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Hi! Welcome to the Winter 2023/2024 issue of the INSPIRE Student Health Sciences Research Journal.

This issue has been written and peer-reviewed by students, 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.

We called out for One Health-related content and you delivered! Look out for the special symbol at the top of themed articles.

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Best wishes,
INSPIRE Student Health Sciences Research Journal Senior Editors

Front Cover

Cover image by **Anatolia Nix:**

I'm a third year Medical Student at the University of Leicester. I created this painting titled "Skull - Lateral View" in watercolour with UV reactive mixed media last year while studying head and neck anatomy. The original fluoresces under UV light. This is the first piece in my ongoing series of multicoloured anatomy paintings, and has been exhibited at the Leicester Museum and Art Gallery.

PLAGIARISM

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Contents

News and opinion

4. **The rising importance of adaptive preventative measures for 'heatwave-resilient' healthcare**
By Zara Hirji

7. **Breaking barriers: innovative strategies for improving healthcare access in remote areas**
by Malaika Mehmood

10. **Organoids in gastroenterology: a One Health approach**
By Phoebe Tarver

Reviews

12. **How is a lack of diversity in medical literature imagery affecting the quality of healthcare?**
By Chidera Stephanie Ayalogu

16. **A systematic review on the use of chlorhexidine mouth rinse for the prevention of alveolar osteitis: dose, regime and risk analysis**
By Liam Fletcher and Freya Lam

30. **The utilisation of genetics to advance the development of pharmaceutical treatments for late-onset Alzheimer's disease**
By Louise Warner

Case report

34. **Asymptomatic presentation of renal arteriovenous malformation: a case report and review of literature**
By George Garratt

Features

37. **The value of medical volunteering**
By Mimi Mostefai

39. **Game for a challenge**
By Phoebe Sussman

Conference report

41. **INSPIRE 'INSPIRing Research' conference report – November 2023**
By Gayathri Kannan

Interviews

47. **Andy Gibson, Mission Rabies**
By Phoebe Sussman

51. **Fatma Sabet, Research fellow in school food system transformation, social activist and Shillingford Organics Farm School creator**
By Mimi Mostefai

Editors

53. **Senior Editors, Winter 2023/2024**

55. **Advisory Board, Winter 2023/2024**

Referees

55. **List of referees, Winter 2023/2024**

New & opinion

The rising importance of adaptive preventative measures for 'heatwave-resilient' healthcare

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Abstract

This is an opinion-style article discussing the impact of heatwaves on human health, demonstrating the intrinsic link between the health of humans and planets. It argues the importance of taking a primary preventative approach to reducing morbidity and mortality during heatwave events. An adaptive approach is argued for due to the ever-changing and developing nature of planetary health as climate change takes effect. Specific emphasis is placed on reviewing and arguing for the use of the novel 'BRACE' framework to achieve this. Further aims of the article woven throughout are to highlight the barriers to achieving resilient healthcare systems in countries that contribute the least to climate change but are the most affected.

From 1998 to 2017, over 166,000 people died globally as a result of heatwaves.[1] One significant example demonstrating the importance of adapting global healthcare systems to large scale climate events, was the record-breaking 2003 European heatwave where over 70,000 people lost their lives in a single instance.[2] Apart from such high-mortality stand-out incidents, the burden of disease during heatwaves is difficult to calculate. As well as 'heat-related deaths', such as dehydration and heatstroke, heatwaves also have many indirect impacts on human health. These include exacerbation of pre-existing medical conditions, malnutrition due to reductions in crop yields, and many further secondary mental health impacts.[3] Between 2000–2016, an additional 125,000,000 people have been exposed to heatwaves,[1] putting more people at potential risk. Because of this vast, vague and increasing burden of disease resulting from heatwaves, having both short-term and long-term effects on human health, it is important that present and future healthcare systems continuously adapt to become more 'heatwave resilient' in the face of our changing climate. The benefits of taking a primary prevention approach will not only come in the form of a reduction in the projected rise in morbidity and mortality, but also by alleviating the added stress predicted to fall on our already overwhelmed healthcare systems.[4,5]

The Building Resilience Against Climate Effects (BRACE) novel framework provides guidance in a five-step process for public health agencies to adaptively manage the health effects of climate change.[6] Steps one and two emphasise (despite its challenging nature) the importance of 'future gazing' when predicting mortality and burden of disease in vulnerable populations as it reflects the nature of climate change's long-term effects on disease patterns.[6,7] This is important at the beginning of the developmental process as understanding who is most affected by heatwaves and why, means that preventative healthcare can be targeted in advance of specific known risk factors that the community is susceptible to. It incorporates a mature understanding that different regions of the world are affected by heatwaves differently due to both geographical and socioeconomic factors,[8] therefore, having healthcare systems tailored for the needs of its community, with the ability to change depending on the changing risk factors, is most effective.

Appreciation of the burden of disease in developing countries is also crucial for global heatwave resilience. A novel probability-based model in India suggested that with rising average summer temperatures, there is likely to be a corresponding 146% increase in heat-related mortality.[3] The significance of this is evident for populations relying heavily on crop yields and locally sourced water for hydration and nutrition. Reduced access to these necessities puts a higher proportion of the population at risk of comorbidities.[1] This will also increase the size of groups at risk from heat-related

deaths and the burden placed on healthcare systems, which may already be stressed or underdeveloped, in treating more vulnerable populations.[8] The sizes of vulnerable populations will be further increased as heatwaves become more intense and frequent.[7] It follows that additional studies, assessing the burden of disease due to heatwaves, across a wide range of locations with differing economic backgrounds will be valuable to informing the developmental process of international heatwave-resilient healthcare systems.

An impactful yet underappreciated challenge to the development of healthcare action plans corresponding to the spread of the burden of disease is that the definition of a heatwave is widely variable – so useful health data that is required to improve healthcare responses is not standardised for comparability.[9] Irregular heatwave thresholds have significant impacts on the reported mortality and morbidity rates. A systematic review and meta-analysis of the impact of heatwave mortality under different heatwave definitions suggests that implementing a new warning system based on a set temperature threshold or increase in temperature from the average, such as those used in the heatwave plan for England, rather than having subjective heatwave definitions may be a viable solution to this problem.[9,10] It is important to also take not only duration but the intensity of the heatwave into account.[11] Access to globally comparable information via the use of a standardised definition would increase the ability of both developed and developing countries to implement the third step of the BRACE framework – assessment of initial public health interventions to produce geographically-specific healthcare adaptation plans for the most concerning health impacts.[6]

A meta-analysis of prognostic factors in heatwave-related deaths suggested that people who were confined to their beds, unable to leave their homes daily or unable to care for themselves had a statistically significant increased risk of mortality during heatwaves.[12] These characteristics are associated with people who are dependent on others for care such as the elderly, children and people who endure health conditions which impact their day to day lives. Relevance of these findings to clinical practice comes in the form of informing recommendations for preventative medicine targeted at personal risk factors as opposed to only considering environmental risk factors. For example, modifying fluid intake routines for the elderly in care homes, who are at high risk of dehydration.[13] Healthcare systems which appreciate the interplay between environmental and personal risk factors can take more effective steps to plateau the trends in morbidity and mortality rates during heatwaves and again alleviate the future stress on themselves.

After the initial evaluation of disease burden and public health responses, step four of the BRACE framework is to develop a climate health adaptation plan.[6] If healthcare systems are prepared before the event takes place, with a warning system triggering a healthcare plan across different sectors, then preventative medicine can be implemented in a more timely manner before large numbers of vulnerable populations require the need for treatment-based healthcare. Although it is still vital for steps to be implemented to improve the treatment of health conditions resulting from heatwaves, preventative strategies beginning at the level of public and community-based healthcare are seen to be of the most benefit to the healthcare systems themselves.[14]

It is evident that many countries view heatwave early warning systems as beneficial in readying public health for a preventative response. Firstly, the CDC extreme heat action plan recommended early warning systems to trigger communication with the public about the possible risks to health, the ways to avoid them, and the importance of air conditioning,[15] which was found to be one of the protective factors for vulnerable populations associated with a reduced risk of heat-related death.[12] Secondly, South Asia's first heat-health action plan incorporated the development of a seven day advance weather forecast early warning system which would trigger their health action plan.[16] Their action plan aimed to incorporate the best practice from other plans which relates, as discussed earlier, to the importance of information free flow between countries to make the best early-warning system and heatwave adaptation plan possible.

Primary prevention methods which aim to prevent disease by limiting risk exposure by individuals, can be taken one step further in the form of primordial prevention. This consists of reducing the risk to populations by changing the environmental conditions around the people themselves.[5] If this is considered in terms of heatwave risk factors, mitigating more intense and frequent heatwaves from even occurring would be the ultimate preventative public healthcare strategy. Therefore, it can also be argued that rather than simply surrendering to the effects of climate change and adapting our healthcare systems to accept it as one of our future health determinants, we should invest more into climate change prevention itself rather than healthcare adaptation strategies which will become increasing difficult to implement without any sort of mitigation.[17] On the other hand, to find a balance between mitigation and adaptation, we can incorporate primordial prevention into our adaptation strategies. The steps that we may take towards adapting our public healthcare response to rising temperatures can also themselves be heatwave mitigating factors. Health systems can be alert to opportunities for improving the environment in their adaptation strategies to provide so called 'co-benefits' to health.[18] One such example from the CDC's extreme heat action plan was the strategic planting of trees to provide shade and cooling effects.[15] Here, primordial prevention comes in the form of adapting the environment to reduce intensity of heatwaves on the surrounding population, but this action also enables us to mitigate climate change using trees to improve the environment. This response can be better implemented through government and local policies than the healthcare sector, demonstrating how multisectoral collaboration to reduce burden of disease is beneficial to healthcare systems.[19]

While encouraging healthcare systems to incorporate all of these important nuances into their strategies to produce the strongest heatwave-resilient healthcare systems, we must understand that there are also many barriers to consider, particularly taking into account developing countries who, while contributing the least to global carbon-emissions, are the ones most affected by them due to their general geographical locations and socioeconomic factors.[8] The World Health Organization (WHO) climate change survey report evaluated the overall progress made by healthcare systems to adapt to climate change. Looking at 101 countries ranging from upper to lower income, the survey found that 47 had underdeveloped or a complete lack of national planning for a healthcare climate strategy, 45% of the countries had low or no level of implementation of a national healthcare related climate strategy and only 42 out of the 98 countries surveyed had an early warning system and health sector response plan in place for heatwaves.[19] The findings from this survey suggest that while the burden of disease from climate change and heatwaves is increasing and is projected to increase,[1,7] while recommendations for preventative strategies may be made specific to local regions,[20,21] certain countries simply do not have the luxury of incorporating climate change into the decision-making of healthcare provisions and distributions.[22] Barriers which obstructed the progress towards ideal 'climate-resilient' healthcare systems were financing, human resources, technology, available evidence and collaboration between sectors – many of which hinder the prioritisation of climate change adaption in healthcare system decision making.[19]

The challenge of the lack of access to finance was recognised in the Paris Agreement, an international treaty which aims to mitigate and adapt resilience to the effects of climate change, including rising temperatures. The agreement recognised the fact that some countries require extra financial, technical and capacity-building support to reach a developed resilient healthcare system.[23] To overcome these financial barriers, there is recognition that developed countries have a role in providing financial aid to countries facing these obstacles and those who are also more vulnerable to the effects of climate change. Secondly, 'climate finance' at the local, national or

international level through different support mechanisms is also accessible to countries and is encouraged in the Paris Agreement.[24] However, the WHO climate change survey report explains the reasons why even providing access to these financial resources may not be enough, many countries still face barriers like not knowing about the opportunities for climate finance, not being connected to the international process or even not being able to produce proposals to apply for climate finance.[19]

In conclusion, heatwave-resilient systems are especially important in countries where populations are at a greater risk of heat-related illness, yet it is often these countries that have the most barriers to overcome. We can consider opportunities for mitigation of climate change within primary prevention adaptation strategies as 'co-benefits' for both immediate human health and climate change which has long-term impacts on human health. Further research into burden of disease, including personal and environmental risk factors, and effectiveness of public health strategies is required to improve primary prevention strategies across the world. One such way this can be made possible is via the assessment of countries' "nationally determined contributions", presented under the enhanced transparency framework of the Paris Agreement, in 2024. This will facilitate the review of the strategies implemented, as required in step five of the BRACE framework, as well as to increase access and awareness of available climate finance. A strong heatwave-resilient system is an adaptive one, it is not just about getting through acute events as they occur, but constantly developing healthcare practices to serve the community and healthcare systems best in the long term too.[25]

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Zara Hirji

Hi, I'm currently a fourth-year medical student at Plymouth University and I love all things planetary health. It's been an interest of mine since first year when I chose a planetary health-related SSU and got to explore the world of determinants of health, policymaking, inequalities and many more global health concepts. Since then, I've constantly been on the lookout for opportunities to explore as many angles as possible. If you also enjoy planetary health or global health, then this is the journal for you! I hope you enjoy reading the rest of the articles in here.

Breaking barriers: innovative strategies for improving healthcare access in remote areas

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Abstract

Access to quality healthcare is a fundamental human right, yet access in remote areas remains a major challenge. This article explores the innovative strategies that have emerged to bridge the healthcare access gap in remote regions. By leveraging technology, community engagement and policy changes, these initiatives aim to enhance healthcare delivery, improve patient outcomes, and create a healthier, more equitable society, reducing disparities in vulnerable regions.

Abbreviations

CHW – community health workers
RCT – randomised control trial
WHO – World Health Organization

Introduction

Access to healthcare is a fundamental human right, but for millions of people residing in remote and underserved areas, this right remains elusive. Geographic isolation, limited infrastructure and resource limitations present substantial barriers to delivering appropriate and effective medical services. This disparity in healthcare access has led to poorer health outcomes and increased morbidity and mortality rates in these areas. Underrepresented populations, such as racial and ethnic minorities, low-income individuals and those living in rural areas, often experience greater health disparities and worse health outcomes compared to the general population.[1] This article explores pioneering approaches that have revolutionised healthcare delivery in remote regions, enabling better health outcomes for vulnerable populations.

Table 1 provides a comprehension of the situation of healthcare and its associated challenges in several different countries, as measured by various health indicators. Afghanistan's maternal mortality rate in 2020 was high, at 620 deaths per 100,000 live births compared to a remarkably low mortality rate of 10 deaths per 100,000 live births in the UK in 2020.[2] The maternal mortality ratio reflects the risks faced by women during childbirth and pregnancy. Higher ratios suggest that more women face life-threatening complications during pregnancy and childbirth. Bangladesh, Afghanistan and Togo have higher maternal mortality ratios, indicating significant challenges in ensuring safe maternal healthcare. In contrast, the UAE, Germany and the UK have lower ratios, suggesting better maternal healthcare and lower risks for pregnant women.

The under-five mortality rate, also known as the infant mortality rate, is a crucial indicator of the quality of healthcare in a country. A higher infant mortality rate suggests that a higher number of infants do not survive their first year of life. Bangladesh, Afghanistan and Togo have higher infant mortality rates, indicating that they may face challenges in providing adequate maternal and child healthcare. In contrast, the first world countries have lower rates, indicating better healthcare systems and more favourable conditions.

The World Health Organization (WHO) measured the impact of communicable diseases on a population's overall health and life expectancy. Higher numbers indicate a greater burden of communicable diseases. Bangladesh, Afghanistan and Togo are just three of the lower income countries that face relatively higher burdens, suggesting challenges in controlling and preventing communicable diseases. In contrast, countries such as the UK have lower burdens, indicating better control and prevention efforts in these countries. The disparities in the impact of communicable disease measured between countries are complex and multifactorial, and some of it is suggested to be due to poor access to healthcare and lower rates of education.

In summary, these statistics serve as a compelling response to action, highlighting the crucial role of improved healthcare access in remote and underserved areas. Access to healthcare is not just a matter of convenience; it is a matter of life and death. By addressing these disparities and expanding healthcare access, we have the potential to save countless lives and improve the overall health and well-being of vulnerable populations in remote regions across the globe.

Telemedicine: a virtual connection

Telemedicine has emerged as a game-changer in providing healthcare access to remote areas. Utilising video consultations, remote monitoring devices and mobile applications, healthcare providers can reach patients located miles away. This virtual approach to healthcare reduces the need for travel and associated expenses. In addition, it allows patients to connect with healthcare providers in the comfort of their home, reducing the anxiety of getting to the healthcare provider. Telemedicine not only facilitates routine medical check-ups but also enables specialist consultations, increasing the scope and quality of care available to patients in remote regions. In a recent study investigating adult patients' perceptions of telemedicine-delivered medical care, a substantial 72% of rural patients expressed moderate to extreme satisfaction with the service.[3] While telemedicine has shown immense potential, challenges such as limited internet connectivity in remote regions and the need for technology literacy among both healthcare providers and patients need to be addressed. Additionally, concerns about data security and privacy in virtual healthcare must be carefully managed. Overall, it can be inferred that telemedicine interventions can contribute to management of chronic conditions, decreased hospitalisations and increased patient satisfaction.

Mobile clinics: medical outreach on wheels

Mobile clinics are proving to be an effective solution for bringing healthcare services closer to remote communities. These medical units equipped with essential medical supplies can reach even the most remote areas, providing a range of medical services. They are staffed by healthcare professionals and offer primary healthcare, preventive services, and health education. Mobile clinics play a crucial role in the early detection and management of health issues, thereby reducing the burden on hospitals and improving health outcomes. A comprehensive study that examined 163 articles, including nine RCTs and 4604 participants, found that mobile clinics had a significant positive impact on chronic disease outcomes. They not only improved clinical results but also demonstrated cost-effectiveness in delivering healthcare services.[4] They serve as a bridge between remote populations and larger healthcare centres, ensuring continuity of care for patients requiring specialised treatment. The sustainability of mobile clinics depends on funding and logistics. Long-term financial support and effective supply chain management are essential to ensure these clinics can continue to reach underserved communities. Moreover, quality control and the training of healthcare professionals on board are critical aspects to maintain the effectiveness of mobile clinics.

