") AND ("AMI" OR "ACS"). Randomised controlled trials (RCTs), clinical trials and meta-analyses were included. Non-English papers were excluded. No arbitrary cut-off date was used, however papers published in the last 20 years were used, to remain up to date with the latest definition of MI.

Out of 189 results, six primary studies were selected, after screening for relevance and proper stratification by sex. Other information was retrieved using reputable websites, systematic reviews, and forwards and backwards citations. **Figure 1** illustrates the process of primary evidence synthesis.[22]

Results and Discussion

Symptom presentation

Examining the relationship between sex and symptom presentation, a US study by Canto et al[23] MI reported 42.0% (95% CI; 41.8-42.1) women and 30.7% (95% CI; 30.6-30.8) men, P<0.001 presented without chest pain/discomfort. This suggests significantly more women than men presented without chest pain/discomfort. The VIRGO study[24] investigated the role of gender on outcomes for young acute MI (AMI) patients, and reported 13.0% women and 10.5% men presented without chest pain, pressure or tightness. Women over 45 had 1.39 (95% CI 1.01-1.92) times the odds of presenting without chest pain compared to men, suggesting women are more likely than men to present without chest pain. Non-chest pain symptoms contribute to delayed help-seeking and access to care and treatment.[25]

Women in VIRGO also presented with more additional non-chest pain symptoms compared to men. Women experienced a mean number of symptoms of 3.4±2.0, and men 3.0±1.9, P<0.0001. The very small p-value suggests a significant difference between the two groups. Asgar Pour et al also looked at this, reporting women with ACS had a mean of 2.94±1.78 typical and atypical symptoms, whereas men had 2.75±1.36.[19] However, despite their more diverse symptom profile, women with atypical symptoms are significantly less likely to be diagnosed with ACS, than with typical symptoms. Despite no direct statistical comparison in mean symptoms, the results seem to agree with the former study, suggesting women present with more symptoms than men.

Canto et al had the largest sample size of 1,143,513, increasing the generalisability to a larger population. VIRGO had a smaller sample size of 2985, so is less generalisable than the first study, however, it spanned 103 US hospitals in geographically diverse locations, thus may be more representative of a broader demographic. Asgar Pour et al's is the smallest, with 438 participants from across eight hospitals and is the least generalisable. The first study is the most favourable in this regard, as due to large sample size, anomalous participants have less skew on results.

Despite its large sample size, in all categories, most of each group in Canto et al's were of White race/ethnicity, with the lowest being 73.1%, therefore is not representative of all MI patients in the US. VIRGO similarly, had a majority of 76% participants being White, decreasing representation of a varied society. This is a limitation, due to 42.2% of the US population being non-White,[26] inaccurately reflecting the US demographic, so cannot be generalised to the entire US population, or allow conclusions to be drawn regarding differences in presentation with ethnicity.

Furthermore, Canto et al had no cohort without MI to compare to, hence findings cannot be generalised to all patients with suspected ACS. However, Asgar Pour et al's study combats this, by comparing between those with and without ACS, stratified by gender and diagnosis, therefore is more applicable to a wider group.

The inclusion and exclusion criteria differ between these two studies, with Canto et al's missing certain data on age, sex and symptoms, and excluding those with a secondary diagnosis of MI or transferred patients, whereas VIRGO included those aged 18-55 hospitalised with AMI. Participant age may contribute to differences; the mean age of women was 73.9, and the second study excluded those above 55, due to the differences in pre- and post-menopausal women, particularly the lack of oestrogenic protection in the latter.[11,27]

Despite the limitations, the data supports each other's findings, suggesting more women than men present without chest pain, with a higher number of women experiencing more additional non-chest pain symptoms. These women are less likely to be diagnosed with ACS.

Symptom perception

Symptom perception was explored by An et al, investigating the gender differences in Chinese patients' ACS attribution of symptoms.[28] They reported 50.9% women and 37.2% men correctly identified their symptoms, although statistical significance is unreported. Contrarily, a Swedish study by Sederholm Lawesson et al reported 59.5% of women and 69.4% men, p=0.04 interpreted their symptoms as of cardiac origin.[29] Concordantly, The VIRGO study reported 54.7% women did not perceive their symptoms to be heart related vs 52.3% men, p=0.379, and were significantly more likely to attribute symptoms to stress or anxiety. However, with such a large p-value, evidence of a significant difference is quite weak. Despite this, 7.4% more women sought medical care before being hospitalised than men, however, significantly more women than men reported that their provider thought symptoms were unrelated.

All three studies used surveys, questionnaires or interviews, which rely upon episodic memory. Consequently, relying upon this being the same across all genders and all participants introduces recall bias, decreasing internal validity due to confounders. This is most prevalent within An et al's study, in which data was obtained 3-6 days post admission. Comparatively, data was collected within 24 hours in the study by Sederholm Lawesson et al, minimising recall bias.

Despite primary data limitations, the alternative is to collect observations from medical records, as demonstrated by Canto et al using secondary data. This was reliant upon subjective interpretation, and lacked standardisation, both in collecting and recording data. In contrast, use of patient interviews in VIRGO was standardised and administered by trained personnel, therefore this primary data may be more reliable, despite its recall bias.

Differences surrounding awareness of ACS symptoms in women may contribute to differing results between the studies. It has been previously identified that there are lower levels of symptom awareness in mainland China, with suboptimal attitudes and beliefs towards ACS, although this has limited capacity for extrapolation and may be outdated.[30] This contradicts the findings from An et al, and may be due to small sample size. Awareness of atypical symptoms, thus the ability to recognise and seek medical help, either directly by recognising their own symptoms, or indirectly by others recognising symptoms, is a predictor of delay in seeking medical attention.[30] In addition to such awareness, other confounders such as international and gender disparities in education, cultural norms, socioeconomic status and healthcare systems may affect health-seeking behaviours.[31] The confounding effect of these behaviours may be reduced in Sederholm Lawesson et al's study, as Sweden is one of the most gender equal countries and has complete healthcare coverage for all citizens, with studies reporting only small gender disparities found in health-seeking behaviour.[31]

Both the studies by An et al and Sederholm Lawesson et al used surveys or questionnaires to obtain data, which have limitations. An et al used the McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey (MAPMISS), which was translated from English to Mandarin. Despite efforts of four experts, translation and interpretation errors may remain, reducing internal validity. Language barriers also affected Sederholm Lawesson et al's study.[29] To ensure high internal validity, individuals with difficulties reading and speaking Swedish were excluded. This minimised the effect of literacy as a confounding variable. However, by excluding this group, firm conclusions could not be drawn about certain immigrant and refugee groups in particular,[29] but also differing educational levels and learning difficulties could act as confounders, reducing generalisability.

An et al's study observed all individuals with ACS, however, Sederholm Lawesson et al's study only observes those with STEMI, so participants make up a subset of those with ACS. Symptomatology may differ by ACS subclassification, due to differences in pathophysiology, and Sederholm Lawesson et al's findings cannot be generalised to all ACS patients.

The incongruence of results and lack of statistical significance suggests no firm conclusions can be drawn on gender differences in symptom perception.

Mortality

Canto et al also investigated the relationship between sex, symptom presentation and hospital mortality for patients with MI. They reported an in-hospital mortality for women of 14.6%, and for men 10.3%. This aligns with an Australian study by Mnatzaganian et al[32] evaluating sex differences in in-hospital mortality following a first AMI. They reported despite adjusting for age, women still had significantly higher crude death rates than males. Both studies share congruence, suggesting women have a higher in-hospital mortality from MI than men.

Changes in the universal definition of MI shortly after Canto et al's study, and diagnostic methods and treatment, means participant inclusion may differ if the study had been conducted more recently, yielding different results. This may affect the reproducibility and applicability of older findings.

With all studies, survival bias contributed largely. All participants who died before hospital admission were excluded, so results may be lower than actuality.

Due to the nature of the variables being measured, observational studies were deemed the most suitable format to record data: observation is the only way to observe natural occurrences. Since no intervention or exposure is being measured in these studies, RCTs would have been unsuitable for data collection.

In-hospital mortality was used as an endpoint to reduce the effect of confounding variables such as quality of follow-up care and recurrence of cardiac episodes.

Limitations

Increased mortality causes are multifactorial, aside from symptom presentation and perception. These include biological differences (genetic, epigenetic and hormonal) and gender differences, affecting both biological and social factors like stress and nutrition, and behaviour.[10] Additionally, factors like time taken from symptom onset to presentation to ED (onset-to-door time), and time taken from patient arrival at ED to percutaneous coronary intervention PCI (door-to-balloon time), provider bias resulting in misdiagnosis, appropriate intervention, follow-up care, co-morbidities, and risk factors such as age, further affect prognosis. This review focuses on exploring symptom presentation and perception as two possible contributors to mortality, not exclusively causing it.

Conclusion

Studies show women are significantly more likely to present without chest pain and experience more symptoms than men. Asgar Pour et al elaborated on this by correlating typical symptom presentation, such as chest pain, and likelihood of diagnosis, suggesting that since fewer women than men experience chest pain, these women are less likely to be diagnosed correctly.

Both Sederholm Lawesson et al's study and VIRGO agree women less often interpret symptoms as heart related than men. However, the study by An et al contradicts these findings. This may be due to awareness differences with gender disparity. Despite the congruence of the former two studies, neither is statistically significant, so no reliable conclusions can be drawn.

Both studies demonstrate a higher in-hospital mortality post-MI for women, although change in outdated diagnostic protocols must be considered and may not be comparable to more recent studies such as from Mnatzaganian et al. Furthermore, due to survival bias particularly affecting mortality rates, these figures may be substantially higher. However, this in addition to potential confounders, does not provide convincing evidence of no difference in mortality between men and women.

The interaction of biological sex and gender with symptom presentation and perception of ACS is significant and does contribute to the dimorphism in mortality. However, there is a dearth of research on the relationship between atypical symptom presentation and incorrect patient perception, and the extent of their contribution to increased mortality in women. There is also no link between the extent of the interaction of sex and gender, and the quantitative effect on outcomes. Consequently, studies should aim to quantify the extent to which sex and gender interplay in symptomatology and mortality and the links between, by ACS subtype. Future sex-specific studies on women should be conducted in cardiovascular research, to ascertain nuanced differences between sexes. Furthermore, it would be beneficial to have accessible information on atypical symptom recognition in GP and community settings and public health campaigns to ameliorate public health awareness. Additionally, using results to inform clinical protocols would greatly increase the prognosis of women, particularly by promoting urgent medial intervention.

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Sareena Khan

Sareena Khan is a second-year medical student at the University of Exeter. She has an avid interest in public health and global health policy, focusing particularly on health inequalities. She is very passionate about obliterating the gender inequalities that exist for women, particularly in cardiovascular health. She presented this article as an oral presentation at the INSPIRE conference recently. She is a firm believer that passions outside of medicine should be explored, and so in her free time she loves to paint, play golf, and explore the Cornish coastline.

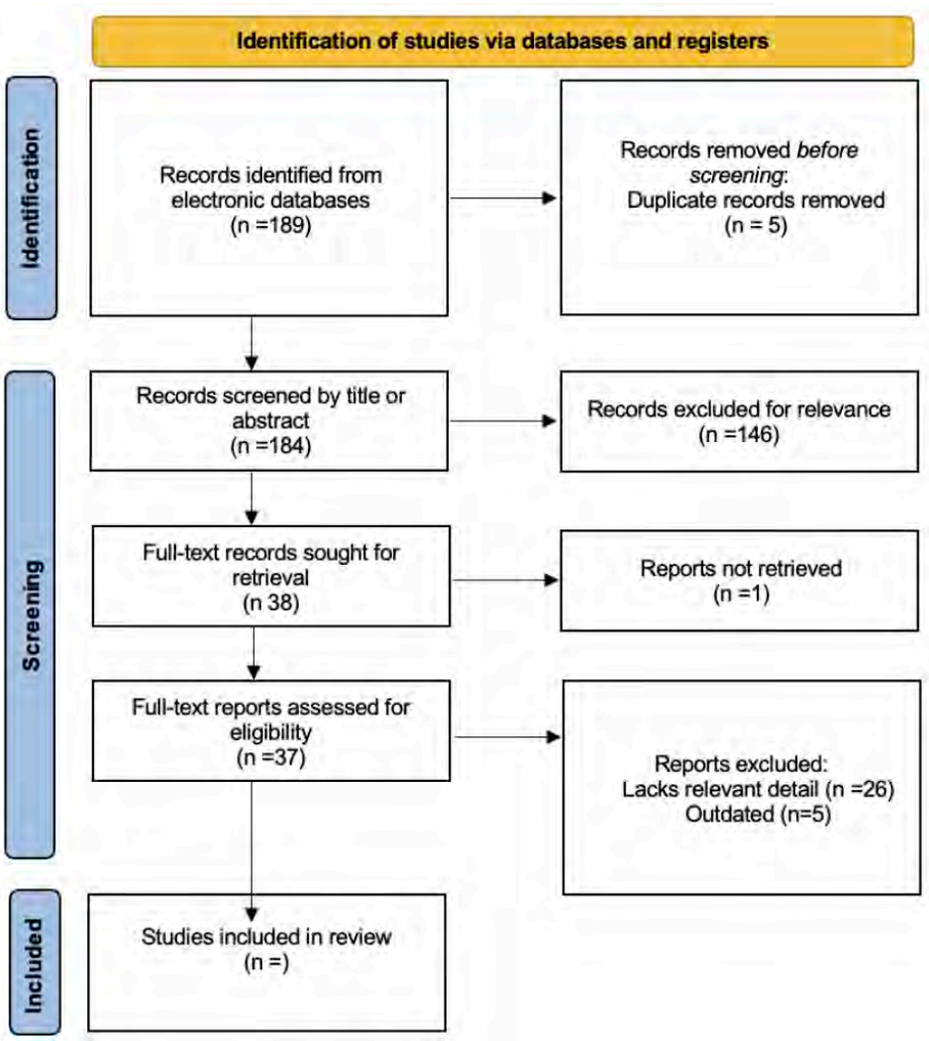

Figure 1. PRISMA diagram outlining primary evidence synthesis of literature for this review. This PRISMA diagram has been adapted from the BMJ Prisma 2020 Statement.[22]