Drone delivery of medical supplies

In areas with limited infrastructure and difficult terrains, the use of drones has emerged as a revolutionary method to deliver medical supplies promptly. These unmanned aerial vehicles can transport essential medicines, vaccines, and diagnostic samples to remote health centres, providing critical support during emergencies and improving the overall efficiency of healthcare delivery. "Time from launch to delivery was 20.77 ± 0.05 minutes. Resupply by foot would take 5.1 hours."[5] This shows that the use of unmanned aerial vehicles is both efficient and this has the potential to be the best way of delivering medical supplies. Although drone delivery is efficient, regulatory frameworks, airspace management, and the cost of implementing and maintaining drone fleets can pose challenges. Ensuring the safety and reliability of medical supplies transported by drones is also utmost.

Community health workers: the local connection

Empowering and training community health workers (CHWs) has proven to be an effective approach to enhancing healthcare access in remote areas. "These individuals, often from the local community, are trained to provide basic medical care, health education and raise awareness about preventive practices. The study revealed that there are few evaluations of mobile health in low-income countries. Although there is sizable documentation, there are limited studies explaining an effect on clinical outcomes.". More studies need to be conducted to evaluate the effectiveness of CHW. By leveraging their knowledge of local customs and languages, CHWs build trust and acceptance among community members, breaking down cultural barriers that may impede healthcare utilisation. They are a vital link between the community and healthcare services. The efficacy of CHWs relies on proper training, supervision and integration into the broader healthcare system. Ensuring that CHWs have access to necessary resources and support is essential for their success. Additionally, rigorous research is needed to better understand the impact of CHWs on clinical outcomes and their cost-effectiveness.

Conclusion

The innovative strategies discussed in this article demonstrate the transformative potential of technology, community engagement, and policy changes in improving healthcare access in remote areas. Telemedicine, mobile clinics, drone deliveries and community health workers are reshaping the landscape of healthcare delivery, making essential medical services more accessible to those who were previously underserved. It is crucial to address the disadvantages and barriers that may hinder their widespread adoption.

In conclusion, while these innovative approaches hold tremendous promise for improving healthcare access in remote areas, careful consideration of their limitations and challenges is essential for their successful and sustainable implementation. As we continue to explore and invest in these innovative approaches, we move closer to achieving healthcare equity and breaking the barriers that have long hindered healthcare access for vulnerable populations in remote regions.

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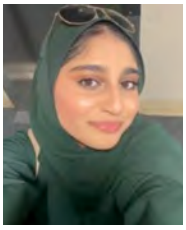

Malaika Mehmood

My name is Malaika, and I am a third year medical student at the University of Plymouth. My journey into medicine was inspired by my personal experiences and my unwavering determination to make a positive impact on people's lives. My primary interests lie in cardiology and paediatrics.

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	Total population[a] (000s)			Life expectancy at birth[b] (years)			Healthy life expectancy at birth[b] (years)			Maternal mortality ratio[c] (per 100 000 live births)	Proportion of births attended by skilled health personnel[d] (%)	Under-five mortality rate[e] (per 1000 live births)	Neonatal mortality rate[e] (per 1000 live births)	New HIV infections[f] (per 1000 uninfected population)	Tuberculosis incidence[g] (per 100 000 population)	Malaria incidence[h] (per 1000 population at risk)	Hepatitis B surface antigen (HBsAg) prevalence among children under 5 years[i] (%)	Reported number of people requiring interventions against NTDs[j]
Data type	Comparable estimates			Comparable estimates			Comparable estimates			Comparable estimates	Primary data	Comparable estimates	Comparable estimates	Comparable estimates	Comparable estimates	Comparable estimates	Comparable estimates	Primary data
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Togo	4 345	4 300	8 645	61.5	67.2	64.3	54.7	57.8	56.2	399	69 a)	63	24	0.38	33	237.5	3.27	5 128 595
United Arab Emirates	6 512	2 853	9 365	75.1	78.4	76.1	65.8	66.2	66.0	9	99 a)	6	3	-	0.8	0.0	0.02	41
United Kingdom	33 239	34 042	67 281	79.8	83.0	81.4	69.6	70.6	70.1	10	-	4	3	-	6.3	-	0.41	0

Table 1. Maternal and infant mortality rate in different countries around the world. An extract from the full table available at https://www.who.int/data/gho/publications/world-health-statistics

Organoids in gastroenterology: a One Health approach

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Abstract

This article presents a summary of the use of patient-derived organoids (PDOs) as a novel research tool for gastroenterology, with a focus on inflammatory bowel disease, in human and veterinary medicine. In addition, it aims to highlight their advantages and limitations over current research models from an ethical perspective. Finally, to draw attention to their potential for contribution to the concept of One Health and the importance of collaboration between human and veterinary medicine resources.

Abbreviations

GI – gastrointestinal
IBD – inflammatory bowel disease
PDO – patient-derived organoid

Introduction

Patient-derived organoids (PDOs) are three-dimensional structures generated from stem cells with the ability to self-organise and resemble in vivo organs.[1] They can re-create components of anatomy and recapitulate basic tissue-level functions of their physiological equivalents, to obtain a bioartificial organ.[2] PDOs play an important role in modelling the pathogenesis mechanisms of diseases, individuals' drug sensitivities (giving rise to personalised medicine), toxicology studies, and much more.[2] Only recently are PDOs finding their applications in veterinary medicine. This article reviews the current use of canine PDOs in comparative gastroenterology and the importance of a One Health approach; a concept recognising the interrelations of human and animal health and proposes a multi-disciplinary approach to tackling problems common to both species.[3]

Organoids in gastroenterology

Gastroenterological research has historically used two-dimensional models of the human gastrointestinal (GI) system using a monolayer of cells to imitate in vivo organ functionality. Gnotobiotics have also been used to replicate the human GI system within mice, involving bacterial colonisation of the gut and subsequent euthanasia.[4] In addition to the ethical issues this method raises, it is evident that mice are a poor model in biomedical research. Around 90% of drugs developed using mouse models have failed in clinical trials,[5] indicating the need for better models. The canine GI system closely resembles that of humans, with a functional and taxonomic overlap of around 60% compared to 10–20% overlap between mice and humans.[6] Furthermore, dogs develop analogous GI diseases such as colorectal cancer and inflammatory bowel disease (IBD) and show similar clinical signs to humans, making them superior models to mice.[4] The practicality and cost of obtaining canine intestinal tissue is feasible as veterinary surgeons have access to these during GI surgery and often take samples for histological use. Canine PDOs provide a more representative model of the human GI system[7] compared to previously mentioned methods, whilst reducing the number of animals used in research. Canine PDOs achieve the 'reduction' and 'replacement' aspects of the 3Rs, an ethical framework for preserving welfare of research animals. 'Refinement' aims to refine tests to alleviate animal stress during research, 'replacement' encourages use of research methods not involving animals, and 'reduction' aims to reduce the number of animals used per experiment.[8]

A recent study

Inflammatory bowel disease is characterised by chronic inflammation of the GI tract[9] and is highly prevalent in both humans in the UK (0.81%)[10] and dogs (approximately 0.9–2.0%).[11] The aetiology of the

disease is currently unknown,[12] and treatment in both species is largely symptomatic.[13,14]

A 2019 study[4] using healthy and diseased dogs (presenting with IBD), created PDOs through collection of adult intestinal stem cells from samples of canine GI tissue. Culture of these cells and visualisation with microscopy demonstrated successful differentiation into crypt epithelial cells.

In IBD, inflammation is mediated through PGE2 which acts through receptors EP1, EP2, EP3, and EP4, in both humans and canines.[4,15] The latest NSAID class 'piprants' target the EP4 receptor and aim to reduce common GI side effects that occur with NSAID drugs, important for IBD patient.[16] The results of this study showed that the EP4 receptor was successfully expressed in the canine PDOs generated, thus deeming this model fit for development of piprant drugs. A limitation to this particular study is that immune and mesenchymal cells, usually detected in abundance in native gut tissue, were absent, supporting the already known fact that the methodologies for generating PDOs require further development to obtain full physiologic functionality.[17] One may question the robustness of these results due to these inaccuracies of the PDO, however, it is clear that canine PDO models provide much improved representation of human tissue than our current mouse models.[6] The use of PDOs for research into IBD treatments could benefit the health of both animal and human patients and facilitate more collaboration between human and veterinary clinicians and researchers.[18]

Conclusion

PDOs present the unique ability to investigate disease processes and develop innovative therapies on highly representative tissue of both humans and animals. They offer a sustainable solution to use of animals in research as fewer animals are needed, overcoming some of the ethical issues involved in research animals. The anatomical similarities shared between humans and canines, coupled with parallels in disease prevalence such as IBD, opens the door for collaboration between human and veterinary fields with PDOs providing an interface for this to happen. Overall, PDOs provide a highly efficient method of biomedical research, transferable across sectors, and collaboration in this way has the potential to accelerate advances in research for the benefit of both disciplines.[19]

Copyright

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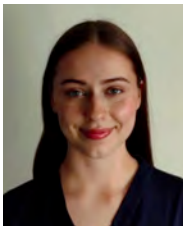

Phoebe Tarver

I am a fourth year veterinary student currently completing my intercalated Master's in Epidemiology. My interests include oncology and veterinary epidemiology. I hope to pursue research throughout my career alongside clinical work and look forward to seeing how the field of One Health can contribute to both veterinary and human biomedical research in the future.

Review

How is a lack of diversity in medical literature imagery affecting the quality of healthcare?

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Abstract

The purpose of this study is to investigate the importance of diverse imagery in medical textbooks in promoting representation, cultural competency, proper diagnosis of medical disorders and inclusiveness in the learning environment. It is essential for medical schools to include imagery featuring a range of skin tones. This inclusion aids future doctors in learning to practise medicine for everyone, not just those of lighter skin tones. As our communities and societies evolve and grow more diverse, it is critical that our medical curriculum evolves as well.

Introduction

As healthcare provides a variety of services for an ethnically diverse society, clinical teaching resources need to be representative to strive for an equal quality of care for all. This essay aims to highlight the overrepresentation of lighter skin tones in comparison to darker skin tones and its impact on the quality of healthcare provided to ethnic populations.

The problem, in part, stems from a lack of ethnic representation in medical literature. Alongside other factors, including socioeconomic status and varying access to care, this eventually leads to disparities in healthcare, specifically racial disparities. The term racial disparity is defined by the Institute of Medicine[1] as the "racial or ethnic differences in the quality of healthcare that are not due to access-related factors or clinical needs, preferences and appropriateness of intervention". Medical literature, comprising journals, articles, and books, primarily serves the purpose of educating on various aspects of medicine, including disease presentation and medical procedures.[2] This is utilised in the training of doctors and, subsequently, practise of medicine. If this information is then biased in terms of imagery and lacks in patient representation, it may not only be ineffective, but also have a negative impact on the health outcomes for certain demographics.

Methods

To comprehensively understand and address the issue of diversity in medical imagery and its impact on healthcare outcomes, a systematic literature search was conducted through various academic databases. This was done using PubMed, Google Scholar, relevant medical education journals, and Plymouth University's library system, which provided access to peer-reviewed journals and articles. The search strategy encompassed key terms such as "diversity in medical imagery", "racial disparities in healthcare", "representation in medical education", and "skin tone variation in clinical signs".

The goal was to search papers that explored and explained the effects of a lack of diversity in medical imagery on healthcare, rather than just identifying it. At the point of interest, there seemed to be a paucity of research on this topic, which meant I had to utilise reputable web articles that offered interesting perspectives still relevant to my topic. To ensure the reliability of these articles, I checked the authors' credentials, verified citations for accurate and relevant sources, and assessed the publication source from reputable platforms. Citation chaining was also used to find sources through other research papers.

Discussion

What is the problem with imagery in medical literature?

Images are crucial for understanding a concept in a more memorable and easily applicable way. This method is particularly useful in

medicine, where images frequently serve as tools to identify and manage patterns of illness. The lack of an array of skin tones in clinical images poses an issue. This lack of representation hinders medical practitioners from effectively applying their clinical knowledge to individuals of colour, making them less equipped to accurately diagnose medical conditions.

Louie & Wilkes (2018) investigated the occurrence of imagery showing pigmented skin tones in medical textbooks including Atlas of Human Anatomy and Gray's Anatomy to see if it approximately aligned with the racial diversity in the United States.[3] Whilst referring to the different races as white, black and other people of colour, and skin tones as light, medium and dark, they found that the books were approximate in terms of race but not in skin tones. In fact, the population of White individuals, Black individuals and other people of colour were 62.5%, 20.4% and 17%, respectively, thus accurately reflecting the population. However, 74.5% of skin tones represented were light whilst only 4.5% were dark, clearly showing an overrepresentation of light skin tones.[3] This is problematic as these books are popular in teaching and yet, fail to sufficiently demonstrate the differences in skin tones which can potentially alter the way treatment is administered. To avoid inadvertently encouraging implicit bias when using imagery as a teaching tool, it is necessary to accurately represent the racial makeup of the patient population.[4] These textbooks could enhance their content by displaying images depicting how medical conditions present on various skin tones such as the Massey-Martin skin colour guide (see **Figure 1**). However, potential challenges may arise from the limited availability of high-quality images illustrating clinical manifestations on darker skin.[5] Regardless, one must consider that not all diseases affect each race equally therefore intentional overrepresentation may be required, where appropriate.

Given that these core textbooks lay the foundation for medical students' understanding of disease identification, the insufficient representation of darker skin tones poses a potential issue. This underscores the necessity for implementing a change in this regard.[6] Implicit racism in medicine can be so subtle that it is hard to pinpoint the issue. Regardless, it is worth understanding due to its effects on the patient's experience of healthcare.

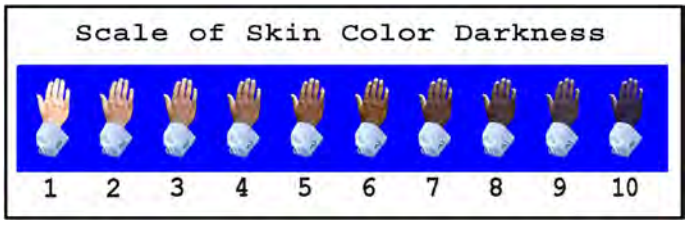

Figure 1. Massey-Martin skin colour guide. Reprinted from Louie P & Wilkes R (2018)[3]

Which areas of medicine suffer as a result of inconsistency in imagery?

This issue of underrepresentation is commonly seen in dermatology. Dermatology is a branch of medicine that deals with the study of the skin and its diseases. Visual presentations on the skin can be an indication of underlying problems like iron deficiency, which clinically presents as pallor but in itself is not a skin condition.[7] Hence, the skin is referred to as a 'window to health'.[8] Despite the primary focus on the skin in dermatology, the problem of underrepresented darker skin tones in medical literature is highlighted in conditions where redness, paleness and rashes are valuable for diagnosis. For example, rashes may manifest on a Black person as a white, purple or a grey colour whereas most textbooks classify rashes as red.[9] Neglecting these visible differences in literature can be harmful, increasing the risk of a delayed diagnosis for those who need immediate care, due to a lack of awareness. Moreover, racially biased literature depicts light skin as the 'norm' and limits the quality and accuracy of differential diagnoses and treatments offered to those with darker skin tones.[10]

Additionally, a study by Massie et al (2019) found that after analysing over 24,000 images in six plastic surgery textbooks, different skin tones were not equally represented in accordance with the US population[4] and another showed that darker skin tones were linked with worse health outcomes.[11] As an example, consider the five-year survival rate for melanoma, which is 67% for Black patients compared to 92% for White patients, primarily due to delayed diagnosis.[11] These statistics vividly demonstrate the possible repercussions of insufficient awareness concerning clinical manifestations in different skin tones, resulting in medical care that may favour White patients while disregarding black and brown-skinned patients.

Besides this, clinical images serve another important purpose – they help convey an individual's diagnosis in a manner that words alone cannot achieve. However, when images inaccurately represent the patient or their condition, confusion can arise – eroding the individual's trust in the doctor's judgment. Such instances might lead patients to assume that the doctor lacks expertise in treating individuals with their specific skin tone. This breakdown of trust can subsequently influence their behaviour, health-related decisions, and most crucially, the dynamic of the doctor–patient relationship.[13]

Problems like these are precisely why representation is crucial in medical education as the limitations highlight the hidden curriculum in medicine. The hidden curriculum consists of the 'uncritical aspects of medical training that impact medical practice'.[3] Decolonisation of the medicine curriculum is crucial to bringing about change. The main focus of this is conquering structural inequalities rather than exclusion based on race.[14] This will mean lecturers and those put in charge constantly question their methods to encompass all students and their future patients. Although the medicine curriculum emphasises the importance of equal care in terms of race, the inconsistent portrayal of races and skin tones in clinical resources contradicts this. Whether or not this is deliberate, the outcomes lead to racial minority patients being pushed aside in medical education, meaning future doctors are not as familiar with complications in minorities. Lipoff, a dermatologist,[15] stated that it is a result of the 'White patient being treated as the default and the Black patient as the asterisk'. As a result, this gives a false idea of the patients that doctors are likely to encounter, creating a sense of unpreparedness in the healthcare setting, contributing to poorer health outcomes in racial minorities.

What factors could contribute to the lack of diversity in medical imagery?

Delving deeper, we can explore the influence of cognitive biases in the authors and teachers of clinical education, as they conclude what is added and discussed in the clinical teaching resources. This is not helped by the lack of racial diversity that are present in the authors. Cognitive biases (sometimes referred to as implicit bias), present in the authors and producers of these resources can affect how they view the importance of inclusive information about different races in their literature. Ryn et al (2015) explains that these biases are likely to develop from their life experiences, some of these maybe occurring at medical school which may ultimately affect how they view other races.6 An example of this implicit bias is in the research findings by Lester et al[15,17] who found that out of 5026 images in common medical teaching resources, coloured skin tones were represented significantly more in sexually transmitted infections (STIs) than in non-STI infections such as acne, 47–58% in comparison with 28%. This literature reflects the reinforced stereotypes of hypersexuality commonly associated with Black people. We need to challenge these statistics in order for subconscious stereotypes to be addressed. Implicit elements like these affect the way healthcare is objectively provided. This is where decolonisation of the curriculum comes into play.