Feature

Student summerships

Sophie Lawrence

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A student studentship is essentially an extended taster day, where you are given—or come up with—a small project to work on during the allocated time and funding to support you. There is no pressure to achieve anything beyond gaining valuable experience and a deeper insight into medical, dental, or veterinary research. In my experience, the facilitators are incredibly helpful and kind, genuinely aiming to inspire the next generation of researchers! Before we hear from those who have been awarded and completed these incredible opportunities, I'll take a moment to go over the application process, why you should apply and share some top tips.

The INSPIRE Research Studentships are open to students in years 1–4 or those intercalating, with opportunities to work with research teams in Plymouth, Bristol, Cardiff or Exeter. These studentships are a fantastic way to build on the interests sparked during the taster days at the start of the year, or even to explore a completely different area of interest.

The application process is fairly straightforward and requires a project plan, your CV (which doesn't need to be extensive—after all, the purpose of Inspire is to encourage medical students into research!), and a statement from your supervising researcher, confirming they're happy with the plan. Projects typically last between 4 to 6 weeks, so it's important to choose a project outcome that is realistic within this time frame.

You'll usually be notified of your success by mid-May, and from there, you can begin developing your project in more detail.

My own project, conducted in the Bristol endocrinology labs in July 2024, involved a week of shadowing researchers and PhD students, followed by 3 weeks of working on my own project. I was given my own set of cells to care for and study, observing their response to various independent variables. This hands-on experience was not only enjoyable but also provided valuable insight into laboratory research—an experience I would have struggled to find anywhere else at this stage in my medical career.

Although I initially found the scheme daunting and a bit intimidating, I'm incredibly glad I applied. If you're interested in exploring an area of medicine/dentistry/veterinary science that is being actively researched or simply want to experience a different side of your subject beyond what your school typically offers, I highly encourage you to apply. There's little pressure other than to fully engage with the opportunity by showing up, being enthusiastic and doing your best. So, what are you waiting for?

Cameron Case, Medicine, University of Plymouth

My experience with the INSPIRE scheme has been pivotal in shaping my passion to pursue a career in research. Through student-selected units, including a recent project with Plymouth Integrative Health and Social Care Education Centre (PICH) exploring healthcare students' attitudes towards interprofessional education, my interests in public health research have grown over my time at university.

Having written for the INSPIRE journal, I was aware of their summer studentship projects. This led me to attend one of the taster days at the University of Exeter run by the Children and Young People's Mental Health (ChYMe) research collaboration. Hearing the portfolio of projects run by the collaboration and first-hand experience from research fellows aligned with my interests in child and adolescent medicine. My personal experience volunteering with Routeways, a Plymouth-based local charity providing respite care for children with SEND, further sparked my interest towards the existing SPaCE project.

Collaborating with the team, I developed a research proposal focusing on neurodiverse parent carers' experience in accessing mental health support. Beyond my aim of conducting a research project, I knew I wanted to strengthen my project management and teamworking skills. This would also provide an opportunity to network with academic foundation trainees and clinical research fellows, understanding the training routes to these research posts. Initially set for four weeks, I extended the project by another four weeks to meet the ongoing development of my aims. The highlight of my studentship by far was the dedication and enthusiasm of my project supervisor, Dr. Tamsin Newlove-Delgado, whose support made me feel genuinely integrated into the team, enhancing both my personal and professional development.

At the project's outset, we defined key aims, focused on producing a research paper and preparing a conference abstract for an oral presentation. I focused my learning objectives towards improving my understanding of different qualitative research methods, writing for publication, and developing public speaking skills for presenting at a conference.

Beginning the research activities, I immersed myself in the interview transcripts and survey responses, implementing reflexive thematic analysis through a critical realist framework, having been introduced to this technique. Navigating my positionality during the coding process proved challenging, especially when dealing with emotionally charged experiences. I initially struggled, finding that I made assumptions from my own understanding when developing concepts, and so I had to actively challenge myself against this. Through discussions with the team, I reflected on the significance of returning to the data source and encapsulating the experience of parents rather than forming my own judgements. To achieve this, I kept reflective memos during the process as a way to guide my analysis more objectively.

I also had the opportunity to participate in patient and public involvement and engagement (PPIE). I spoke with a group of parent carers about their reasons for involvement, learning about their own passions and practical involvement within the development of research goals and outcomes. I was able to present my results and preliminary themes, incorporating their feedback to finalise the generated themes and illustrative quotes. This experience highlighted the value of co-developing research goals with public groups who are directly impacted, emphasising the importance of advocacy in shaping meaningful outcomes.

In terms of my revised project outputs, I have developed a qualitative research paper as a first author. Once this has been reviewed our aim is to submit this for publication. This process allowed me to refine my writing style and tone to present qualitative data in a holistic and objective manner. I also developed the paper into a conference abstract. I have since presented this as an oral presentation both regionally at the Inspire Research Conference and nationally at the Royal College of Paediatrics and Child Health Conference in Glasgow.

This experience has solidified my ambition to pursue a career in academic research. It has inspired me to apply for the specialised academic foundation programme and consider the academic clinical fellowship pathway post-foundation training. I am very fortunate to have established a network of experts for guidance along the way as a result of this studentship.

For anyone curious about research, I recommend exploring the opportunities provided by the INSPIRE scheme. This has undoubtedly ignited my passion, and I am excited to see where it leads me next.

Millicent Brodie Cooper, Dentistry, Cardiff Uni ersity

Last summer, I completed a 3-week INSPIRE Summer Studentship at Cardiff, my home university. I was first introduced to the scheme at a 'taster session' run by the Improving Dentistry research group at my school. Having heard about the fascinating projects previous students had undertaken, I left the session – quite literally – inspired to apply.

Having already had some exposure to research during my dental degree, I was keen to gain a deeper understanding of how academic projects operate in real-world settings. So, after approaching a potential supervisor with my project idea, I submitted a short application just before the Easter holidays and, a few weeks later, was delighted to learn I'd been accepted. The process was refreshingly straightforward and accessible.

My project, titled 'An Investigation into the Content of Dentistry-Related Smartphone Applications', explored the availability, functionality and content of mobile apps related to dental health, focusing on their potential to support evidence-based care and improve patient outcomes.

As the lead investigator, I designed and managed the project; conducting a systematic review of free, publicly available dental apps across the Apple App Store, Google Play Store and Microsoft Store. My research team gathered key information about each app's purpose, target audience, features and technical elements, such as the app's privacy settings and offline functionality. I was responsible for training others to carry out this process consistently, providing

a fantastic opportunity to strengthen my leadership and teamwork skills.

One of the unexpected highlights of the studentship was experiencing Cardiff in the summer. The city takes on a different energy during the quieter months and I could enjoy events I would usually have missed out on during my evenings and weekends. The programme is very flexible – I spent my last week working remotely from home, meaning I didn't miss out on valuable family time which is so precious during our all-too-brief period of warmer weather! Additionally, the stipend ensures you don't lose out by partaking; particularly if, like me, you would usually have worked through the break.

Undertaking this project has given me real insight into how collaborative research operates. I strengthened my academic writing and analysis skills, was introduced to platforms like the Open Science Framework (OSF), and, perhaps most importantly, confirmed that research is something I truly enjoy. The studentship has already opened doors to future opportunities, such as a possible publication, presentations and prizes.

INSPIRE has also played a key role in shaping my long-term aspirations within academic dentistry, as I have now secured an Academic Dental Foundation Training (ADFT) post for September. I believe the skills, experience and confidence I gained through this studentship gave me a competitive edge when applying.

My advice to future applicants would be: if research interests you, go for it! Reach out to a supervisor whose work excites you, don't be afraid to propose your ideas and enjoy the process. INSPIRE is what it says on the tin and could be the first step in your academic journey.

Phoebe Sussman, Veterinary Science, University of Bristol

During my second year at vet school, I carried out an INSPIRE Summer Studentship where I spent a month working in Professors Linda Wooldridge's laboratory, studying T-cells and immunoassays targeted to stimulate and optimise T-cell function.

It was a very interesting month where I learned a lot about working within research and immunology. I also developed a lot of new skills, which I wouldn't have been exposed to during the veterinary degree; I was able to gain experience with lab work, carrying out cell cultures and working to keep sterility under hoods, something which looks easier than it is! I also learnt a lot about flow cytometry and FloJo, a software used to interpret flow cytometry results. Learning to use the software was definitely a good challenge but I was able to create beautiful graphs when I did manage to get it to work! Alongside developing my practical skills and helping to set up some pretty interesting experiments, the studentship was a great opportunity to talk to researchers and PhD students about their pathways into academia and gain advice on working within research. This has really been a pivotal step in my journey through vet school, as it really opened my eyes to the different opportunities which were available to vet students within research. Equally, this month counted towards my clinical Extra-Mural Studies (EMS) requirements; it was a great way to get a chunk of clinical EMS out the way early in the degree, taking pressure off my third and fourth year. Additionally, EMS can be expensive — the studentship provides you with a stipend for the number of hours you work, which makes this placement a lot more accessible. Overall, this experience was very enjoyable, and it definitely inspired me to pursue more opportunities to get involved in research. I would highly recommend a studentship to anyone considering going into research or even if you are just curious about what it's like to work in academia. It is just a great opportunity to dip your toe into research and understand what goes on behind the scenes in some of the leading research groups within the GW4 (University of Bristol, Cardiff University, University of Exeter and University of Plymouth).

Alex Turlea, Medicine, University of Exeter

I applied for the INSPIRE student summership to enhance my understanding of the clinical auditing process and data analysis, whilst also gaining hands-on experience in the research field.

As part of the summer project, I was fortunate enough to start auditing clinical data on patients with gestational diabetes mellitus, offering the team valuable insight into the insulin requirements in pregnancy. The observational database created around the rapid insulin titration algorithm in patients with gestational diabetes can be used to explore questions around basal insulin dosage previously not answered.

Building upon the work I did in the student internship I have successfully submitted an abstract and presented a poster at Diabetes UK. This is a leading professional conference for healthcare professionals involved in diabetic care, where I was able to attend and present my research to colleagues and other students.

This experience has been instrumental in advancing my career, providing me with skills in auditing and creating a scientific poster for a conference. I hope to take this further and progress into an academic career after graduation.

My advice for students looking to apply for this year's summership grant is to have clear objectives on what they want to achieve over the summer and to not get discouraged by obstacles, and communicate with their supervisors when issues arise.

Supervisor's comments from the INSPIRE outcome report submitted at the end of the summer:

Alex has been fantastically studious and enthusiastic during the INSPIRE project. She has overcome several hurdles to data access and achieved a fantastic amount in a short period of time. I have thrown her in the deep end of research and she has swum! The data she has collected and started to analyse will be invaluable in improving the care and outcome for women with gestational diabetes in the UK and beyond. I am very happy to continue to support her with her ongoing involvement in this project and beyond. Very well done!

Feature

Citations and revelations: inside our Journal Club

Anjali Rameshwaran and Freya Hanson
Year 1, Medicine, University of Bristol
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In a world where deadlines loom and group projects haunt our dreams, INSPIRE Bristol student ambassadors said *no more* to isolated reading and *yes please* to lively debate, collective eye-rolls at dodgy research design, and bonding over baffling abstracts.

That's how our Journal Club was born — part think tank, part therapy session, part pizza-fuelled chat fest.

Who are we?

An eclectic group of Bristol med, dental and veterinary students who gather on a monthly basis to discuss a chosen article, combined with some pizza and controversial opinions (follow our insta @inspirebristol to stay up to date with journal club dates).

What do we do?

- Pick a journal article
- Break it down: methods, results, analysis etc
- Ask big questions like "Was this even proofread?!"
- Leave knowing a bit more about critical appraisal, different methodologies and what the paper actually adds to the world

Why should you care?

We realised that motivating oneself to sit down and read an academic paper alone in a uni room for fun, was a feat harder than climbing Everest. Because reading alone is fine. But reading together? That's where the magic (and laughter) happens.

Join us if you…

- Love research but hate reading in isolation
- Have ever wanted to embrace your inner nerd and want to read research papers but could not be bothered
- Want to build confidence in understanding complex ideas
- Appreciate good banter and rogue research topics
- *And to sweeten the deal*, we have some exciting speakers coming along to some of our future sessions…

Bring your brain. Bring a snack. Join INSPIRE. Follow INSPIRE Bristol to stay up to date:

Anjali Rameshwaran

Freya Hanson

Hi! Our names are Anjali and Freya, and we are currently first-year medical students at the University of Bristol! This first year of getting immersed into university life and all things medicine has been incredibly exciting and really piqued are interests into all the different avenues and possibilities that medicine encompasses. One of the highlights of this year has been joining the INSPIRE student ambassador team as the INSPIRE Bristol social media reps. This has been a lovely creative outlet, and it's wonderful to promote all the great events and opportunities happening this year. Another highlight was helping to set up and run the INSPIRE Bristol journal club. In fact, we ran the first session where we read a riveting article about the use of AI in answering public health questions. We would love if everyone followed INSPIRE Bristol along and joined the journal club!