Despite the strong influence of racial disparities in medical education upon patient outcomes, some may argue that the lack of trust present in the doctor–patient relationship with Black patients

also plays a significant role in their absence in medical research and literature. The deep-rooted distrust present in the majority of the Black community may stem from individual experiences of racism and discrimination from healthcare professionals along with the history of harmful clinical practises like the Tuskegee syphilis study.[18,19] Consequently, this results in a reluctance to adhere to clinical treatment and participate in drug trials meaning there is less information about certain diseases for Black people in comparison to their White counterparts.

Even though the majority of this research is based on the American population and American healthcare, the same implicit biases which lead to racial disparities are present in the UK healthcare system tool.[20] This has been highlighted in the current pandemic climate of the UK where ethnic minorities have been affected most by the virus, with the highest number of deaths.[20] In such cases, it would be unfair to attribute the outcomes solely to genetic differences.[21] Instead of placing blame on genetics, it is crucial to address the healthcare disparities arising from biased literature and implicit racism, which contribute to these unfortunate deaths. A lack of diversity in medical education is an example of racial inequality which is reflected in care provided to people of colour.

What is the way forward?

Barriers to a good quality of healthcare need to be dissolved or else they can have negative consequences on those affected. Efforts have been made by medical professionals to tackle these inequalities and create more awareness. One such initiative comes from a third year medical student, Malone Mukwende, who published a clinical handbook called 'Mind the Gap' which aims to bring attention to the clinical signs that do not present the same in a darker skin tone and to educate healthcare professionals on how to identify these differences.[22] For example, consider Kawasaki disease, an acute inflammatory disease of the blood vessels which presents as a red rash in lighter skin tones but as a barely visible heat rash on black skin tones.[22] Please see **Figure 2** for another example. Resources like this will be beneficial in educating of these significant differences that affect health outcomes and is a great example of student advocacy.[6] Despite the impressive response to this book, it is disappointing that a separate book needs to be created in order for there to be an inclusive solution. Just as Lipoff says, 'You can't make skin of colour a lecture that students get once a year. It can't be 'otherized' or put in a separate textbook.'[15] This is a powerful statement that emphasises the pattern of teachings regarding skin colour.

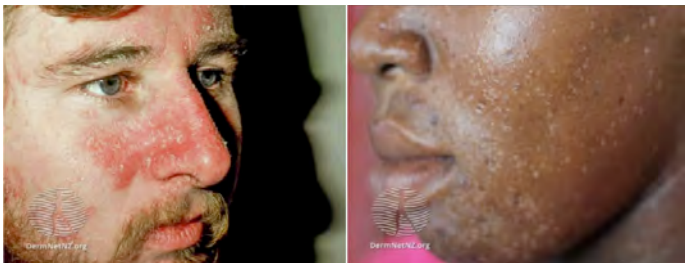

Figure 2. Presentation of Seborrheic Dermatitis on lighter skin and darker skin. Images reprinted from DermNet[23]

Recently, the General Medical Council (GMC) issued a statement acknowledging the need for ethnic representations in patient case studies to diversify the curriculum and the resources used to educate medical students, so that they have the 'opportunity to gain knowledge and understanding of the needs of patients from diverse social, cultural and ethnic backgrounds'.[24] As this new change in the curriculum is relatively a new thing, it is not certain if the change will be the determining factor in better patient health outcomes, but with the GMC speaking out and the NHS incorporating images of darker skin tones in their patient information websites, it is a good place to start.[14,25]

Conclusion

The studies presented highlight a critical issue concerning the underrepresentation of darker skin tones. This issue carries a dual impact, influencing both the competence of doctors in treating patients of colour and the satisfaction of these patients with the quality of healthcare received. As a medical student and person of colour, who has received a dermatology handbook devoid of skin tones similar to my own, I feel passionately about the need for change to provide medicine that is created for all.

To enhance doctor–patient relationships and optimise patient wellbeing, the need to eradicate barriers present in healthcare such as racially biased literature is crucial. As medical institutions prioritise inclusivity in training and educational materials, we have an opportunity to promote improved healthcare outcomes for diverse patients and foster culturally competent doctors. In doing so, we can work towards eradicating inequalities that have marginalised and isolated Black and Brown patient populations.

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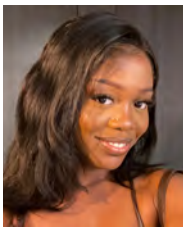

Chidera Stephanie Ayalogu

Hello, I'm a fourth-year medical student at Plymouth Medical School. My fascination with the intricacies of the brain has led to a strong interest in neurology and psychiatry. The inspiration for this essay stems from my first-hand experiences as a student and those of my loved ones in healthcare. These encounters have ignited my passion for advocating and raising awareness about the importance of this topic.

Review

A systematic review on the use of chlorhexidine mouth rinse for the prevention of alveolar osteitis: dose, regime and risk analysis

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Abstract

Background
Alveolar osteitis (AO) is a complication following dental extractions. There is evidence for the use of chlorhexidine (CHX) in the prevention of AO. Recent systematic reviews have several limitations and do not include recent trials. Our aim was to assess the efficacy of CHX rinse in the prevention of AO and describe which dose and regime is optimal and potential adverse reactions.

Methods
MEDLINE, EMBASE, SCOPUS, Web of Science and Cochrane databases were searched for randomised controlled trials (RCTs) comparing the use of CHX rinse with no treatment, placebo rinse or saline to reduce the incidence of AO in patients undergoing an extraction. The Critical Appraisal Skills Programme checklist and risk of bias 2 tool was utilised for quality assessment. Treatment effect was assessed using absolute risk reduction, relative risk reduction and the number needed to treat to benefit (NNTB). Meta-analysis was performed using risk ratio. Fixed effects meta-analysis was used for sensitivity analysis.

Results
Of 230 RCTs identified, nine were included. 0.12% CHX rinse is more effective at reducing the incidence of AO compared to a placebo rinse yet offered no benefit over saline. There is no evidence to suggest 0.2% is more effective. Rinsing twice daily for seven days postoperatively may be optimal, however this cannot be confirmed by the data currently available. 4.3% of participants experienced minor adverse reactions; bad taste, dysgeusia and staining were common. The evidence is limited by a high risk of performance bias and failure to comprehensively account for risk factors.

Conclusion
0.12% CHX rinse is an effective and safe treatment to prevent AO. CHX is no more effective than saline, however, this evidence is significantly weaker. The most efficacious dose and regime may be 0.12% twice daily for seven days postoperatively. Further trials are needed to confirm these results.

Keywords

Chlorhexidine, rinse, alveolar osteitis.

Abbreviations

AO – alveolar osteitis
ARR – absolute risk reduction
CASP – Critical Appraisal Skills Programme
CHX – chlorhexidine
CI – confidence interval
LTF – loss to follow-up
M3M – mandibular third molar
NHS – National Health Service
NNTB – number needed to treat
PICO – patient-intervention-comparison-outcome
RCTs – randomised controlled trials
RoB2 – risk of bias 2
RRR – relative risk reduction

Introduction

Alveolar osteitis (AO) is a complication following permanent tooth extraction. Reported incidence is between 1% and 38% in mandibular third molar (M3M) extractions.[1] AO is characterised by halitosis and intense pain unrelieved by analgesics. Other symptoms include lymphadenopathy, insomnia and dizziness.[2] Blum[3] defines AO as 'postoperative pain inside and around the extraction site, which increases in severity at any time between the first and third day post-extraction, accompanied by a partial or total disintegrated blood clot within the socket'. The pathophysiology of AO is poorly understood. Birns[4] hypothesised that AO is the result of increased local fibrinolysis leading to the disintegration of the blood clot and alveolar bone exposure. Risk factors for AO include surgical trauma, surgeon inexperience, oral contraceptives, smoking and poor oral hygiene.[5]

In 45% of patients with AO, multiple post-extraction visits are needed for symptomatic relief, placing a burden on the National Health Service (NHS) and dental professionals. Societal costs due to time off work and the effect this has on patients must also be highlighted.[6] Therefore, an effective prophylactic treatment would be beneficial. Various interventions have been suggested, notably chlorhexidine (CHX), which has been widely reported in the literature to reduce the incidence of AO. CHX is a broad-spectrum antimicrobial agent and is used extensively in dentistry to prevent biofilm formation.[7]

Current evidence for the use of CHX is conflicting. Several studies have shown CHX, in rinse or gel formulation, reduces the incidence of AO.[6,8,9,10] However, Yengopal et al[11] did not identify sufficient evidence to support the use of CHX. There are several limitations of these studies. Wang et al,[10] Rodriguez-Sanchez et al[9] and Yengopal et al[11] failed to exclude studies that combine CHX with antibiotics, confounding the contribution of CHX. Taberner-Vallverdú et al[8] presented conflicting grades of recommendation and included only one non-randomised trial which assessed a CHX rinse against a control. Regarding dosage and regime, a review by Mínguez-Serra et al[12] found the optimum regime to be twice daily for seven days postoperatively using 0.2%. However, this study is outdated and included non-randomised trials which failed to report on the methodological quality of the evidence. Although the most recent review was published in 2021,[10] it failed to include the most recent randomised controlled trials (RCTs). Additionally, none of the reviews to date were focused on CHX rinse. CHX rinse requires little patient education to be implemented effectively and therefore we felt a focused review on this topic would be advantageous. As a result, we identified a need in the literature to provide an up-to-date summary of the current evidence accounting for the limitations discussed.

The primary aim of this review was to assess the efficacy of CHX rinse in the prevention of AO. Our secondary aims were to describe what doses and regimes were used and any adverse reactions that occurred, providing insight into which dose or regime may be optimal and if the benefits of CHX outweighed its adverse reactions. By doing this, clinicians will better be able to educate patients on how to prevent post operative complications such as AO.

Methods

Search methods

A search of Ovid MEDLINE, EMBASE, SCOPUS, Web of Science and Cochrane databases was conducted on 12 July 2022 and reported in line with PRISMA guidelines for relevant trials up to July 2022. **Appendix A** displays the search strategy, including the search terms used and Boolean operators applied. In addition to database searches, the reference lists were consulted to supplement the literature search.

Selection criteria

Inclusion criteria

We only considered completed RCTs up to July 2021. Articles needed to have satisfied the patient-intervention-comparison-outcome (PICO) criteria: 'In patients undergoing an extraction, does the use of a CHX rinse reduce the incidence of AO to a greater extent when compared to no treatment, a placebo rinse or saline?' A depiction of this criteria can be seen in **Figure 1**. We did not require a specific concentration or dose of CHX to be used. We did not limit our review to M3M extractions and considered articles that extracted one or more permanent tooth from any site. The required primary outcome was the incidence of AO. Studies needed to have clearly defined their criteria for a diagnosis of AO. No date or language restrictions were applied.

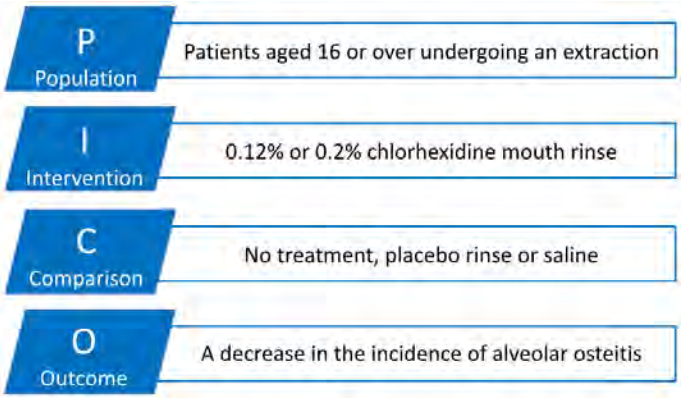

Figure 1. PICO question to be explored in this review.

Exclusion criteria

We excluded review articles, replies and expert opinion pieces. Any trials that compared CHX rinse to an active intervention, combined CHX with another form of treatment, or focused on CHX in other formulations, such as gel, were excluded.

Selection of studies

Articles sourced from our literature search were recorded and duplicates removed using EndNote Online. All remaining articles were screened and evaluated independently by two reviewers (LF and FL) to eliminate bias or errors in methodology. Firstly, articles were screened based on their title and abstract and excluded if the above criteria were not fulfilled. Full text articles of the remaining publications were retrieved and assessed for inclusion eligibility. The results obtained from each author were compared and any differences were discussed and resolved. This process produced a set of publications that satisfied all aspects of the PICO criteria.

Outcome variables and analysis

Our primary outcome was the incidence of AO. Secondary outcomes included the dose and regime of CHX administration and reported adverse effects. To analyse and compare treatment effects both within and across studies, absolute risk reduction (ARR), relative risk reduction (RRR) and the number needed to treat to benefit (NNTB) was calculated by the reviewers where this was not provided by the trial authors. Meta-analysis was performed using the Review Manager software provided by the Cochrane Collaboration. This permitted subgroup analysis which was required due to the variation in CHX concentration and controls used, allowing us to determine if differing results could be attributed to varying methodology. Risk ratios (RR), 95% confidence intervals (CI) and p-values were used to assess and compare the treatment effect. Statistical heterogeneity was assessed using the I2 test and a null hypothesis test where $p<1$ was considered to represent significant statistical heterogeneity. The Mantel-Haenszel statistical method and random effects

analysis, owing to heterogeneity in participants, interventions, and intervention delivery, was used to perform the meta-analysis. A narrative summary was provided for secondary outcomes that were not meta-analysed.

Sensitivity analysis

We pre-specified two sensitivity analyses: i) Including only trials classified as 'low risk' for random sequence generation and allocation concealment; ii) Fixed effects meta-analyses. The latter allowed us to identify the presence of small-study effects.

Quality assessment

To assess the methodological quality of the publications, both authors independently utilised the 'Critical Appraisal Skills Programme' (CASP) checklist for RCTs.[13] We reported our bias analysis summary using the CASP checklist assessment in line with the Cochrane Collaboration's recommendations.[14] Additionally, the risk of bias 2 (RoB2) excel tool for RCTs provided by the Cochrane Review Group was used to allow a more robust bias analysis.[15] The GRADEPro software online was used to grade the certainty of evidence for each outcome.

Results

Study selection

Our literature search yielded 230 articles once duplicates were removed. After title and abstract screening, 203 articles were excluded. The full content of the remaining 27 articles were retrieved for evaluation. Of these, 18 were excluded in line with our exclusion criteria. Consequently, nine articles were included in this review. **Figure 2** illustrates the selection process and **Appendix B** lists the full text articles excluded including our justification.

Study characteristics

Study design and participants

All included studies were published between 1990 and 2021 and were parallel group RCTs, except one that used a split mouth design.[16] In all studies, participants were healthy individuals aged 16 or over requiring at least one M3M extraction, excepting one study where participants required any tooth extracting[17] and one that only included heavy smokers.[16] Mean age varied from 21.4[18] to 43.4.[17] Sample size ranged from 53[16] to 744.[17]All follow ups were between days three and seven. A summary of the trials can be seen in **Table 1**.

Interventions and controls

All studies compared a CHX rinse to either saline solution,[18,19,20] a placebo solution,[21,22,23] or water.[16,17,24] Most studies used a concentration of 0.12%, except two that used 0.2%[19,20] and one that failed to specify.[24] Rinsing regimes varied: two studies prescribed a single preoperative rinse[18,24]; two studies asked participants to rinse twice daily for seven days postoperatively.[17,19] Three studies used preoperative rinsing followed by twice daily for seven days[16,20,23]; and two studies prescribed twice daily rinsing for seven days preoperatively, followed by seven days postoperatively[21,22]

Outcomes

All studies report the incidence of alveolar osteitis (AO) and all, except one,[24] state the dose and regime used. Five studies report the presence or absence of adverse events.[17,20,21,22,23]

Quality assessment

Risk of Bias (RoB2) analysis

Most studies within this review show concerns regarding the randomisation process, with only three studies reporting sound methodology.[16,18,23] Two studies were at high risk of bias due to deviations from the intended interventions and missing outcome data.[18,22] This is due to their high LTF without supporting evidence suggesting that this had a minimal effect on their ability to conduct an intention-to-treat analysis. All studies are at low risk of bias due to inappropriate methodology regarding the measurement of the intended outcome. Two studies show either some concern or a high risk of bias regarding the selection of the reported results owing to missing data.[22,23] Overall, only one study presents a low risk of bias across all domains.[16] These results can be seen in **Figure 3**.

Treatment effect analysis

Incidence of alveolar osteitis

Of the seven studies that reported the incidence of AO by subject, four reported strong evidence for the use of the intervention over the control (ARR: 4.6-25%, RRR: 37.8-63%, NNTB: 4-21.88, p <0.04).[17,21,23,24] Two reported no evidence for the use of the intervention over the control (ARR: 2.8-4.4%, RRR: 11.8-21.2%, NNTB: 22.7-35.7, p >0.05).[19,20] The remaining study did not report p-values, however the incidence of AO across all treatment groups was between 17.9% and 23.7% (ARR: 1.2-4.8%, RRR: 5.1-24.5%, NNTB: 17.2-83.3).[18] A summary of the treatment effect can be found in **Table 2**.

Four studies reported the incidence of AO by extraction site and all presented strong evidence for the use of the intervention over the control (ARR: 10.3- 37.8%, RRR: 44.2-61.9%, NNTB: 2.6-9.7, p <0.041).[16,21,22,23]

Regarding our meta-analysis, risk ratio was lowest when comparing 0.12% CHX rinse to a water rinse (RR: 0.39, 95% CI [0.25, 0.59]) and highest when comparing 0.12% CHX rinse to saline (RR: 0.86, 95% CI [0.42, 1.76]). No statistical heterogeneity was present within subgroups (I^2 = 0%). Heterogeneity was greater for subgroup differences, however, this was insignificant (I^2 = 46.2%, P=0.11). Overall, these results favour the use of a CHX rinse compared to the control (RR: 0.55, 95% CI [0.44, 0.68]). These results can be seen in **Figure 4**.