Photos provided by Inspire Bristol Journal Club

Interview

The Heart at Play Foundation Interview and Podcast

Eunice Pak

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I was very privileged to talk to Patty Rivera, the director of the Heart at Play Foundation, a non-profit organisation catering to persons with developmental disabilities from underprivileged communities based in Manila, the Philippines. The Heart at Play Foundation was founded by Patty's mother in the early 2010s, working to empower the special needs community in Manila by providing free dance movement therapy classes to children with autism and other developmental disabilities.

Can you tell me a bit more about yourself?

I'm Patty, or Teacher Patty, or Coach Patty to my students, and I'm currently the co-founder and executive director of the Heart at Play Foundation (THP). I manage The Heart at Play, alongside my older sister Therese Rivera.

I am a student of Master's in special education from the University of Phillippines, Diliman Campus, and I'm also trained in Applied Behavioural Analysis. I got my certification as a registered behavioural technician two years ago.

So I've been dancing for 24 years and started competitive dancing when I was 15 years old, representing the Philippines in international competitions. And I have been teaching dance professionally for 11 years now, about the same time that I've been a disability advocate through our work in the Heart at Play Foundation. So, by trade, I am a professional choreographer and a competitive dancer, but I have since expanded my expertise to inform the work we do in the Heart at Play Foundation.

Can you please tell me briefly a bit about what the Heart at Play Foundation does, along with its ethos and mission?

The work we do in the Heart at Play is catering to persons with developmental disabilities, including, but not limited to, autism spectrum disorder, Down's syndrome, cerebral palsy, Möbius syndrome and other forms of developmental disabilities. We cater to economically underprivileged or indigent families here in our capital, Metro Manila. We provide them with alternative therapies, so primarily dance or movement therapy, as well as monetary support if the need arises. We've recently also acknowledged the necessity of providing support to the people who take care of these developmentally challenged learners too, so we occasionally have support group meetings with the moms and guardians to check in with their mental health and disposition.

Can you tell me how the idea of the Heart at Play Foundation originated and how you got around to making this inspiration a reality?

Coming from a family of dancers, The Heart at Play Foundation started as a family initiative inspired by teacher Anna Rivera, who pursued a Master's in Special Education and discovered the potential of using dance therapy as a therapeutic tool for individuals with special needs during her immersion in the US.

She identified wo gaps in the existing methods:

1. Limited accessibility for those with severe disabilities: most dance movement therapies catered only to individuals with mild to moderate conditions.

2. Lack of focus on memorisation and structured sequences, which are essential for working and long-term memory development. Upon returning to the Philippines in 2012, she sought to make dance accessible for individuals with profound disabilities, leading to the development of a pioneering methodology. I became involved at 14 by initially tagging along, and 12 years later, the initiative has grown into a registered NGO with aspirations to formalise and expand its therapeutic approach. Now, the foundation is on the verge of a major milestone: establishing the first performing arts and therapy centre for individuals with special needs in the Philippines, marking a legacy of passion transformed into meaningful impact.

Patty's top tips on setting up an NGO*: <10 steps for the beginner

1. Distinguish between advocacy and foundation
- An advocacy is an informal movement.
- A foundation requires formal registration and government compliance.

2. Secure initial capitalisation
- A foundation is still considered an incorporation, therefore you are required to provide documentation on your initial capitalisation (at the time of THP's registration, the minimum amount required was 1,000,000 Philippine pesos, approx, US$20,000).

3. Register with the government – the Bureau of Internal Revenue (BIR) and Securities Exchange Commission.
- As a legal entity (Inc.), the foundation must be registered for tax purposes.

4. Draft Articles of Incorporation
- A formal document outlining the mission, structure and governance of the NGO.

5. Appoint a Board of Trustees
- Identify board members and key staff responsible for decision-making and operations.

6. Comply with tax requirements
- NGOs must pay taxes and file reports with the BIR and other relevant agencies.

7. Quarterly compliance and reporting
- Regular financial and operational reporting to maintain legal status.

8. Ensure proper governance and accountability
- Maintain transparent financial records, ethical practices and operational efficiency.

9. Plan for long-term sustainability
- Beyond paperwork, an NGO needs funding strategies, donor relations and community engagement for long-term success.

*Requirements might vary from country to country

Can you briefly tell us about the use of dance therapy as a form of alternative therapy for children with developmental disabilities?

Alternative therapies like music therapy, hydrotherapy and dance movement therapy (DMT) are gaining recognition alongside conventional treatments such as occupational therapy and speech and language therapy.

The Heart at Play Foundation has developed its own Dance BEST© (Behaviour, Emotional, Executive Skills, and Sensory Targeted Movement Therapy) methodology, which addresses five key domains:

1. Physical domain:
- Improves gross, fine and oral motor skills, balance, agility, strength, and body awareness.
- Enhances daily self-help skills like dressing, grooming and self-protection.

2. Psychosocial domain:
- Builds social skills for individuals with autism, helping them engage in socially acceptable behaviours.
- Enhances self-esteem and confidence through dance mastery and public performances.
- Provides emotional catharsis for non-verbal individuals, offering a healthy outlet for expression.

3. Cognitive domain:
- Engages left and right brain functions to enhance sequencing, working memory and long-term memory.
- Improves attention, focus, impulse control and executive functioning.

4. Sensory domain:
- Helps manage sensory processing dysfunction, a common issue in children with developmental disabilities.
- Provides exposure to auditory, visual, tactile and proprioceptive stimuli, improving sensory regulation.
- Encourages multitasking and neural pathway development.

5. Behavioural domain:
- Reduces self-injurious behaviours by redirecting impulses into dance movements.
- Helps students self-regulate, improving behaviour in everyday settings (e.g. meals, public outings).

- Promotes functional communication, allowing students to express their needs without the use of disruptive behaviour.

The Dance BEST© program has led to measurable improvements, such as reducing self-injurious incidents like hitting and scratching, and enables children to participate in family meals, public outings and other social activities without displaying disruptive behaviour that was previously present.

The program supports lifelong intervention by helping individuals with developmental disabilities a) regulate sensory overload, b) build a stronger mind-body connection, c) learn daily living skills and ultimately d) integrate with the broader society whilst pursuing a self-actualised life.

What are the current limitations towards children with disabilities in Filipino society?

1. Lack of accurate data and research
- No up-to-date, specific statistics on developmental disabilities.
- Disability data lumps physical and developmental disabilities together, making it difficult to assess needs.
- Without proper data, budgeting and service deployment remain inadequate.

2. Stigma and lack of awareness
- Parents often hesitate to disclose their child's disability due to social stigma, misinformation and cultural beliefs.
- This lack of transparency hinders policy making and prevents early interventions.
- Standardised awareness campaigns are needed to combat disability stigma and to promote inclusion.

3. Gaps in services across the lifespan
- Early intervention services exist, but support dwindles as individuals reach adulthood.
- Few employment training centres for persons with special needs.
- Lack of specialists to provide lifelong support from childhood to adulthood.

4. Limited opportunities for severe disabilities
- Job opportunities are often limited to verbal individuals or those with mild to moderate disabilities.
- Those with severe cerebral palsy or self-injurious behaviour are left with no employment prospects.
- More businesses need to adopt inclusive employment strategies.

5. Government involvement and economic support
- Healthcare subsidies for developmental disabilities are insufficient.
- The cost of autism care for Filipino families can be up to 20% of their income, while average family income is less than $500 USD.
- Need for government-backed incentives for businesses to hire people with disabilities.
- Stronger legislation is needed to promote accessibility, inclusivity and employment incentives for people with special needs.

What are some event highlights over the years for the Heart at Play?

In 2019, our foundation represented the Philippines' disability community in Singapore's largest inclusive concert held at the National University of Singapore. We flew out a 54-man delegation, where they performed a culturally inspired routine in front of the government ministers, including then Singapore president Halimah Yacob. If that meant they would need a shadow to assist them, that was okay with us – so it was a combination of dances performed independently and with parents and guardians. Almost everybody on our flight had never been out of the country before. So this experience was quite literally the trip of a lifetime for them, and we're so grateful they got to have that right before the pandemic, it was just life-changing being a part of that scene!

What are your thoughts on the future for the Heart at Play Foundation?

So two key goals for us:
1) Program development. We have to continue developing our modality, and we are now focusing on behavioural interventions. So all of our programs are now geared towards catering to the behaviour because we believe it's the precursor to learning – to learn skills in order to flourish in life.

2) We hope to build our very own centre by 2026; the centre is not just for performing arts, nor is it just for therapy. It's going to be a one-stop shop that caters to both – so we'll provide a holistic curriculum for persons of all developmental disabilities across the ages.

I would like to thank Patty for her time and for giving us her insightful thoughts and sharing of her experiences. I wish THP all the best in future endeavours!

For more information about the Heart at Play Foundation, please visit their website at www.theheartatplayfoundation.org, and tune in to the INSPIRE podcast to hear the full interview and for poignant stories that would melt your heart!'

Photos provided by The Heart at Play Foundation.

Interview

Interview with Yvonne Wren, Professor of Speech and Communication at the University of Bristol

Deepa Sharda
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With cleft lip and/or palate (CLP) affecting approximately 1 in 800 live births, it is one of the most common congenital conditions in the UK. Evidence based research and multidisciplinary teams are essential to helping these patients overcome the complex medical, social and psychological challenges they may face as a result of the condition. With her wealth of experience and research, Yvonne Wren, Professor of Speech and Communication at the University of Bristol, is at the forefront of CLP research. Yvonne has been Chief Investigator of The Cleft Collective Cohort Study since 2020; its aims are to 'investigate the biological and environmental causes of cleft, the best treatments for cleft and the impact of cleft on those affected and their families'. In this interview, Yvonne shares with us her journey into research, common challenges faced by CLP patients, the impact of the Cleft Collective research to date, and finally how best primary care practitioners can support CLP patients.

Tell us a little bit about you and your journey into your current research.

I always liked the idea of a career in research when I was first qualified but I thought it was a pipe dream, the kind of thing that people like me didn't do.

My first degree was in Speech Pathology at the University of Manchester and that qualified me to work as a speech and language therapist. I worked in clinical roles in hospitals and community for ten years before taking up an opportunity to do a funded PhD at Bristol Speech and Language Therapy Research Unit, which was then based at Frenchay Hospital. That coincided with the births of my two older children and so took five years to complete, after which I did the usual route of multiple fixed term research associate contracts. I worked part-time during most of this period and had my third child and then applied for an NIHR PostDoc Fellowship. I was one of few who were not medics or dentists applying to that scheme and was thrilled to hear I had been successful.

This was a pivotal time for me as my research up to that point had been focused on children with speech sound disorder. During the NIHR Fellowship, I became involved in the Cleft Collective and set up the speech substudy. Through this, I became more involved with the clinical and patient communities in the field of cleft lip and palate, and this led me to taking on a more multidisciplinary role across the Cleft Collective as well as establishing processes for robust Patient and Public Involvement (PPI) for the study.

Now I lead the Cleft Collective and also the new Programme Grant Cleft@18-23. But my roots in speech and language therapy are still evident through the work I lead outside of the University of Bristol with colleagues at North Bristol NHS Trust and Cardiff Metropolitan University.

What are some common speech and communication challenges faced by individuals with cleft lip and/or palate?

When a child is born with a cleft palate, they are unable to close off the nasal cavity during speech. We do this all the time without realising – except when we make the nasal sounds 'm', 'n' and 'ng'. Without the facility to close off the nasal cavity, speech can sound hypernasal but also the consonants that require oral pressure cannot be produced. These are the sounds 'p', 'b', 't', 'd', 'k', 'g', 'f', 'v', 's', 'z', 'sh', 'zh', 'ch' and 'j'.

Surgery to repair the palate makes it possible for the oral and nasal cavities to be separated which is important for feeding as well as speech. However, it doesn't mean that there will be no future problems with speech.

As a child grows, sometimes a hole (fistula) can form in the palate where air can escape and which can impact speech. In other cases, the gap between the pharynx and the soft palate (the moveable muscle part at the back of the palate) becomes too great and the soft palate can no longer make contact with the back of the throat to close off the nasal cavity. At other times, the original repair of the cleft may break down. In each of these cases, further surgery is needed.

Children born with a cleft palate can also have articulation problems which is when the way in which they produce speech sounds in the oral cavity is different to others. There are characteristic features of articulation associated with a cleft palate and often a child will

produce some speech sounds such as 't' or 's' further back in the mouth or in a different manner to usual. This will alter how their speech sounds and might impact their intelligibility. Children – and adults – who show these characteristics need speech and language therapy to help them make changes to their speech.

Children who are born with a cleft lip and without a cleft palate have fewer problems with their speech though some might show a few difficulties with the sounds that are produced with the lips such as 'p', 'b' and 'm'. Most of the time however, children born with only a cleft lip will sound like other children of the same age.

How does your research address these challenges to enhance therapeutic interventions?

In the Cleft Collective, we are collecting data on surgical and speech and language therapy and dental interventions. Interventions vary from one child to the next depending on how they present – but there are some common elements. By collecting data on a large number of children – as we do in the Cleft Collective – we are able to determine which interventions are associated with better outcomes. In order to do this, we collect data on outcomes as well. This includes patient reported outcomes but also outcomes measured at clinical assessments and audit visits. There are many outcomes which are important in the clinical care of individuals born with a cleft. As well as speech, facial growth and appearance are important as is oral health and well-being. We collect data on each of these outcomes as well as important confounders such as socio-economic status and presence of an identified syndrome.

What are some key findings from your research and how have they influen ed the cleft lip and palate patients and their families?