Adverse reactions to CHX

Out of a total of 1043 participants exposed to CHX, there were 15 reports of a bad taste, 18 cases of dysgeusia, 10 reports of staining to the oral tissues, one case of stomatitis and one case of brief stomach upset.

Sensitivity analysis

Owing to insufficient low risk of bias studies, a sensitivity analysis using the pooled treatment effect from low-risk studies alone was unable to be completed. Fixed effects meta-analysis showed little difference in the estimated treatment effect compared to our random effects meta-analyses, showing that the small sample size in some studies did not overestimate the treatment effect. This meta-analysis can be seen in **Appendix C**.

Certainty of evidence and level of recommendation

The results pertaining to the primary outcome of this review were graded to have very low certainty. This is due to the high risk of bias across the included studies and imprecision of the results. Despite this, the cost-effectiveness, ease of implementation, and minimal adverse events associated with CHX rinse, as shown by the moderate certainty level for this outcome, outweigh the uncertainty of these results. This allows the authors to make a conditional recommendation for the use of 0.12% CHX rinse to prevent AO. As discussed, a recommendation cannot be made regarding the dose

and regime. These recommendations can be seen in **Figure 5**.

Discussion

Summary of evidence

Our primary aim was to assess if the use of a CHX mouth rinse was effective at reducing the incidence of AO following tooth extraction. Our meta-analysis has shown six RCTs to favour the use of a CHX rinse to reduce the incidence of AO[16,17,21,22,23] whilst three showed little to no additional protection over saline.[18,19,20] Methodological heterogeneity regarding the controls used could explain the differing results. Studies that supported the use of CHX rinse used water or a placebo solution as the control, whereas those that did not used saline. Saline solution provides protection against post-operative complications such as AO,[25] yet water offers no antimicrobial properties, and it is unknown if the placebo solutions afforded any protection. This is most notable for the study conducted by Ragno and Szkutnik[23] as they failed to define the content of their placebo solution. Participants who used saline would have had a lower incidence of AO compared to those that used a control with no antimicrobial properties. Naturally, the results show that CHX is effective at reducing the incidence of AO when compared to placebo rinses, however, may offer no additional protection against AO over saline.

We also sought to describe what doses and treatment regimens were used to gain an insight into which regime may be optimal. Due to a variation in population selection criteria, controls used, methodological quality and the use of intraoperative irrigation in some studies, we were unable to identify a preferred rinsing regime. The optimum regime would be one producing the desired effect with minimal exposure to CHX, thus reducing side effects. It would be reasonable to conclude that a two-week course is less preferable, as the same benefits can be achieved using a one-week course.[16,17,23] However, more trials directly comparing regimes are needed to confirm this. Mínguez-Serra et al[12] supports this conclusion, reporting that the optimum regime was twice daily for seven days postoperatively using 0.2% CHX. Our results do not support the use of 0.2% over 0.12% as both studies that utilised 0.2% failed to show any benefit. This is most likely due to the methodological heterogeneity discussed as it is probable that a higher concentration would offer the same benefits. Nonetheless, when increased adverse effects are taken into consideration, 0.12% seems to be the most sensible choice.

Our final aim was to describe the potential adverse reactions that can occur when using CHX rinse to gain an understanding of whether the benefits of CHX rinse outweigh its potential adverse reactions. A total of 45/1043 (4.3%) participants exposed to CHX experienced an adverse event. Bad taste, dysgeusia and staining were commonly reported, which is consistent with the findings by Gürgan et al.[26] There were no reports of major adverse events such as hypersensitivity or anaphylaxis. However, it is likely that these results do not reflect the true prevalence of adverse events within the population if CHX was to be implemented widely as the protocol of four studies was not designed to detect the presence of adverse events[16,19,18,24] and a further four studies excluded participants with a CHX allergy.[16,17,19,21] The prevalence of a perioperative hypersensitivity to CHX is stated to be 9–10%,[27] yet only two major adverse events due to CHX have been recorded in dentistry within the UK.[6] The evidence suggests CHX rinse is safe to use and serious adverse reactions to CHX are rare. However, clinicians must be aware of the potential for CHX to induce both minor and major adverse events when prescribing CHX.

Strengths and limitations

This review provided a focused, comprehensive assessment of the current literature regarding the use of a CHX rinse to prevent AO. Robust statistical analysis, via meta-analyses and sensitivity analyses, and critical appraisal, using the CASP checklist and Cochrane RoB2 tool, was undertaken. The quality of evidence was graded to provide a clear clinical recommendation for practitioners. The systematic methods employed to identify the included studies were stringent, with the inclusion of published literature in all languages, alongside grey literature searching, to avoid publication bias.

Our quality assessment highlighted the limitations within the current evidence, notably the high risk of performance bias. Consequently, the treatment effect of CHX is likely to be overestimated. Interestingly, the studies at greatest risk of performance bias are those that do not support the use of CHX over saline, supporting the conclusion that CHX offers no benefit over saline. However, caution must be exercised with this conclusion. Two out of three of the studies using saline failed to account for risk factors at baseline,[18,19] notably tobacco use. Tobacco use increases the likelihood of acquiring AO by 3–4 times.[28] It is possible these risk factors were unevenly distributed between treatment and control groups in favour of the control, giving a higher incidence of AO in the treatment arm. In contrast, all studies that support the use of CHX excepting Ahmed et al[24] accounted for some risk factors at baseline, of which all include tobacco use, and so are at lower risk of producing spurious results. However, the risk factors accounted for were far from exhaustive in all studies. This highlights the need for future RCTs to comprehensively account for risk factors to minimise potential extraneous variables.

The loss to follow-up (LTF) in most studies was minimal, most probably owing to the short duration of these trials. However, two studies present a high risk of attrition bias.[18,22] Importantly, Berwick and Lessin[18] excluded and replaced participants that were LTF. Although they state that this affected the treatment and control groups evenly, this was not supported by quantitative data. This is a particular limitation in this trial design as those who were LTF were more likely to be asymptomatic and were potentially replaced by symptomatic patients. It is possible the incidence of AO was higher amongst participants within the sample and whether this affected the groups evenly is uncertain.

Conclusively, owing to the factors discussed, the evidence which does not support the use of CHX rinse is significantly weaker. However, the RCTs supporting the use of CHX rinse are not free from methodological concerns, as performance bias and a lack of comprehensive risk factor analysis is a significant limitation in all studies.

Moreover, the statistical methods of two studies fail to account for clustering effects in their extraction site analysis,[22,23] potentially leading to an inappropriate reduction of p-values.[29] Therefore, caution must be exercised when inferring conclusions from this data. This is most notable for the data reported by Larsen[22] as no subject-level analysis was performed. Additionally, only one study reported 95% confidence intervals[17] and so the precision of these results is unclear.

Finally, although the scope of this review was not limited to M3M extractions, only one study reported data for teeth from other locations. Therefore, care must be taken when applying these results to teeth from other sites.

Implication for practice

Current guidelines emphasise smoking cessation advice and oral hygiene education as the best prevention for AO.[30] Unfortunately, AO can still occur despite patients' efforts, especially after M3M extraction. In these cases, we rely on intra-socket obtundents, costing around £45 per pot, and mild analgesics. This diagnostic approach means patients present already in intense pain and adds to the financial burden of the NHS. CHX rinse is a useful preventative tool and is readily available, affordable (around £4) and requires little patient education to be implemented effectively. However, whether CHX rinse is superior to hot salty mouth rinses is uncertain. Therefore, clinicians should make a judgement on which treatment they advise considering the patient's presenting risk factors and any previous tolerance or reactions to CHX.

Conclusion

There is sufficient evidence to recommend the use of 0.12% CHX rinse to prevent AO. CHX is no more effective than saline, although this is supported by poor quality evidence. There is no evidence to suggest that 0.2% CHX offers any benefit over 0.12%. The use of CHX twice daily for seven days postoperatively may be optimum, however this is unable to be corroborated by the data. The adverse reactions caused by CHX are largely benign, yet clinicians must be prepared for a medical emergency in the event of anaphylaxis. This review has highlighted the high risk of performance bias and failure to comprehensively account for risk factors in current RCTs. Further trials are required accounting for these limitations before CHX can be recommended as a suitable preventative treatment to prevent AO.

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Authorship The authors of this project, Liam and Freya, are solely responsible for the conception, design, acquisition, analysis, drafting and approval of the final version.

Declaration of Interest None

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I am currently completing my Dental Foundation Training in Bristol. I am currently enjoying the variation that dental practice brings but I look forward to future academic roles where I can continue to improve my academic capabilities. My hobbies include swimming, running and going to the cinema.

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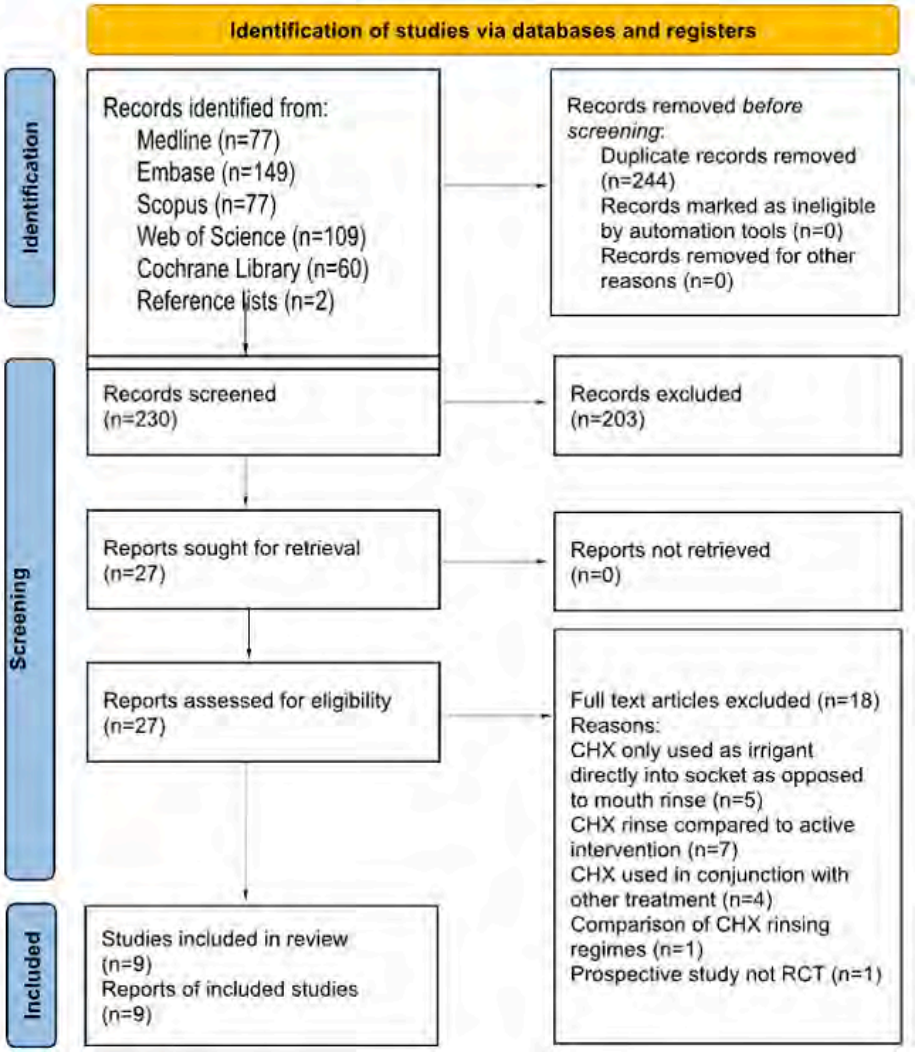
I am currently completing Dental Foundation Training in Bristol. I am completing a two-year post and am currently working in Primary Dental Care Services. This role allows me to treat patients with additional needs which I find extremely rewarding. My hobbies include watching television, going to the gym and spending time with my Vizsla, Chester.

CHX, chlorhexidine. RCT; randomised controlled trial, PICO; patient-intervention-comparison-outcome.



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org

Figure 2. PRISMA fl wchart showing the selection process of articles.

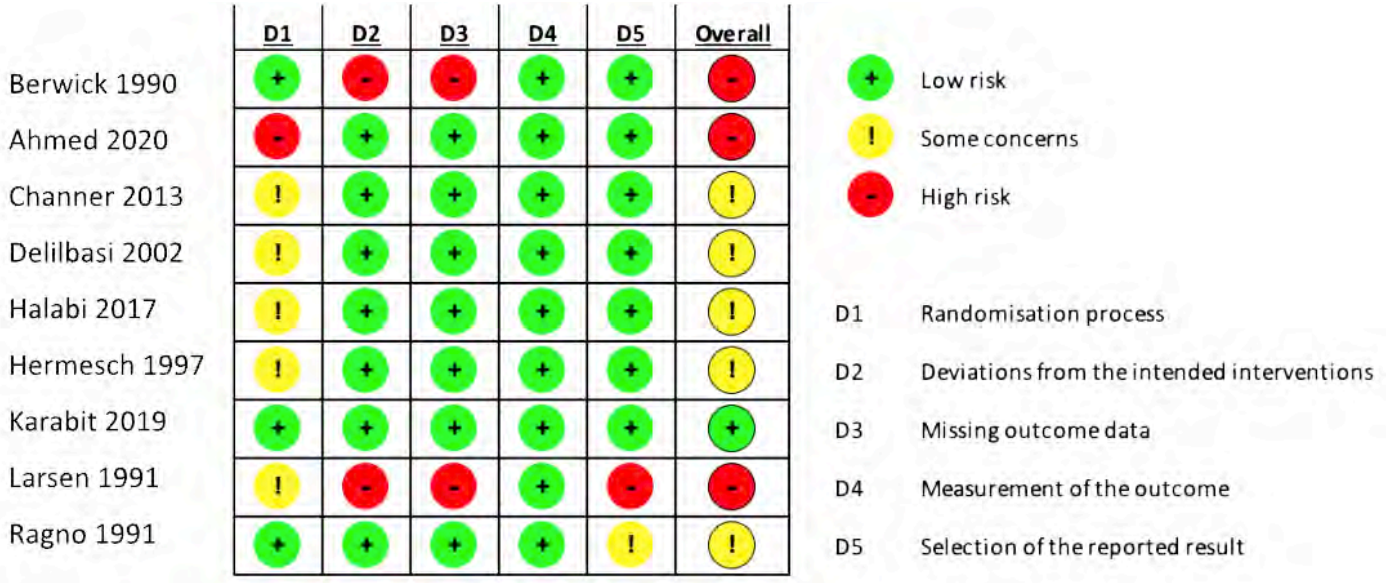


Figure 3. Risk of Bias Assessment of included studies.

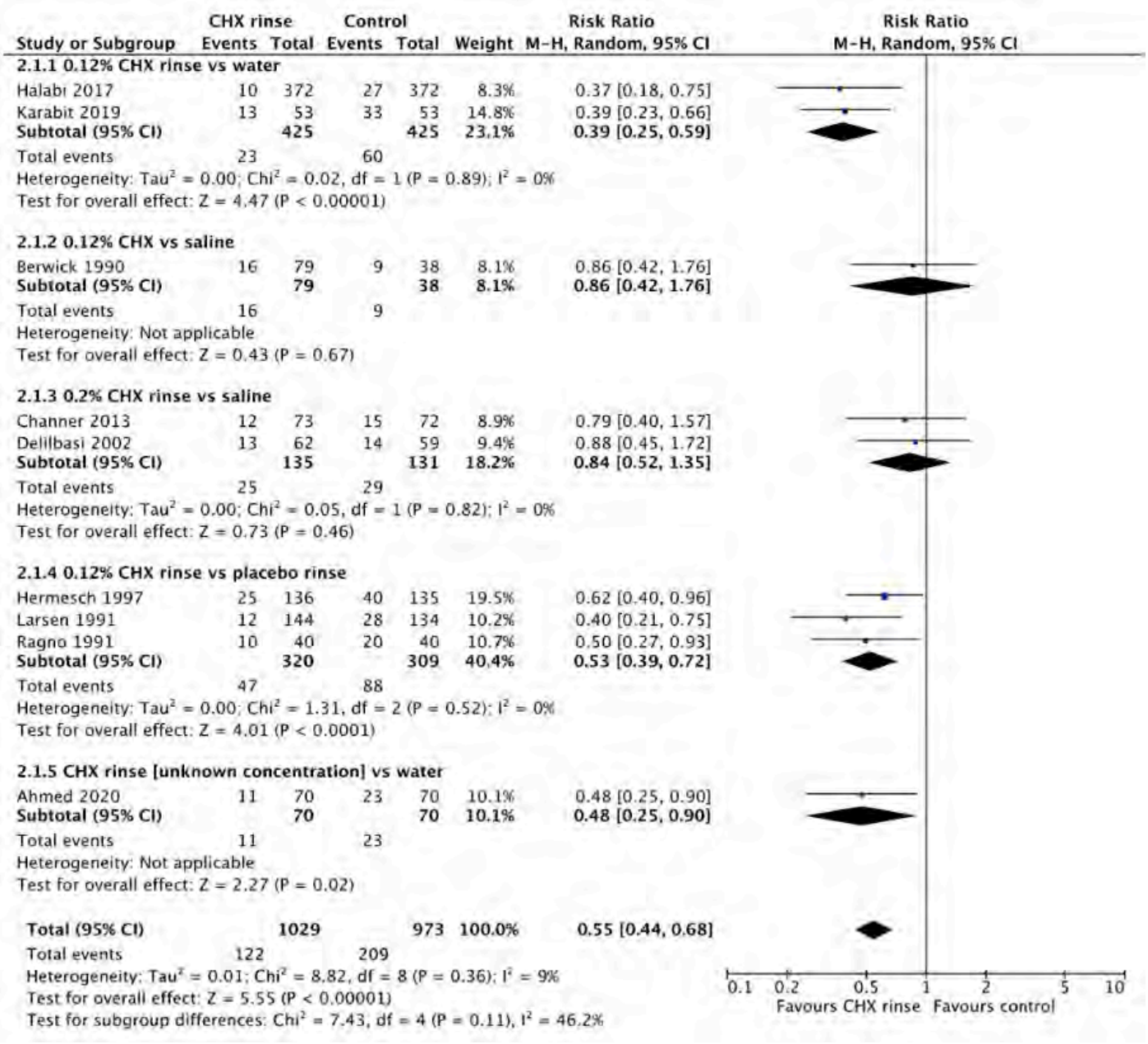


Figure 4. Meta-analysis for CHX rinse (0.12% or 0.2%) versus the control for risk ratio of alveolar osteitis.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CHX mouth rinse	no treatment, a placebo rinse or saline	Relative (95% CI)	Absolute (95% CI)		
Incidence of alveolar osteitis												
9	randomised trials	very serious	not serious	not serious	serious[a]	none	122/1029 (11.9%)	209/973 (21.5%)	**RR 0.55** (0.44 to 0.68)	**97 fewer per 1,000** (from 120 fewer to 69 fewer)	⨁◯◯◯ Very low	IMPORTANT
Dose and regime analysis												
9	randomised trials						Due to a variation in population selection criteria, controls used, methodological quality and the use of intraoperative irrigation in some studies, we were unable to identify a preferred rinsing regime				-	IMPORTANT
Adverse events												
5	randomised trials	not serious	serious[b]	not serious	not serious	none	45/1043 (4.3%)		not estimable		⨁⨁⨁◯ Moderate	CRITICAL

CI: confidence interval; **RR**: risk ratio

Explanations

a. Risk ratio 0.55, 95% CI [0.44, 0.68]
b. Incidence of adverse events varied significantly despite similar sample sizes.