Some of our research has a direct impact on how we care for children born with cleft lip and palate and their families today. For example, during the COVID lockdowns, data we collected from families about their experiences of receiving support from their regional cleft team remotely were used to inform care and change practice at some of the cleft centres. In other research using Cleft Collective data, we found that the lockdowns had not had a negative impact on the development of children's speech and language skills, which was reassuring to both clinical teams and to families.

In other work, our research is helping to build a picture which in time will increase our knowledge of what causes clefting. Using genetic data which was extracted from the biological samples collected from children and their parents, we have identified new genes for cleft. However not everyone who has the gene has a cleft so we know that there must be some environmental factors which cause the gene to be activated. We will use the data we have collected in the Cleft Collective to determine which lifestyle factors are important in the relationship between the environment and genes. With this information, we can provide public health advice to reduce the likelihood of a child being born with a cleft.

As an expert in the fiel , what do you think are some key things dentists and wider clinicians should be aware of when treating cleft lip and palate patients?

Individuals who were born with a cleft of the lip or palate or both have experienced a lifetime of clinical care. From the moment they were born – or even before – they have received specialist care from a multidisciplinary team. Therefore, even if they present with symptoms or features which appear common to the general population, their experience of them might be different. So, in many cases, if their needs are related to their speech, their teeth, their well-being, their hearing or their appearance, it is important to consider whether a re-referral back to their specialist cleft team would be appropriate.

Yet of course, an individual who was born with a cleft is much more than just their cleft. So, understanding who they are and what is important to them will be unique as with any other patient. The key thing therefore is to listen and observe. Our work with the patient community has taught us that sometimes as clinicians we think we know what a patient needs – but if we ask them, we might learn that while we thought they were concerned about their appearance, it was actually their hearing that was bothering them.

What are the upcoming goals planned for the Cleft Collective?

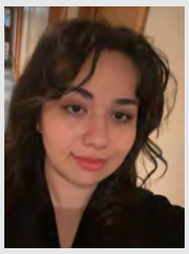
The Cleft Collective is a resource – and our primary goal is to continue to grow the resource so that it can be the best possible. As a study team, comprising operations and research staff, we are keen that people know that the Cleft Collective is available for them; that it has a huge dataset which is still expanding; and that it can be accessed and used by simply completing our proposal form.

We have a lot of dental information in the Cleft Collective, both from parent and participant questionnaires and also from clinical assessment. We are keen for dentists and orthodontists to use the data to ask clinically relevant questions.

To find out more, look at our website https://www.bristol.ac.uk/dental/cleft-collective/ or get in touch with us at cleft-collective@bristol.ac.uk

Senior Editors, Spring 2025

Hajer Al-Shakarchi



Year 4, Dentistry, Cardiff University

Being an INSPIRE editor has been an excellent opportunity not only to deepen my understanding of academic writing, but also learn from the experiences of other students in the field. As an editor, I have developed an eye for detail and clarity, alongside an appreciation for the collaborative process that underpins publishing. Overall, publishing research as a student is an incredibly valuable experience that goes far beyond building a CV- it allows you to contribute to the advancement of your field and build a strong foundation for your post-grad career. I highly recommend getting involved with INSPIRE and I am grateful to have been part of the editorial team this year!

Moyowa Arenyeka

Year 5, Medicine, University of Plymouth

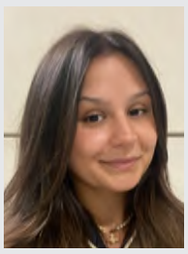
The INSPIRE scheme has been instrumental in consolidating my interest in medical research by providing a plethora of opportunities for me to gain greater insight into the field. Through this scheme, I have served as a peer reviewer, editor and article author, attended taster days, participated in a residential summer school and more. Being welcomed back to the INSPIRE team as a member of the Advisory Board has been a great privilege, which has enabled me to contribute positively, whilst gaining further exposure, to the world of research. I am grateful to have been given the chance to work with INSPIRE as it has substantially expanded my perspective and skillset, bolstering my professional development.

Umaima Arif

Year 5, Medicine, Cardiff University

Hi! I am a final year medical student with a heavy passion for research, writing and travel. My current clinical interests include internal medicine and oncology as well as global health and humanitarian medicine. Most recently, I have been interested in the role of immunotherapy and biologic therapy for gynecological cancers, which has been the focus of my recent SSCs and my current elective in Canada. Because research publication and writing has always been a particular passion of mine, I deeply appreciate being part of the editor team for the INSPIRE Student Journal, as it enables me to encourage other students' research interests as well as spread the word regarding new prospects and versatile developments in different fields - something I believe to be the core of one's medical career. Outside of the journal, I try to further my experience through peer-reviewing, leading research in the Refugee Health Society, and teaching for Cardiff Muslim Medics. I hope that further experience will enable me to grow into a well-rounded, conscientious practitioner who is open to learning more about the world and my colleagues' impressive works.

Victoria Bak



Year 2, Medicine, University of Exeter

Hi! I am currently a second-year medical student at the University of Exeter. In the future, I hope to become an academic clinician. I have a range of interests including women's health, neuroscience, and endocrinology. I am particularly interested in translational medicine, which involves applying research findings directly into clinical practice. Additionally, in an age where social media is widely used, it is essential to consider effective strategies for communicating medical research and best clinical practices to the broader population, ultimately ensuring optimal health outcomes for everyone. The INSPIRE journal and initiative provide an excellent opportunity to have your work showcased. As an editor, I have learned how to manage papers behind the scenes, which has been both interesting and enjoyable. In my spare time, I enjoy playing the piano, going to the gym, and dancing. I hope you enjoy reading this journal.

Dilshan Jayakody

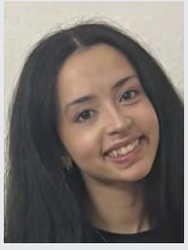
Year 5, Medicine, University of Plymouth (On to Intercalation - Master's in Cardiovascular Research, King's College London)

My journey in medicine is driven by my passion for addressing health disparities and inequalities, and I'm deeply involved in several research projects aimed at improving healthcare outcomes for our vulnerable populations. I'm also passionate about quality improvement projects in planetary health and sustainability. My research interests led me to discover INSPIRE, and I feel honoured to be part of a like-minded editorial team. In the future I aspire to become a Surgeon, with interests in Trauma Surgery and Cardiothoracic Surgery. In my free time, I love cycling and mountain biking, enjoying the thrill of navigating challenging terrains. I also really enjoy watching sports, whether it's live or down at the pub with friends!

My experience working with INSPIRE has been incredibly enriching. I've gained valuable skills in copy-editing, social media management, and interview/podcast. I've thoroughly enjoyed every aspect of handling submissions from our talented peers across the Great West 4 and around the World.

I hope readers find as much joy in reading this issue of INSPIRE as we did in creating it!