Figure 5. Certainty of evidence for primary and secondary outcomes.

Table 1. Characteristics of the Randomised Controlled Trials Selected

Author, Date, and Location	Study Design	Participants			Inclusion criteria	Exclusion criteria	Stratification Variables	Treatment		Regime	Outcome(s) Measured		Follow up
		Number (Extraction site no.)	Age range (Mean± SD)	Male/ female				Intervention(s)	Control		Outcome	Definition	
Ahmed, T. et al., 2020 Karachi, Pakistan	Parallel group RCT	140 I: 70 C: 70	I: (33.7±8.8) C: 34.8±9.2)	56/84	20-50 years of age with asymptomatic mesioangular impacted M3M	NR	Not used	CHX rinse	Water	20ml 30s twice -1min total-preoperatively	Incidence of PO AO	Exposed alveolar bone accompanied by moderate to severe pain within 3 days PO	3rd day PO
Berwick, M. J. E. and Lessin, C. M. E., 1990 (Unknown location)	Parallel group RCT	80 I (group 1): 20 I (group 2): 20 I (group 3): 20 C: 20	16-40 (21.4)	40/40	Healthy patients requiring M3M XLA	Pericoronitis; abx treatment; pregnant females	Not used	**Group 1**: 0.12% CHX rinse + IO irrigation using 15/15ml CHX/ saline dilution **Group 2**: 0.05% Cetylpyridium rinse + IO irrigation using 15/15ml cetylpyridium/ saline dilution **Group 3**: 0.12% CHX rinse + IO irrigation using 30ml saline	30 ml IO saline irrigation (0.09% NaCl) (no rinse)	10ml 1min preoperatively	Incidence of PO AO	Denuded socket with or without necrotic debris or fetid breath.	Between 3rd and 7th day PO
Channer, K., A., et al., 2013 Jamshoro, Pakistan	Parallel group RCT	214 I (Group 1): 73 I (Group 2): 69 C: 72	20-40 (30.44± 5.20)	129/85	Healthy patients with impacted M3M between 20-40 years of age	Acute pericoronitis; CHX allergy and penicillin	Not used	**Group 1**: 0.2% CHX rinse **Group 2**: 0.2% CHX rinse + Augmentin* (bid 7d PO)	Saline rinse (0.09% NaCl)	15ml 30s bid 7d PO	Incidence of PO AO	Loss/ necrosis of blood clot or exposed alveolar bone and throbbing pain at surgical site not relived by mild analgesia	3rd and 7th day PO

Delilbasi, C. et al., 2002 Ankara, Turkey	Parallel group RCT	177 I (group 1): 62 I (group 2): 56 C: 59	(24)	82/95	Patients in good general health requiring at least 1 M3M XLA	Pericoronitis; abx treatment; females who were pregnant, lactating or taking oral contraceptives	Not used	**Group 1**: 0.2% CHX rinse + IO irrigation using 15/15ml CHX/ saline dilution **Group 2**: 0.2% CHX rinse + IO irrigation using 15/15ml CHX/ saline dilution + Augmentin (bid 5d PO)	Sterile saline rinse (0.09% NaCl) + 30ml IO saline irrigation	15 ml 30s preoperatively followed by bid 7d commencing 24hrs PO	Incidence of PO AO Adverse reaction to CHX	Pain unrelieved by analgesia and presence of exposed/ necrotic debris	3rd and 7th day PO†
Halabi, D. et al., 2017 Valdivia, Chile	Parallel group RCT	744 I: 372 C: 372	(43.4)	363/ 381	Adults requiring XLA (any tooth) with one of the following RF: smoker; previous surgical site infection; and/or traumatic XLA	CHX allergy; abx treatment; abx prophylaxis requirement; pts living in rural areas; pts needing XLA in operating theatre	Tobacco use; previous infection; traumatic XLA	0.12% CHX rinse	Sterile water rinse	15ml 30s bid 7d commencing 24hrs PO	Incidence of PO AO Adverse reactions to CHX	Increasing PO pain intensity for 4d within/ around the socket and total/ partial breakdown of blood clot +/- bone exposure Hypersensitivity, dysgeusia or pigmentation	7th day PO (phone call 4th day PO to encourage attendance)
Hermesch, C. B. et al., 1997 Texas, USA	Parallel group RCT	271 (479) I:136 (239) C: 135 (240)	18-52 (22.3)	101/170	Healthy pts ≥ 18 years of age requiring at least one impacted M3M XLA	Pregnant or lactating females; Abx treatment within preceding 2w; abx prophylaxis requirement; pericoronitis; CHX allergy	Gender; tobacco use; no. of impacted M3M; tobacco use	0.12% CHX rinse with 11.6% alcohol	Placebo rinse identical to intervention minus CHX	15ml Bid 30s 15d commencing 7d prior to XLA	Incidence of PO AO Adverse reactions to CHX	One or more of the following: loss/ necrosis of blood clot, exposed alveolar bone, persistent or increasing pain at surgical site not relieved with mild analgesics	7th day PO (telephone evaluation 3rd- 4th day PO) †

Karabit, Z.Z., Al Kattan, F. Z., 2019 Damascus, Syria	Split mouth RCT	53 (106) I: 53 (53) C: 53 (53)	18-26	31/22	Smokers (over 20 cigarettes per day) requiring XLA of bilaterally symmetrical mesially impacted M3M	Abx prophylaxis requirement; CHX allergy; systemic disease; adrenaline contraindication; females who are lactating or taking oral contraceptives		0.12% CHX mouthwash	Distilled water	Bid 7d commencing 1d preoperatively and resuming 1d PO	Incidence of PO AO	Presence of pain, blood clot or whether socket was covered or uncovered	3rd and 5th day PO
Larsen, P. E., 1991 Ohio, USA	Parallel group RCT	139 (278) I: 72 (144) C: 67 (134)	≥ 18	61/78	Pts requiring surgical XLA of bilaterally impacted M3M	Acute infection; abx treatment; abx prophylaxis requirement	Gender; females taking oral contraception; tobacco use	0.12% CHX rinse	Placebo rinse (identical to intervention minus CHX)	15ml 30s bid 14d commencing 7d preoperatively and resuming 1d PO	Incidence of PO AO Adverse reaction to CHX	Persistent or increasing PO pain beginning after the 3rd day with necrotic tissue in socket, exposed bone, loss of blood clot or abnormal healing	7th day PO †
Ragno, J.R., and Szkutnik, A.J., 1991 Washington, D.C., USA	Parallel group RCT	80 (160) I: 40 (80) C: 40 (80)	≥ 18	51/29	Healthy pts ≥ 18 years of age and have at least 2 M3M	Pts taking mediation (except birth control pills)	Gender; tobacco use; females taking oral contraception	0.12% CHX rinse + IO irrigation using 15ml CHX	Placebo solution + IO irrigation using 15ml placebo solution	15ml 30s preoperative rinse followed by bid 7d commencing 1d PO	Incidence of PO AO Adverse reactions to CHX	Loss/ necrosis of blood clot, foul odour, increased PO pain unrelieved by mild analgesia and absence of gross infection Any adverse reactions reported by patients	3rd and 7th day PO

AO; alveolar osteitis, M3M; mandibular 3rd molar, Abx; antibiotic, bid; twice daily, s; seconds, min; minute, hrs; hours, d; days, w; weeks, no.; number, XLA; extraction, I; intervention, C; control, ml; millilitres, NR; not reported, IO; intraoperatively, PO; postoperatively RF; risk factors, SD; standard deviation, G1; group 1, G2; group 2, G3; group 3

*Augmentin= Amoxicillin 500mg + clavulanic acid 125mg

†Patients who experienced symptoms prior to the planned follow up were seen earlier for clinical evaluation

Table 2. Results for outcomes of interest: incidence of alveolar osteitis and adverse reactions to CHX.

Study	Subject based incidence of Alveolar Osteitis						Extraction-site based incidence of Alveolar Osteitis						Adverse effect of CHX: number (%)
	Intervention(s) (%) †	Control (%)	Magnitude of Treatment effect [95% CI]				Intervention(s) (%)	Control (%)	Magnitude of Treatment effect [95% CI]				
			ARR (%)	RRR (%)	NNTB	P-value			ARR (%)	RRR (%)	NNTB	P-value	
Ahmed, T. et al., 2020	11/70 (15.7)	23/70 (32.8)	17.1	52.1	5.8	0.018							NR
Berwick, M. J. E. and Lessin, C. M. E., 1990	**G1:** 7/39 (17.9) **G3:** 9/40 (22.5)	9/38 (23.7)	**G1:** 5.8 **G3:** 1.2	**G1:** 24.5 **G3:** 5.1	**G1:** 17.2 **G3:** 83.3	NR							NR
Channer, K., A., et al., 2013	12/73 (16.4)	15/72 (20.8)	4.4	21.2	22.7	>0.05							NR
Delilbasi, C. et al., 2002	13/62 (20.9)	14/59 (23.7)	2.8	11.8	35.7	>0.05							Staining of dentures/ oral mucosa: 10/118 (8.5) Dysgeusia: 18/118 (15.3) Reports of bad taste: 12/118 (10.2) Total number with adverse event 40/ 118 (34))
Halabi, D. et al., 2017	10/372 (2.7)	27/372 (7.3)	4.57 [1.5-7. 7]	62.6	21.88 [13.0-69. 3]	0.006							No adverse effects
Hermesch, C. B. et al., 1997	25/136 (18.4)	40/135 (29.6)	11.2	37.8	8.9	0.031, 0.041‡	31/239 (13.0)	56/240 (23.3)	10.3	44.2	9.7	0.014	Stomatitis: 1/ 136 (0.7) *
Karabit, Z.Z., Al Kattan, F. Z., 2019							13/53 (24.5)	33/53 (62.3)	37.8	60.7	2.6	0.039, 0.041‡	NR
Larsen, P. E., 1991							12/144 (8)	28/134 (21)	13.0	61.9	7.7	0.01	No adverse effects
Ragno, J.R., and Szkutnik, A.J., 1991	10/40 (25)	20/40 (50)	25.0	50	4	0.04	14/80 (17.5)	29/80 (36.3)	18.8	56.8	5.3	0.008	Reports of bad taste: 3/40 (7.5) Brief stomach upset: 1/40 (2.5) Total number with adverse event 4/ 40 (10)

BCP; birth control pill, NR; not reported, CI; confidence interval. G1; group 1, G3; group 3, ARR; absolute risk reduction, RRR; relative risk reduction, NNTB; number needed to treat to benefit

*Hermesch et al. (1997) reports several adverse events following surgery and treatment including paraesthesia, infection, trismus, gingivitis, glossitis, abnormal healing, nausea, sinusitis, headache, dysphagia, oedema, haemorrhage, pain, pharyngitis, and a rash. It is acknowledged that the majority of these are a result of surgery. The one incident of stomatitis in the intervention arm was deemed to be definitely/ possibly attributed to CHX.

‡Karabit and Kattan (2019) and Hermesh et al. (1997) are ambiguous in there reporting of p-values, reporting two values instead of one when comparing AO incidence between the treatment and control.

†Data only reported for intervention groups that satisfy the PICO Question.

Appendices

Appendix A

A screenshot showing an example of the search strategy used in Medline on Ovid and the number of articles found. A table format is included for ease of reading.

	Search term	Number of articles
1	Dry socket/	825
2	(Dry socket* or alveolar osteitis or alveolalgia or alveolalgias or alveolar osteitides or alveolar periostitides or alveolar periostitis).ab,ti.	671
3	Chlorhexidine/	9127
4	(Chlorhexidine or CHX).ti,ab.	13652
5	Tooth Extraction/	20281
6	(Extract* or remov*).ti,ab.	1580276
7	1 or 2	1059
8	3 or 4	15435
9	5 or 6	1587978
10	7 and 8 and 9	77

# ▲	Searches	Results	Type
1	Dry Socket/	825	Advanced
2	(dry socket* or alveolar osteitis or alveolalgia* or alveolar osteitides or alveolar periostitides or alveolar periostitis).ab,ti.	671	Advanced
3	Chlorhexidine/	9127	Advanced
4	(Chlorhexidine or CHX).ab,ti.	13652	Advanced
5	Tooth Extraction/	20281	Advanced
6	(Extract* or remov*).ab,ti.	1580276	Advanced
7	1 or 2	1059	Advanced
8	3 or 4	15435	Advanced
9	5 or 6	1587978	Advanced
10	7 and 8 and 9	77	Advanced

Appendix B

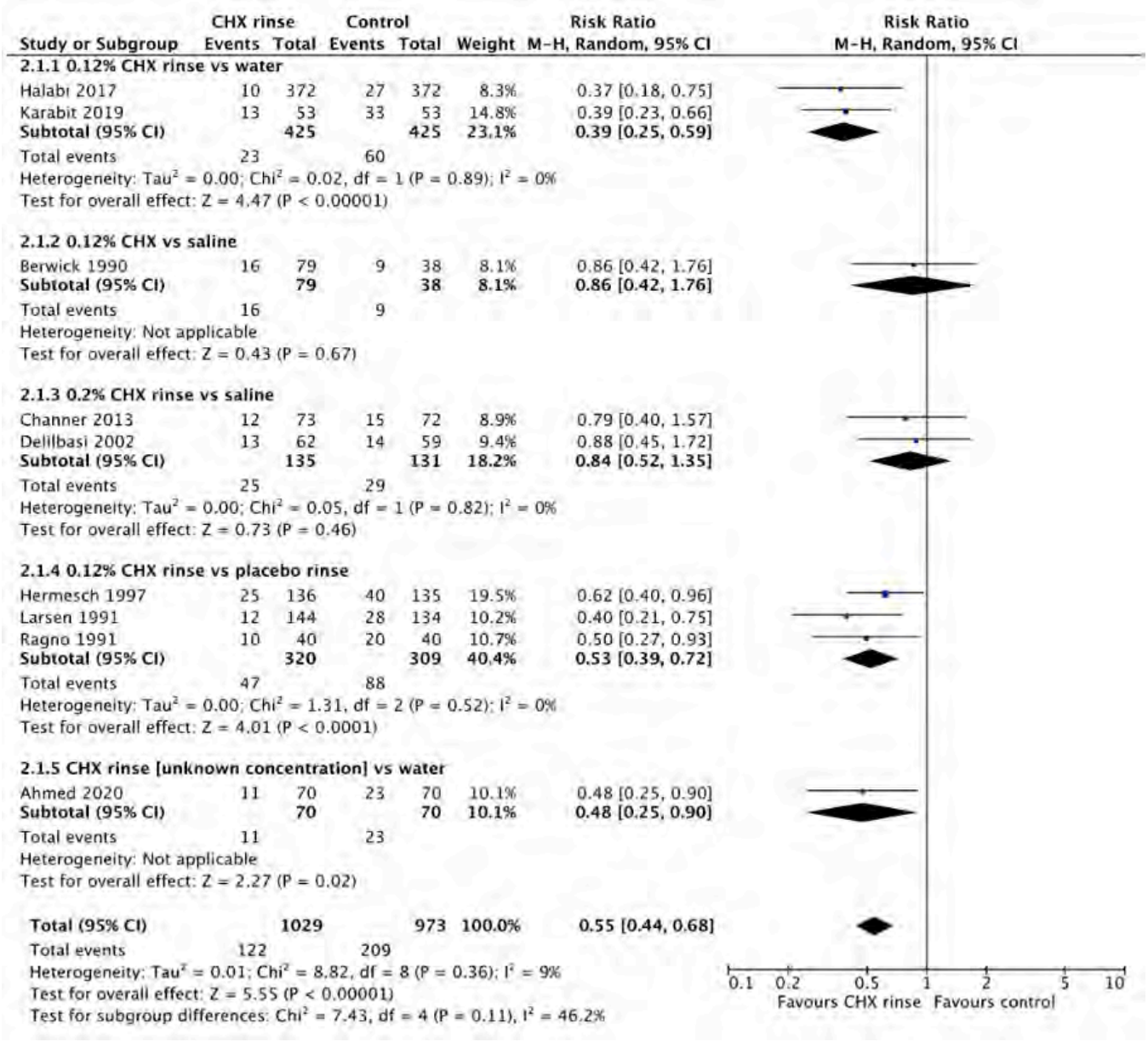
Excluded articles after full text assessment along with their reason and justification for exclusion.

Articles Excluded	Reason for Exclusion	Rationale for Exclusion
Sridhar, V. et al., 2011	Nonrandomized prospective study	Level of evidence insufficient
Metin, M. et al., 2006	Comparison of CHX rinsing regimes	Does not satisfy comparator aspect of PICO question.
Reddy, P. A. et al, 2020 Jadhao, V. A. et al, 2018 Chong, J. K. H., et al., 2016 Haupt, A. M. et al., 2015 Field, E. A. et al, 1986	CHX used as irrigant directly into socket as opposed to mouth rinse	Irrigation post-operatively by a clinician would allow better access of the CHX solution into the socket. This method of application does not reflect what could be achieved with mouth rinsing alone.
Mohanty, R. and Jha, C., 2020 Abu-Mostafa, N. et al., 2019 Divya, R. et al., 2019 Cho, H. et al, 2018 Abu-Mostafa, N. et al., 2015 Younus, S. et al., 2014 Hita-Iglesias, P. et al., 2008	CHX rinse compared to an active intervention rather than a control	Does not satisfy comparator aspect of PICO question.
Osunde, O. D. et al., 2017 Istvan, K. et al., 2017 Bonine et al., 1995 Tjernberg, A. et al., 1979	CHX rinse used in conjunction with other treatment	Addition of another treatment would confound the contribution of CHX in the treatment arm.

CHX; chlorhexidine, PICO; population, intervention, control, outcome.

Appendix C

Sensitivity analysis showing fixed effects forest plot the for CHX rinse (0.12% or 0.2%) versus the control for risk ratio of alveolar osteitis.



Review

The utilisation of genetics to advance the development of pharmaceutical treatments for late-onset Alzheimer's disease

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Abstract

Alzheimer's disease (AD), common in our elderly population, is set to almost double in prevalence within the next few decades. Current medications focus on symptom control and relief, but no treatments hinder disease progression. However, targeting genes associated with late-onset Alzheimer's disease (LOAD) to further the advancement and development of treatments for LOAD has been hypothesised. A literature search was completed on PubMed to investigate this. The search provided knowledge of the *APOE* gene and its contributions to the pathophysiology of LOAD, inciting key findings regarding AD treatments that can target apoE proteins, such as LDLRs, LXRs and recently, the development of mAbs. Several trials on mice, using fluvastatin to target apoE protein receptors, produced various benefits, such as decreased amyloid-beta plaques and increased Aβ clearance. Further mice trials to increase apoE quantity and lipidation using LXR and RXR's, provided similar benefits, and sometimes a reversal of all AD symptoms. Human drug trials did not reproduce similar therapeutic benefits and these drugs resulted in side effects such as liver toxicity. In addition, several mAbs such as donanemab, have been instrumental in AD research but they still produce severe side effects for patients, including micro haemorrhage and oedema. Genetic knowledge can help researchers develop appropriate drugs to target mechanisms associated with the *APOE* gene and LOAD pathology. However, more drug research is needed to investigate and mitigate dangerous side effects.

Abbreviations

ABCA1 – ATP-binding cassette transporter A1
Aβ – Amyloid beta
AD – Alzheimer's disease
APOE – Apolipoprotein gene
apoE – Apolipoprotein E
ARIA – Amyloid-related imaging abnormality
CNS – Central nervous system
LDLR – Low-density lipoprotein receptors
LOAD – Late-onset Alzheimer's disease
LRP1 – Low-density lipoprotein receptor-related protein 1
LXR – Liver X receptors
mAb – Monoclonal antibody
PET – Positron Emission Scan
RXRs – Retinoid X receptor agonists

Introduction

What is Alzheimer's disease?

Alzheimer's disease (AD) is the most common type of dementia and is defined as a neurodegenerative disorder that progressively worsens over time, gradually affecting memory.[1] AD is extremely debilitating and is increasing in our elderly population. As of 2019, over 850,000

people in the UK over 65 were diagnosed with AD.[2] Statistics predict that with the current growing rates this will be over 1.5 million in 2040.[2] In 2012 an estimated 13% of people over 65 years old had AD.[3] AD is divided into two subsections, early-onset familial, or late-onset (>65 years old); they account for 5% and 95% of cases respectively.[4] Early symptoms of AD include loss of short-term memory, causing patients to show mild cognitive impairments. As AD advances, disorientation, language impairment, extreme behaviour changes, and difficulty with motor and sensory functions begin. Eventually, major organs and key bodily functions begin to deteriorate, and most cases of AD result in death. After diagnosis, the average life expectancy is between three and nine years.[5] The high occurrence and lack of suitable management make AD a crucial area for medical research. Currently, there is no treatment available that successfully reverses or permanently halts AD progression.[6] This paper examines the potential of genetics in targeted pharmaceuticals, signifying the utility of genetics in this area of medicine.

Genetics of Alzheimer's disease

Unfortunately, the pathogenesis of late-onset Alzheimer's disease (LOAD) is complex and multi-faceted, making it difficult to underpin the genetics. Lifestyle and environmental factors also impact an individual's lifetime risk of LOAD, further complicating the pathophysiology.[7] Consequently, no mutations are identified as being solely responsible for LOAD, but over 30 at-risk loci have been acknowledged through genome-wide association studies, and over half of these loci have some association with the *APOE* gene.[8]

The *APOE* gene is located on chromosome 19 and presents as three different polymorphic alleles: *ε2*, *ε3* and *ε4*, with *ε3* being the most common.[9] The *ε4* allele is associated with the biggest disease risk, with a single copy estimated to increase your risk of LOAD by three-fold, and two copies increase your risk by 9-to 15-fold.[9] The *ε4* allele is present in 13.7% of the general population but in approximately 40% of AD patients.[10] ApoE is the only cholesterol carrier in the brain and a major carrier in peripheral tissues. It plays a major role in lipid metabolism, homeostasis, and inflammatory response regulation. In the central nervous system (CNS), apoE is produced by astrocytes and will transport cholesterol to neurons in the brain via apoE receptors, such as low-density lipoprotein receptors (LDLRs).[11]

The amyloid cascade hypothesis suggests that AD degeneration is caused by amyloid beta (Aβ) accumulation in the brain.[12] This occurs through changes in Aβ metabolism, either through increased production or reduced clearance.[13] Increased Aβ in the brain will enhance oligomer formation, which eventually leads to severe damaging effects on synaptic function. In addition, inflammatory responses will occur and will lead to plaque formation. Over time, this leads to oxidative stress in the brain and causes various biochemical changes.[14] This cascade ends with increased Aβ and hyperphosphorylated neurofibrillary tau tangles, consequently leading to neuronal injury and cell death, producing the symptoms of AD.[14]

Pathological studies have investigated the implication the *APOE-ε4* gene has in AD pathogenesis. The pathogenesis can be categorised into a gain of toxic function, loss of physiological function, or both. A gain of toxic *APOE-ε4* gene function involves a decrease of Aβ clearance, increased Aβ aggregation in cells and increased neuronal toxicity. Post-mortem studies then confirmed that the *APOE-ε4* gene enhances inter-neuronal Aβ plaques accretion and neurotoxic Aβ oligomer formation.[15,16] A loss of physiological function in the brain encompasses decreased integrity of the blood-brain barrier, decreased synaptic function, and increased inflammatory function, which leads to neuronal injury, further increasing the vulnerability of the brain to the toxic *APOE-ε4* gene. This vulnerability leads to further damage, which produces the symptoms seen in AD patients. However, research found that *APOE-ε2* carriers have less chance of developing LOAD and, in a cross-sectional study, *APOE-ε2* was associated with decreased Aβ accumulation in participants with normal cognitive functions. In participants showing signs of cognitive deficit, *APOE-ε2* was slightly neuroprotective against Aβ depositions, concluding that *APOE ε2* does not have any part in the AD pathogenesis and aids in reducing the risk of LOAD.[9] But when both *APOE-ε2* and *APOE-ε4* alleles are present, the neuro-protectiveness of *APOE-ε2* will not outweigh the neuro-destructive nature of *APOE-ε4*.[9]

The latest AD research focuses particularly on gene-targeted therapies, involving the *APOE* gene. This review examines papers investigating this new research and the pharmacological approaches produced as a result.

Methodology

A literature search on PubMed was conducted to understand AD genetics. The search criteria excluded results from before 2003, ensuring up-to-date information and excluded papers not focused on LOAD, as the pathophysiology between early onset and LOAD is different. The filter "best match" was applied, to ensure the top papers answered the search title. Initially, the search term was 'Alzheimer's disease, "genetics"'. When selecting meta-analysis and systematic reviews, this search produced 6980 results, with the abstracts of top papers including the keywords LOAD, *APOE* and treatment. Next a more targeted search of 'LOAD, *APOE* gene' was completed to understand more about LOAD and the implications that *APOE* has to this subtype. Finally, a search of 'LOAD, *APOE* treatment, genetics' was completed. Relevant papers were identified through abstract keywords of monoclonal antibodies, aducanumab and donanemab. From papers found, citation chaining was used to ascertain more research papers and reviews, and from these papers, key information and findings were synthesised. In addition, a Google Scholar search provided recent figures on Alzheimer's prevalence.

Discussion

Modifying Aβ levels

In the brain, apoE mainly binds to LDLRs, such as low-density lipoprotein receptor-related protein 1 (LRP1), which are strongly linked to cholesterol homeostasis and clearing Aβ depositions.[11] In LOAD, LRP1 levels decrease, resulting in Aβ and cholesterol build-up, two hallmark signs of LOAD.[10] Consequently, researchers investigated whether overexpressing LDLRs could reduce Aβ build up, subsiding its destruction, and potentially being utilised as a therapeutic mechanism.[9] Research in mice that overexpress the amyloid precursor protein gene (APP transgenic mice), supports this theory, showing that LDLR deficiency increased Aβ deposition, whereas in LDLR overexpression it decreased Aβ depositions but also increased Aβ clearance.[17] One supporting study administered 5 mg/kg/day of Fluvastatin in 8-week-old mice. Studies have suggested that statins could help reduce AD risk. The exact mechanism is not understood; however, it is hypothesised that statins influence Aβ metabolism.[18] Their results showed that fluvastatin increased Aβ clearance and LRP1 expression at the blood-brain barrier, but no results showed decreased brain cholesterol levels. Although these studies' positive results provided a solid foundation, the research is new and further trials are needed.[18] Another study, also involving wild mice, tested caffeine and rifampicin, as these compounds have been reported as having a protective effect against AD, by potentially enhancing the clearance of Aβ from the brain. There were three groups: 40mg/kg caffeine daily, 20mg/kg rifampicin daily, and a control group, with approximately 4 mice per group. The study identified that these two structurally different compounds both contribute to LRP1 upregulation and increased Aβ clearance. However, researchers suggested other factors could explain these results, hypothesising the presence of an undiscovered receptor to regulate Aβ clearance.[19]

Both articles demonstrate major advances in LOAD therapy by lowering Aβ levels in the brain, eliminating plaque build-up, and focusing on one fundamental pathological aetiology of LOAD. However, further analysis reveals several flaws, including a lack of

understanding about the specific mechanism of action of these drugs, and that experts have suggested other possible receptors, indicating the need for more research. In addition, Quosa's 2012 study has higher validity compared to Shinohara's 2010 study, their use of genetically "normal" mice decreased the skewing of results, whereas genetically modified APP transgenic mice could increase drug effectiveness, making their results unreliable. Also, using mice creates a shared barrier for both papers, as it is untransferable for human application without further research.[18,19]

Targeting apoE quantity and lipidation

Due to implications in lipid homeostasis, LOAD-related pathways can be influenced by apoE lipidation. LXRs are regulators of lipid homeostasis. It is theorised that LXR's effect on LOAD is due to the regulation of ABCA1 expression, which affects apoE lipidation. Poor lipidation diminishes apoE's ability to break down Aβ.[20] LXRα/LXRβ deficient APP transgenic mice research showed this, as they had increased Aβ deposits and consequently AD signs in their brains.[21] LXRs T0901317 and GW3965 were developed to improve Aβ clearance and apoE production in neuronal cells. A study of Aβ plaque-free mice involved giving 50mg/kg a day of T0901317 for seven days. Results showed T0901317 increased expression of ABCA1 in their hippocampi, increased apoE, and improved contextual memory deficits[22] Similarly, a study involving GW3965 showed enhanced transcription of apoE and ABCA1, reducing Aβ levels in mice[23] Both LXRs improved Aβ clearance and altered apoE production in neuronal cells. Long-term administration showed 50% reductions in Aβ plaques.[24] However, first-generation LXRs were unsuitable for further development, due to high liver triglyceride levels. Newer LXRs had similar side effects in clinical trials, resulting in no drugs achieving FDA approval.[20]

The most popular RXR is bexarotene, an FDA-approved drug used to treat T-cell lymphoma.[25] A study of oral bexarotene in mice showed increased clearance of soluble Aβ. Within 72 hours of receiving bexarotene, 50% of Aβ was cleared.[26] However, clinical applications are limited due to reported liver toxicity. Additionally, in a double-blind placebo human clinical trial of 20 AD patients, bexarotene showed no impact in reducing Aβ or any AD symptoms, and it showed poor CNS penetration. The only effect was increased serum triglycerides, concluding that bexarotene cannot be administered outside clinical trials.[27] Analysis of the paper found their research weakness was the species barrier.[27] The effectiveness and penetration of drugs vary between mice and humans. The papers provide a basis for how we can utilise drugs but conclusively point towards the need for further research to investigate supplementary factors causing cholesterol levels to rise in the periphery.

Monoclonal antibody treatment

The newest treatment is monoclonal antibodies (mAbs). Aducanumab, a disease-modifying human mAb, became the first FDA-approved mAb in 2021.[28] Aducanumab selectively binds to Aβ, both oligomeric and fibrillar, meaning it directly targets the pathophysiology of LOAD.[29] In a double-blind, placebo-controlled randomised phase I trial PRIME, 165 participants with mild AD and positive Aβ positron emission scans (PET) were given a placebo or 1,3,6 or 10 mg/kg infusion of aducanumab for 12 months.[30] Results showed significant reductions in Aβ PET; for participants in the 3,6 and 10 mg/kg group there was a decline in Aβ, but in the 10mg/kg group, some participants now had negative Aβ PET.[31] The PRIME study showed concurrent results in *APOE ε4* carriers and non-carriers.[30] Nevertheless, the study had limitations, including a small sample size and reduced region sample, as they only included USA participants.[30] The next two phase III trials, EMERGE and ENGAGE were completed, with doses based on *APOE ε4* carrier status. Participants were given a low dose, high dose or placebo. In the low-dose group, carriers received 3 mg/kg and non-carriers received 6 mg/kg, in the high-dose group carriers received 6 mg/kg and non-carriers received 10 mg/kg. This was every four weeks for 72 weeks.[32] Post hoc analysis showed higher dose groups demonstrated greater reductions of Aβ plaques. However, futility analysis prompted the early termination of the trial, prompting questions about the validity of the trial's findings. The trial admits to lacking diversity in their population, further biasing their results.[32]

Both studies reported postponed clinical effects of aducanumab, estimating six-month delays in clinical improvement.[30,32] Throughout trials of aducanumab, there have been no reported deaths.[29] However, severe side effects include ARIA.[28] There are two types: ARIA-E (oedema) and ARIA-H (micro haemorrhage or hemosiderin deposition).[28] In the PRIME study, ARIA-E was the prevailing side effect, occurring in higher dose groups amongst *APOE ε4* carriers, with 41% suffering brain oedema.[30] Similar figures were reported in the phase III trials, where 35% of participants suffered ARIA-E.[31] Research on aducanumab has shown other side effects including headaches, nausea, and confusion. Due to disparities in research, further studies are needed to effectively judge the drug's efficacy against its risks.[28]

Donanemab, an immunoglobulin G1 mAb, was trialled after the initial results of aducanumab. Donanemab is designed to directly target insoluble Aβ and help remove Aβ plaques via phagocytosis.[33] TRAILBLAZER-ALZ 2 was a double-blind, placebo-controlled, phase III trial to assess the efficacy and adverse events caused by donanemab.[33] Participants aged 60–85 years were categorised into low/medium or high tau populations after receiving a mini-mental state exam and Aβ and Tau PET scans.[33] Donanemab showed 80% clearance in the low/medium group after 76 weeks and produced meaningful clinical benefits.[33] However, ARIA-E occurred in 24% of participants in the donanemab group, and three patients died after ARIA, two of these were *APOE ε4* carriers.[33] This trial had limitations, including population bias due to a majority white population.[33] Overall, this study concluded that donanemab slows AD clinical progression and has fewer ARIA incidents.[33]

Conclusion

Current research indicates that applying our knowledge of genes and targeting them, has had huge advancements in the treatment for LOAD. This highlights the importance of combining genetics and precision medicine, to aid researchers in developing even more effective LOAD treatments. Targeting LDLR receptors with different compounds has led to Aβ plaque decline, increased Aβ clearance, increased apoE expression and reversals of AD symptoms. LXR and RXRs help increase apoE quantity and lipidation, reproducing many of the same desirable effects as the LDLR targeting compounds. However, most research was done in mice and has not produced positive results in human trials. They have resulted in toxic side effects and no change in symptoms. Monoclonal antibody therapy has been the most promising development to come from genetics research into AD medication, the most successful of these being donanemab. However, severe side effects persist, regardless of the treatment of choice, making monoclonal antibody therapy less than ideal for some patients with AD, especially for *APOE ε4* carriers. In the future, further human clinical trials and randomised control trials are needed, hopefully, producing a more efficacious drug that can safely target the *APOE* gene, and the pathologies associated with it, to reduce LOAD in the general population.

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Louise Warner

Hi! I'm a third-year medical student at the University of Exeter. My interests in medicine are currently surgery, neurology and oncology, particularly focussing on genetics and the potential they could have in helping develop safer and more successful treatments for patients in the future.