Tayha Jupe

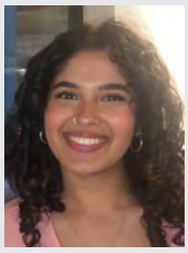


Year 4, Medicine, University of Bristol

Hello, I am Tayha, a fourth-year medical student at the University of Bristol. During my intercalation, my interest in research grew, leading me to join INSPIRE as an editor. I've thoroughly enjoyed gaining insights into the publication process and understanding the journey a paper undergoes from submission to acceptance. My interests include dermatology, plastic surgery, women's health, microbiology, and pharmacology, making this role a perfect opportunity to explore these fields further. Outside of my studies, I enjoy reading and playing badminton. INSPIRE is an excellent platform for students to engage with research, and I encourage everyone to explore its content. Research is vital to advancing all areas of medicine, especially as we move towards a more sustainable and evidence-based healthcare system.

Senior Editors, Spring 2025

Gayathri Kannan



Year 4, Medicine, University of Bristol

Hi! My name is Gayathri and I am a fourth-year dental student at Cardiff University. I have a particular interest in the evolving world of clinical research and how this can be incorporated into patient-centred treatment to facilitate a higher standard of care being delivered. Being a part of INSPIRE for three years as an editor and as a part of the advisory board has allowed me to hone my critical appraisal skills and gain insight into the vast knowledge available out there through all the splendid papers being submitted to us. Aside from INSPIRE, I am currently the careers representative for my dental school which allows me to really encourage undergraduate students to look beyond the obvious choice for their future career!

Sophie Lawrence

Year 3, Medicine, University of Plymouth

Hello, I am Sophie, a third-year medical student at Peninsula. I initially got involved with INSPIRE through the research program, which eventually led me to do a summer project with the same lab. My current research interests include cancer endocrinology and the role of APP in the pathogenesis of Alzheimer's, breast and prostate cancer. I have enjoyed my time as the editor for the INSPIRE journal and have found it fascinating to read the research papers from various universities and explore new and innovative research. Outside of medical school, I love running and anything else outdoors, including walking my three cockapoos.

Alvin Leung

Year 4, Medicine, University of Bristol

Hi! I am a fourth-year medic from the University of Bristol. My main clinical and research interests are dermatology and venereology, and I am also passionate about tackling inequalities in healthcare. It has been a pleasure working as an editor for the INSPIRE Student Journal, perusing through the innovative literature that we have received, as well as delving into topics that are less familiar to me previously. In my spare time I enjoy travelling, strolling in art galleries and a nice cup of coffee.

Eunice Pak

Year 5, Medicine, Cardiff University

Hello! I am Eunice, a final-year medical student at Cardiff University aspiring to be a clinical academic. Within medicine, I like the fields of internal medicine and children's health. I have previously undertaken research work in clinical pharmacology and paediatrics, having presented in several international conferences. Being an editor for the INSPIRE journal has enabled me to understand the process behind publications, working with an excellent team of editors and reviewers to produce the manuscript in your hands. I also enjoy teaching, opening my eyes to new medical innovations and reading about, or even producing, works on medical humanities- including art, music, literature and history. In my spare time I enjoy hiking, watching tennis, listening to music, singing, playing board games and maintaining my blogs.

Deepa Sharda

Year 5, Dentistry, University of Bristol

Hello! My name is Deepa and I am a fifth-year dental student at the University of Bristol. Unlike most dental students, I studied A-Level English literature and have always had a love for writing and the world of academia. Teaching and education is definitely my passion, for 2 years voluntarily worked with students with English as a second language; I now work with the University of Bristol as a Widening Participation tutor, encouraging students from less advantaged backgrounds to study health sciences/ dentistry. I resonate with these students and understand some of the barriers they face; hence feel joy in giving back. I love to share my enthusiasm and passion for dentistry with the upcoming generation and hope to do this through the Inspire journal too. I'm so grateful to be a part of the Inspire scheme, helping to spread fantastic research, educate others and learn a lot myself!

Phoebe Sussman

Year 5, Veterinary, University of Bristol

Hi, I'm Phoebe, I'm a veterinary student from the University of Bristol, currently taking an intercalation year to study for a Masters in Global Wildlife Health and Conservation. I have a strong interest in the sustainable use of veterinary medicines, antimicrobial and anthelmintic resistance. This past summer, I carried out a research project working with World Horse Welfare to investigate anthelmintic resistance within working equid populations in Panama. This project really piqued my interest in rural agricultural communities and their access to veterinary care as well as the control of veterinary medicines in different countries. I am also very interested in zoonotic disease and One Health, and I hope to focus my masters project on the impacts of environmental health on the health of wildlife populations and hence the disease risk of communities living adjacent to wildlife. It will be crucial for veterinarians, medics and dentists to work together to begin to tackle some of the large problems affecting humans and animals. Journals such as INSPIRE provide such an incredible platform for vets, medics and dentists to come together, and I am very grateful to have been a part of this process and act as an editor.

With thanks to all the previous editors and advisory board members 2024/2025

List of referees, Spring 2025

Dharesh Raj Amarnath,
Newcastle University

Uashar Badakhshan,
University of Exeter

Larai Bowers,
University of Exeter

Millie Brown,
University of Plymouth

Florence Chang,
Cardiff University

Lucas Gadaleta,
University of Exeter

Caroline Gu,
University of Exeter

Jonathan Heng,
University of Bristol

Emma Hillier,
University of Bristol

Hang Long Li,
University of Hong Kong

Hussein Malik,
University of Bristol

Ahmed Mansoor,
Cardiff University

Mafa Mohlala,
University of Plymouth

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University of Bristol

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www.bristol.ac.uk/vet-school/research/inspire
www.bristol.ac.uk/dental/courses/undergraduate/inspire

Bristol Medical School Co-Leads: Dr Anu Goenka, Senior Clinical Lecturer in Paediatric Infectious Diseases and Immunology; Dr Becky Foster, Associate Professor in Microvascular Medicine.
Bristol Veterinary School Lead: Dr Alex Tasker, Senior Lecturer in One Health Trusted Research Environment
Bristol Dental School Leads: Dr Mark Gormley, Consultant Senior Lecturer and Mr Alexander Gormley, Clinical Research Fellow

Cardiff Uni ersity

Cardiff School of Medicine Co-Leads: Dr William Davies, Reader (Basic Science), Dr Emma Tallantyre, Clinical Reader
Cardiff School of Dentistry Lead: Dr Heather Lundbeck, Clinical Lecturer in Paediatric Dentistry

University of Exeter

www.exeter.ac.uk/faculties/hls/studying/catp/doctors/inspire

Lead: Dr Jane Smith, Senior Lecturer, Faculty of Health and Life Sciences

University of Plymouth Peninsula School of Medicine and Dentistry

www.plymouth.ac.uk/about-us/university-structure/faculties/health/inspire

Leads: David Parkinson, Professor of Neuroscience;
Vehid Salih, Associate Professor in Oral & Dental Health Research,
Dr Alex Cresswell-Boyes, Lecturer in Oral Sciences

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