Case report

Asymptomatic presentation of renal arteriovenous malformation: a case report and review of literature

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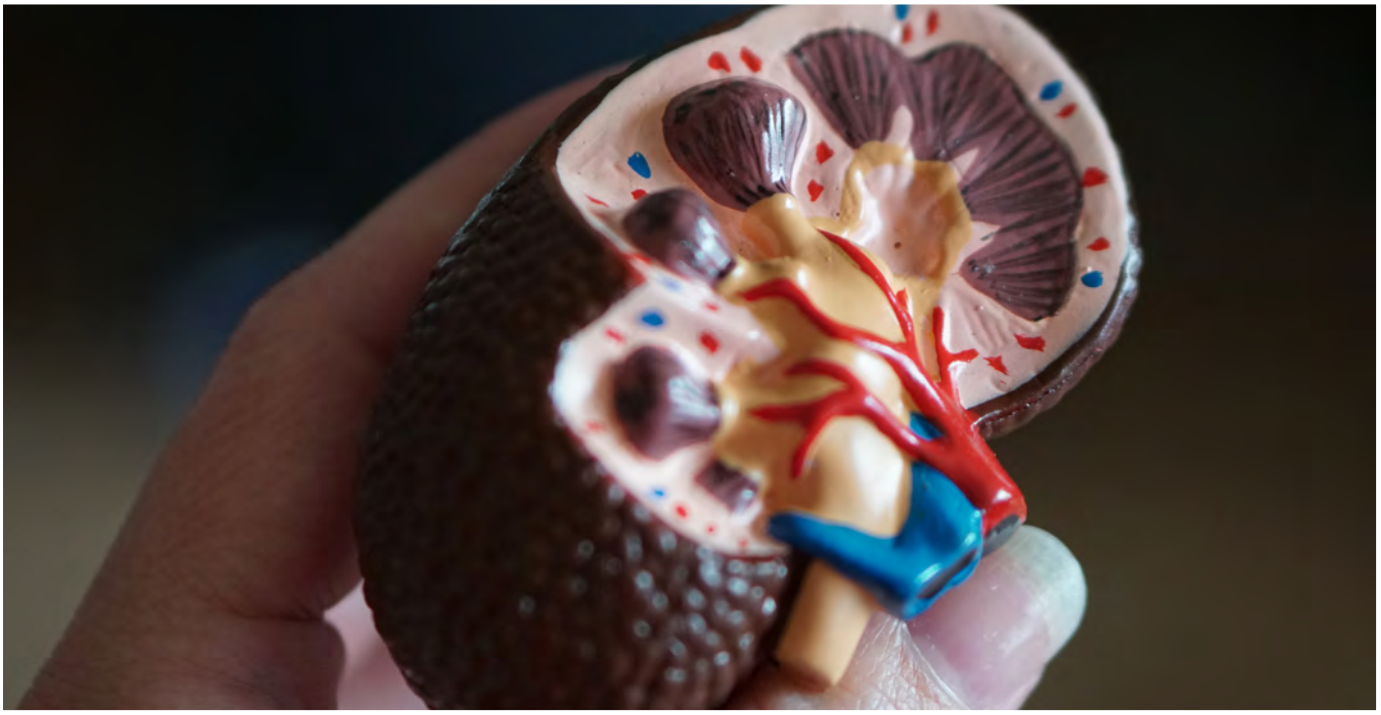

Abstract

Renal arteriovenous malformations (AVM) are a rare finding with fewer than 200 cases reported in the literature. Most commonly, RAVM present symptomatically with haematuria; other presentations include high-output heart failure, refractory hypertension, spontaneous rupture, and a renal mass. We present the clinical and computed tomography findings of an asymptomatic 34-year-old man with an incidental finding of a large (3cm) acquired left RAVM. We discuss the treatment options, by way of a full and relevant review of the literature, and illustrate the need for future research into the natural history of RAVMs, with the possibility of active surveillance as a management option in RAVMs.

Abbreviations

AVM - arteriovenous malformation
BP - blood pressure
CT - computerised tomography
DMSA - Dimercaptosuccinic Acid
eGFR - estimated glomerular filtration rate
IgA - Immunoglobulin A
RAVM - renal arteriovenous malformation

Introduction

Arteriovenous malformations (AVMs) are a rare finding in the kidney with fewer than 200 cases reported in the literature.[1] AVMs are abnormal connections between arteries and veins where blood does not flow through the standard capillary network, but instead through an abnormal vessel network termed a nidus.[2] Incidental findings of renal AVMs are even rarer with less than 30 asymptomatic cases described.[3] AVMs of the kidney are classified as congenital, acquired or idiopathic, and intra or extrarenal. Acquired AVMs are the most common type making up approximately 80% of all renal AVMs, with specific causes including iatrogenic, commonly by renal biopsy or surgery, and trauma, infection or malignancy.[3,4] Anatomically, AVMs are sub-classified into three types: angiomatous, in which a single artery feeds multiple interconnecting distal branches and draining veins; cirsoid, where multiple arteries interconnect by varix-like malformed vessels to form a vascular bed;[5] and cavernosal, where a pre-existing arterial aneurysm invades then erodes into an adjacent vein.[2] 75% of congenital cases present with haematuria,[6] whereas acquired causes are more likely to present with cardiovascular changes, like hypertension, spontaneous rupture with or without haemodynamic collapse, cardiomegaly, and high output heart failure due to increased venous return causing increased preload.[5] Other presentations are from mass effect, like a renal mass, varicocele if on the left, and abdominal distention.[7]

Most cases of incidental asymptomatic renal AVMs are small, defined as less than 2cm.[3] We report the case of a large, 3cm, asymptomatic acquired AVM.

Case report

A 34-year-old male was referred to the urology department with an incidental left renal mass detected on a routine ultrasound scan. The patient had a background of IgA nephropathy diagnosed in 2012 by left renal biopsy, which was well managed on ramipril with a BP of 138/89, eGFR >90, and creatinine of 91 as of May 2021. The patient had no other medical conditions, his performance score was 0, and he was asymptomatic, reporting no episodes of haematuria. A CT arteriogram was conducted which showed a 3cm well-defined left renal pelvic cavernous type AVM **(Figure 1)**, which was fed by a distended anterior branch of the left renal artery with increased blood shunted into a distended renal vein within the left kidney. The aetiology was thought to be secondary to the previous renal biopsy taken in 2012. The differential renal function was assessed by a DMSA scan showing 53% on the right and 47% on the left kidney with the AVM. A multidisciplinary team of urologists and interventional radiologists decided upon a watchful wait approach due to the patient's asymptomatic presentation, with future interventions, namely nephrectomy or embolisation, only considered when local or cardiac symptoms and potential risks outweigh the risk of treatment.

Literature review

A literature review was conducted using PubMed with search criteria "renal arteriovenous malformation" of English articles after the year 2000, this resulted in 80 relevant papers.

From the literature the possible treatment options are: [2,4]

1. Conservative treatment. A less preferred option with the risk of spontaneous haemorrhage, but without operative risk and loss of renal parenchyma. Little data exists on the progression of asymptomatic renal AVMs, although a case report of five congenital renal AVMs showed that with hypertension management alone no other treatment was required.[5]

2. Surgical

   a. Partial nephrectomy. This option has technical difficulty in large AVM, and in the case, the large, cavernous saccular mass was central within the kidney and seemed to be directly feeding to the main renal vein. This is a possible option available to centres with access to robotically assisted surgery, allowing the AVM to be removed while maintaining renal parenchyma.
   b. Radical nephrectomy. One case showed that nephrectomy gave good six-month outcomes regarding renal function and cardiac status.[4] However, this option tends to be used in life-threatening intra-abdominal haemorrhage or haematuria[8] and does lead to significant loss of healthy renal parenchyma. Radical nephrectomy has also been shown to be a good modality in cases with concomitant tumour, a rare cause of acquired renal AVMs.[2,5]
   c. Renal autotransplantation with on-table dissection is an option for experienced centres of renal transplant.
   d. Ligation of the AVM, which is typically for segmental branches of the renal artery.[4]

3. Embolisation by interventional radiology. Minimally invasive options are the most common treatment modality for renal AVM, with one study reporting that embolisation was used in 77% of renal AVM[3] and a case series reporting its use in 92% of cases.[8] Emobilisation can be by coil, alcohol, liquid embolic or gelfoam to embolise the feeding artery of the AVM. The modality of choice is at the discretion of the interventional radiologist on the vasculature and hemodynamic factors. Embolisation is thought to be the go-to treatment for renal AVMs as it preserves unaffected renal parenchyma function, rarely has side effects, and has a reported 91.7% success rate in treating haematuria, with normal post-procedural blood pressure and renal function.[8] However, it is not without risk, including pulmonary embolism,[9] dislodgement and migration[10] with coils, and with all modalities post-embolisation syndrome and the risk of recurrence.[10]

The possible complications of renal AVM have been well documented. What is unclear is when AVMs present and how many cases go on to never present or cause complications. High output heart failure is a well document presentation of AVMs, typically presenting in patients aged over 30.[10] The need for cardiology involvement in these cases is complicated, high output heart failure can cause hypertrophic cardiomyopathy which has a worse prognosis than that of a radical nephrectomy. Because of their rarity, little data exists on the best management of these cases, so does treatment need to be tailored to the complication or to the anatomy of the AVM itself?

Conclusion

The natural history of renal AVMs is poorly understood, and data does not exist on the prognosis of conservative management in the cases of incidental asymptomatic renal AVMs. Little is known about which of the treatment modalities has the best efficacy and which is most appropriate for given cases. While small asymptomatic AVMs can be treated conservatively with watchful waiting, interventional ambivalence still exists for the treatment of asymptomatic cases of large renal AVMs. The decision of if or how to treat these patients needs to be taken on an individual basis after careful consultation with the patient and consideration of individual patient factors. More research is needed as to the best treatment modality for RAVMs.

Consent

Verbal informed consent was obtained for discussion of this case report and use of accompanying images.

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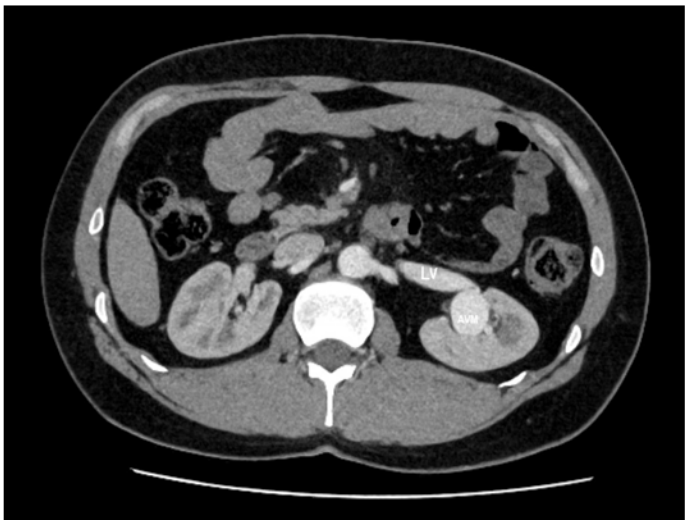

Figure 1. Axial CT showing 3cm Left Renal Arterial Venous Malformation of the Patient

George Garratt

George Garratt is a final year medical student at the University of Leicester, having completed an intercalated MRes on retinal development George aspires in becoming an active medical researcher of the future.

Feature

The value of medical volunteering

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Whilst the meaning of words can evolve with time and historical events, the word "volunteer", deriving from the Latin word voluntarius meaning "willing" or "of one's choice", epitomises its origins in its current implications and uses. Today, the Oxford English Dictionary defines volunteer as, "one who voluntarily offers his or her services in any capacity; one who of his or her own free will take part in any enterprise".[1] In the medical field, volunteering is often associated with care, services and aid in the context of humanitarian crises, public health emergencies, or low- and middle-income countries with roots in colonialism and a reciprocal "the helper and the helped" dynamic. However, medical volunteering is prevalent closer to home perhaps more than we might be aware. One such UK-based non-profit registered charity is Festival Medical Services (FMS): the charity aims to provide efficient and high-quality medical services at UK-based events with the underlying vision of broader and far-reaching transformative change via the utilisation of funds raised to support global health-related charities. Following the completion of my First Responder Emergency Care Level 3 Certification, I have volunteered with FMS as a first responder in pre-hospital teams for several years.

Though volunteering describes an act that is selfless, it is a rewarding undertaking with much to be gained by the volunteer themself. The value of medical volunteering as a medical student, I believe, is conspicuous and incontestable; there are opportunities to develop one's clinical and communication skills and to acquire new ones. However, as I learnt through accruing experiences at different events, the learning extends beyond that which is tangible and related to skills refinement. I will henceforth attempt to outline this by recounting a memorable pre-hospital experience.

Despite cumulating a breadth of pre-hospital experience across a variety of events, before each shift I am always overwhelmed with excitement. This excitement is also entwined with anticipation and apprehension as to what the imminent shift will engender. Thoughts that pervade my mind include, "Do I still remember all the key details from my training to be able to manage difficult patient cases? What if I encounter an outlandish presentation? Am I capable of managing this effectively? Will I be able to find my way around the vast perimeter of land hosting the festival/event?" On one hand, we dare not to utter the hapless and ill-omened "Q-word" (quiet) in fear of awakening the superstition that turmoil will be unleashed. On the other hand, though we do not wish for individuals' ill-health, we hope that the shift will not be so "Q-word" as to be uninteresting. Indeed, I, alongside others, always hope for there to be a balance.

During one of my very first shifts, the aforementioned balance was disproportionately skewed towards there being a series of critical incidents. As a volunteer, you often meet the team members you are working with during shifts for the very first time at the start of the shift, thereby adding to the complexity of managing critical incidents. However, there had been a premonition amongst the current working team that the next act would foment some unrest and inspire intrepid daredevil behaviour amongst the young crowds, having notoriously done so when they performed several years ago. Thus, we were fortunate in that the former team judiciously chose to remain past the handover period and extend their working

hours into their free time. Such prudent preventative measures did make me wonder whether the knowledge, both of performers and spectators, that there are medical teams at festivals may perpetuate the normalisation of health-detrimental behaviours, as we were soon to experience. Is this just? And is there a way of ensuring that medical teams' resources are equitably distributed?

As the havoc-wreaking act began to perform, as anticipated, there was a crescendo influx of patients into the medical tent. Initially, most presentations were panic attack-related due to the formation of mosh pits and the rapid inundation of fans into the spectator viewing area, or related to the acute sequelae of excessive alcohol consumption and possibly the consumption of illicit drugs as well. The latter patients, on the whole, were either nauseated, already vomiting, or found unconscious. Thus, the atmosphere in both the medical tent and the arena was heightened. This situation could have easily overwhelmed me as a rookie first responder; however, I kept my head down and focussed on my predetermined role. This involved bringing patients in, ensuring their safe positioning an appropriate distance away from one another, exploring their presenting complaint, and rapidly taking some basic observations before summarising and feeding my findings back to the nurse in charge. However, the number of patients entering the tent imminently and almost exponentially skyrocketed and, as a result, I quickly assumed the role of "scribe" whilst also dealing with the simplest of cases. Being one of the most junior team members, my assumption of this role was a means to release the more experienced and qualified team members to focus their attentions on delivering high-quality patient care to a group of increasingly sicker patients. Indeed, amongst the second influx of patients, several were critically unwell: one with greatly reduced consciousness, one with a traumatic musculoskeletal injury, one patient with epilepsy who presented actively seizing, and the most critically ill of all was a patient in cardiac arrest.

Per our predetermined and assigned roles, the more senior team members flocked to help out with the cardiac arrest. Adult Life Support (ALS) was swiftly commenced on the patient and their transfer via ambulance to the on-site medical centre was rapidly arranged. I continued my role of ensuring that patients' details were being documented and scribed; however, was also assigned to the role of "runner", if necessary. Moreover, to ensure sufficient privacy, dignity, and confidentiality for the cardiac arrest patient and so as not to distress further other unwell patients, my next role was to try to clear out the medical tent as much as possible. Thus, despite the tent teeming with people and the circumambient chaos, the medical team was strategically organised in our mobilisation and activities.

I left this shift feeling somewhat hopeless due to the minute role I assumed, taking on a "follower" over frontline roles. However, personal reflection alongside a whole team debriefing enabled me to recognise the value and salience of my roles in the smooth running of the team and management of events as well as to learn more about my own personal qualities, character traits and values. Moreover, through the debriefing, I learnt more about effective clinical governance in medical volunteering. Firstly, medical volunteering does not in any way equate to less accountability or a lower quality of care due to a presumed lack of regulations, supervision, or fewer high-level systems in place as in hospitals. On the contrary, the debriefing was organised to establish a timeline of events, and promote resolution and welfare for the staff involved, with opportunities to establish and act on learning points. It was a real comfort to understand from the debriefing that the decisions taken, and interventions carried out, were agreed to have been appropriate and timely by senior medical staff and non-clinical managers. Furthermore, the debriefing highlighted the paramountcy of safeguarding everyone's health, whether a patient's or a colleague's, for the sustainment of high-quality healthcare. Secondly, this experience illuminated how, by simply sharing the same values as others, one can rapidly and truly become part of a community. I experienced how forthright communication was key to achieving this, but also that I was able to quickly build rapport with colleagues by being empathetic, kind, respectful and supportive, whenever needed.

In terms of learning about myself, I feel that I had been enlightened as to my demeanour and how I carry myself in such high intensity situations and unfamiliar territories. Clinical skills simulation sessions, often with a small audience and although made to be as realistic as possible, can only teach you so much about yourself in this sense. Whilst at times during the shift I may have felt slightly overwhelmed, I feel that I was able to navigate these feelings quietly and composedly by remaining calm, level-headed and keeping a clear mind, and by being flexible, adapting to the unforeseen circumstances. If I ever felt out of my depth, I felt confident to call for more senior support, something that can often feel unnerving as a medical student on clinical placements for fear of disturbing or vexing senior staff with an issue that may be "trivial", or for being deemed "incompetent" or unknowledgeable.

Thus, in addition to amassing clinical and communication skills, an invaluable learning point from this experience was my better appreciation of and confidence in my own capabilities, as well as the individual resilience that I started to build whilst being immersed in a supportive, highly-professional team delivering excellent medical care.

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Feature

Game for a challenge

by Phoebe Sussman

Year 4, Veterinary Sciences, University of Bristol

In August 2022, I made my way to South Africa to take part in the Vets Go Wild Impact course, to learn about wildlife medicine. After a long journey from London Heathrow to Port Elizabeth, we loaded up onto minibuses and began the drive to Amakhala Game Reserve. During the drive, the vastness of the landscape was apparent. The topography in the Eastern Cape is characterised by mountain ranges and valleys which are largely grassveld (an Afrikaans term which can be loosely translated to 'prairie'). These areas of land are uncultivated with indigenous grass growing freely and the odd sighting of an impala or kudu; a very different sight to that of the green patchwork fields making up the British countryside. After a few hours we had arrived. Amakhala Game Reserve was established in 1999 as a joint conservation effort between six families who had previously used the land to farm sheep and cattle. The reserve's 18,000 acres has since undergone a re-wilding process to provide habitats for native South African wildlife. Visitors can expect to see a range of species including giraffes, lions, elephants, rhino, buffaloes and cheetahs. Over the next two weeks, we would shadow Dr William Fowlds and Dr Emily Blaxter, getting the chance to work with many of these species and a taste of life as a wildlife vet.

The bread and butter of wildlife work in South Africa is darting animals to anaesthetise them for various procedures or translocation. During the course, we worked as the ground team, monitoring the anaesthetic for many antelope species, giraffes, lions, and black and white rhinos. It was incredible to see these species up close and a great opportunity to practice our basic clinical skills. During the first week, we focused on the translocation of kudus and impalas. In the field, monitoring anaesthesia can prove quite difficult; a lot of the time you are working whilst the animal is being transported in the back of a truck with limited resources. If you can feel a pulse whilst driving over the rough South African terrain, then you'll fly through monitoring pulses in first opinion practice. After honing our monitoring skills working with kudus and impalas, we then moved on to bigger animals. A particular highlight was feeling the pulse of a black rhino whilst the reserve's team replaced its tracker. They are such forceful creatures, and it was a surreal experience to feel the gentle buzz of its pulse. Working with giraffes was another incredible experience. To help maintain genetic diversity and prevent inbreeding, we translocated two juvenile giraffes to another reserve. This proved quite an exercise as the height of the giraffe poses a logistical challenge when they are knocked down by the dart.

To reduce the impact of the fall, a team ran behind the giraffe and encircled it with ropes to help control the fall; a slightly astonishing race requiring the coordination of people, ropes and the giraffe. Once the giraffe was knocked down, we immediately reversed the anaesthetic. Three people then laid on the neck to prevent the giraffe from rising whilst we placed a halter, blindfold and ear plugs. These helped to reduce the sensory stimuli and protect the giraffe's eyes. The giraffe then stood up and we guided her onto a big trailer with the halter and ropes, applying and removing pressure at just the right moments. This was a truly unforgettable experience. During the course, we also helped to place a contraceptive implant into a lioness to prevent the lion population becoming too large. This was a slightly nerve-racking experience; prior to carrying out the procedure, we had to scare off a lion which was mating with the lioness. Rattling guns and making loud noises from the game-viewer, eventually he left. We were then able to carry on but we had to carefully watch for his return. On this day, I had the chance to place my first ever IV catheter. Luckily, it was a little bit easier than most domestic species – lions have pretty big veins compared to domestic cats!

Although much of the course was practical, we had a series of lectures to bring us up to speed with the crucial theory behind wildlife medicine and conservation. It became apparent that the work of a wildlife vet stretches far beyond medical procedures. Wildlife vets play a crucial role within One Health, the field focusing on the intersection of animal health, environmental health and human health. Wildlife, in particular, can carry many zoonotic diseases (diseases which are transmissible to humans) such as rabies and anthrax. Wildlife vets work to surveil these diseases and prevent the spill-over into human populations. Additionally, advocacy to protect habitats and promote environmental health will only help to prevent future outbreaks of serious diseases from occurring. When the environment is unstable, disease prevalence will only increase. Hence, wildlife vets play a central role in the control of wildlife diseases which may have significant human health impacts. We also discussed the socioeconomic impacts of conservation, and the large problems surrounding poaching. Conservation needs to positively impact the surrounding communities for it to be successful. Without communities valuing these animals, they will be at a high risk of poaching. There is a huge market for the illegal trade of wildlife products, and poaching provides an opportunity for many to make money and support their families. A multi-faceted approach will be required to disincentivise poaching and the team at Amakhala is working to increase job opportunities within these communities, provide education on the importance of wildlife to children, and encourage greater animal welfare of domestic species to stimulate a greater perceived value of animals as sentient beings. However, the illegal wildlife trade will continue to threaten critically endangered species, meaning that there is a large necessity for anti-poaching campaigns.

Although wildlife populations are declining due to human activity, learning about the work of wildlife vets such as Dr William Fowlds and Dr Emily Blaxter has been hugely inspiring. I often reflect on my time at Amakhala as a very formative experience; it is fairly remarkable to witness these animals in their natural habitat. Their extinction would be deplorable, but as future veterinarians we have the unique opportunity to protect them and work towards building an environment which benefits both humans and animals.

Photographs kindly provided by the author.

Conference Report

INSPIRE 'INSPIRing Research' conference report – November 2023

Gayathri Kannan

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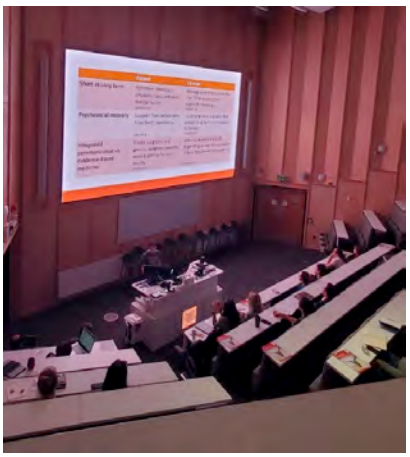
On the 18 November 2023, I was extremely grateful to attend the INSPIRE 'INSPIRing Research' conference taking place at the Centre for Student Life in Cardiff. The event was attended by over 120 medical, dental and veterinary students from eight UK Universities. The event was informative, engaging and insightful with a positive environment that I felt was extremely enriching for the young professionals present – cultivating a sense of confidence surrounding independent research.



Following a brief history of the INSPIRE scheme, a number of short research talks were delivered by students – all to an extremely high standard. Throughout the presentations, Mentimeter was available for the Q&A, giving guests the freedom and opportunity to ask questions whenever possible.

The research talks started off with **Adam Maher**, a veterinary science student at Bristol, who focused on the current challenges of burn care in the healthcare system. Following this impressive presentation, he aims to publish his secondary data in a journal next year and at a conference focussing on care for individuals affected by burns.

Next, **Annalisa Willmott**, a fifth-year dental student at Cardiff, delivered an insightful presentation on the effects of short promotion materials of UK mouthwash on oral health. The research covered both positives and negatives of the promotional materials and highlighted the evidence-based approach that is so prevalent in current NHS dentistry.

Courtney West, a medical student at Exeter, gave an informative insight into RET gene mutations which are associated with risk of medullary thyroid cancer. West's presentation focused on exploring the treatment options for addressing this particular medical issue and she went on to win the award for the best oral presentation, after which I was able to conduct a short interview with her:

Courtney West pictured receiving her award with Professor Tarr's parents Michael and Susan Tarr

Well done on an extremely engaging and interesting presentation. It was delivered at an incredibly high standard, a well-deserved win. In terms of your research, would you like to expand your findings further and take it elsewhere and if so, where?

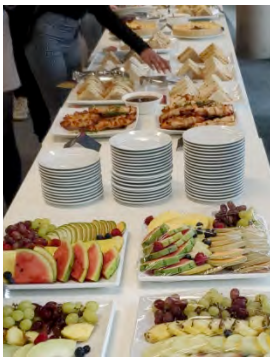
The research I presented was developed from the project I undertook as part of my intercalated year; I have since developed the project further with the aid of my supervisor and a summer studentship from the Society of Endocrinology. My aim with this project is to submit it for publication as I believe the findings could help shape official guidelines in the management of incidentally found RET variants.

There are still many unanswered questions surrounding this project particularly around what are the contributing factors in causing medullary thyroid cancer if the penetrance is as low as I found, and I would like the opportunity to work on this. However, I am still new to research and this is a substantial project that may take time to come to life. Therefore, in the meantime I am trying to expand my knowledge of the research space, how it works and what options are out there. With the overall plan for next steps being to apply for the specialist foundation programme with a research placement to be able to continue participating in research, specifically genomics research throughout my career.

Tomas Nicolas at Plymouth followed with a topical issue about how smoking can change the oral biome and presented his interim data as a part of a longer study that was due to be finished at the end of the year. The implications of smoking can cause vasodilation problems resulting in blood pressure issues but, interestingly, Nicolas identified that there was no difference in blood pressure between smokers and non-smokers – an unexpected result that paves the way for further exploration.

To round off the oral research presentations, **Annabelle Lim** – a medical student at Cardiff – delivered an extremely colourful presentation on routine MRI surveillance of people with multiple sclerosis for which she went on to win best runner up oral speaker.
I was immensely impressed at the standard of oral presentations by the students of various different ages, seeing the thought and effort that has gone into their long-term research and the ability to which they were able to deliver their ideas to an audience of specialties different to the focal topic.

Plenary speaker, **Dr Arman Eshagi** of UCL, gave a relevant and intriguing talk on the use of Artificial Intelligence (AI) in healthcare. He commenced his talk by revisiting what AI actually is which was refreshing to see as there is so much buzz around this topic that people can forget what it actually is at its core. Dr Eshagi went on to explore the use of AI in viewing the progression of Alzheimer's, designing radiographic reports and neurological diseases, presenting evidence on the accuracy of the results by the AI when cross-referenced by a clinician. Personally, I found that the idea that stood out most to me was the concept of 'self-supervising AI' which involves providing the AI with a large data set from which it then proceeds to learn on its own, which can assist with diagnoses, prognoses and predicting systemic disease. This concept was fascinating to me and I thank Dr Eshagi for such an eye – opening talk.



Everyone then dispersed for lunch and to look at the poster presentations that were displayed across the floor. It was wonderful to see the work that had gone into these posters. The presentations produced were a result of the hard work of students of medicine, dentistry, and veterinary science across all years. The display was incredibly informative with a variety of ideas and provoking thoughts put forward by such intelligent young minds.

After the break, the second plenary speaker **Alex Newberry,** a former Law student now working for Welsh Government, broke up the scientific flow, providing a fresh perspective on the ethics that go into research and healthcare. Newberry discussed data collection, privacy concerns and discussed data ownership. I felt that Newberry was able to give an insight into aspects that healthcare students will have to face as they mature into young professionals, particularly down the research route. Newberry also mentioned the idea of positive research culture which aptly segued into the Hackathon presentations.

The INSPIRE Hackathon was a challenge surrounding the themes of research and innovation to encourage undergraduate students of Cardiff University, Bristol University, Plymouth University and Exeter University (institutions that are a part of the GW4) to tackle a problem and devise solutions using big data for an emerging issue surrounding healthcare, humans and animals – a task that would involve a One Health approach. This is slightly different to the traditional concept of a 'Hackathon' which refers to exercises surrounding computing.

Dr Alex Tasker, Senior Lecturer at University of Bristol, presenting.

The presentations started off with an overview of the challenge presented to the candidates – each team was provided with an image of a bat on a tree indicating Nipah virus and their mission was to plan around a Nipah virus outbreak with the One Health approach in mind. Using analytical techniques to analyse large datasets (big data), the candidates had to present solutions to the emerging problem of the Nipah virus and how various sectors, such as agriculture and the general public, could be managed in order to control this outbreak.
Judging was completed by the audience who were provided with a Mentimeter code where there were different categories with sliders from 1 to 10 to indicate how well the proposed approach adhered to each aspect.

The categories were as follows:

1. Scope – How well did they deal with the complexity of this problem?
2. Interdisciplinarity – Who and what did they include in their response, and how did they bring together different expertise and experiences?
3. Pragmatism – What real-world considerations did they anticipate?
4. Feasibility – Have they shown understanding around the importance and potential of big data and data science to inform their decisions?

All teams delivered their presentations with confidence and assurance indicating the level of thought and time that had gone into analysing the problem that they were faced with. After a close competition, the Exeter University team was deemed the winner of the Hackathon challenge.

Team Bristol: Shraddha Sriraman, Jenn Chae, Elin Hardwick and Sruthi Nair
Answers by Sruthi Nair

You mentioned in your presentation an approach of tackling the virus from the point of view of a pig farmer. How did you go about conducting research to achieve this perspective?

To answer this, we firstly looked at what pig farming would look like in a country like Babi by extrapolating data from what South-East Asian rural Pig farming looked like. Then we looked at the problem from the perspective of our imaginary Farmer in Babi, Farmer Mo and structured what our interventions would be based on the problems he would most likely face in getting support. For example, how he would sell his produce and not be out of pocket if his pigs had to get culled. We also looked at whether it was currently possible to test pigs for infectious diseases, as this is an important step in our plan. The vet in our team Elin had lots of baseline knowledge about pigs and infection which was very helpful and to help supplement our ideas she found a few papers.

You talked about a farmer connecting app, please could you tell us more about this?

We thought that as smartphones are very common in South-East Asian countries it would be useful to have a method to connect farmers when they're going through something as difficult as isolations and the potential culling of pigs. It would alert farmers when a nearby farm had an outbreak, governments would be able to communicate to farmers using the app and farmers would be able to share advice about how to implement biosecurity. It would also be used to report pigs for testing and allow tests to be ordered. This hopefully would enable people to still feel connected, access support and share ideas. Furthermore, it would help governments keep track of the spread of the disease.

What do you feel that you have gained out of participating in the Hackathon?

I think the most important thing that we gained was a greater understanding of inter-disciplinary work. Our team was mostly medics, but we also had a vet. Her perspective of the problem really changed the way we decided to tackle it and I think will change the way we look at healthcare problems in the future. We have also gained a greater understanding of the complexities of infectious outbreaks and the sheer volume of things you have to think about, not just keeping people safe but making sure their livelihoods are intact. Lastly, I think we also learned how important targeted interventions are.

Team Cardiff: Riya Rao; Tsz (Eunice) Pak; Tsz (Vanessa) Yeung; Samuel Njoroge; Hamza Khan
Answers by Tsz Pak (Eunice)

Thank you for such an engaging presentation and representing Cardiff! How did you find the process of doing something new such as this Hackathon that involved concepts like big data which is not something you tend to come across in a healthcare degree?

I found the process extremely exciting and enlightening because big data is such a massive topic whether or not in the healthcare field, as its application crosses so many sectors of our daily lives. Learning how to solve problems in healthcare such as via policy making, involving multiple stakeholders, expanded my horizons on thinking from different perspectives and thinking on a broad societal point of view. Moreover, learning how to use machine learning and AI models in solving problems in healthcare is a very cool and innovative concept which I would be keen to explore more in the future, through learning techniques such as coding.

Your network model was very impressive, what went into making that?

One of our team members studies Data Science and has the template as a basis for the model. Another team member has basic knowledge on machine learning and how it can be applied to create transmission modelling and statistics, so it was really down to their contributions!

What was the most exciting part of preparing a presentation for this challenge?

The most exciting part is having to have different team members contributing their own point of views and coming to a common conclusion towards the solution of the problem through brainstorming. I learnt a lot of important One Health concepts throughout the discussion process, different public health issues and ways of tackling emerging diseases in a country. It was also particularly interesting to apply the machine learning models into the project as it brought about real-life applications of the use of machine learning.

Team Exeter: Riyea Akhtar, Tobi Akinlolu, Charles Britton, Shaima Chbib, Fasika Estefanos, Frances Eslabra, Ieva Jakaityte, Pavel Loginovic; Grace Maani, Tom Owen, Sana Poormohammadreza, Bodrun Nahar Sheikh, Siddharth Shukla, Joshua Tyrrell

Team Exeter University at the Centre for Student Life.

During your presentation, all of the team members were very actively involved - how did you delegate responsibilities and manage to come together as a team to incorporate different ideas to tackle such a multi-faceted problem?

Riyea Akhtar: To ensure a comprehensive approach in addressing the multi-faceted challenge, our team strategically convened in person initially to collectively define objectives and outline a holistic solution framework. We then divided into groups according to our individual skills and strengths. One group focused on the data aspects and the other delved into epidemiological considerations. Throughout the project, whether virtually or in person, we reviewed our individual research findings and collaboratively shaped our presentation. This process not only facilitated an exploration of the problem but also ensured that all concerns were addressed.

What was your favourite part of compiling the presentation?

Bodrun Nahar Sheikh: One of the most rewarding aspects of compiling the orientation for the Hackathon was the teamwork and spirit of our team. As a big group from Exeter University, we had students with previous degrees and different backgrounds. We utilised each other's expertise in different areas to formulate a comprehensive strategy for the Nipah virus outbreak. We had a number of group meetings, in person and online, and these sessions were filled with dynamic discussions and everyone's input was valued. Another aspect was that the research process allowed us to learn more about various topics of public health, epidemiology and medical ethics, fostering both individual learning and teamwork.

What have you learnt most from the process of completing this challenge?

Shaima Chbib: During this process, we collectively learned about teamwork, and taking a One Health, holistic approach towards this complex, multi-factorial issue. It was interesting to observe this issue through other peoples' perspectives based on their experience and area of expertise. It was interesting to explore alternative solutions, both short-term and long-term when dealing with this outbreak. With our diverse group, we benefited from each members' different strengths, and made our discussions fruitful, insightful and made it a great opportunity for all of us to learn from one another. It was also a great opportunity to learn research techniques and presentation skills.

I really enjoyed this experience and am very grateful to have such an excellent team.

What does winning mean for you and do you have any plans to take this research further?

Obatobi Akinlolu: Well, it was a close call. When we won, it was a relief to feel that all our hard work had paid off and the challenges we faced were all worth it. It was exciting to see the power of teamwork as well as how a common interest can bring people together.

I'm not sure about the rest of my group but attending the conference really helped me see real and practical ways to get involved in research and help make a difference in areas I am passionate about. I am actively seeking and creating opportunities for myself and I've been inspired to reach out to academics that may be able to help me. I am really looking forward to my future career in academia.

Thank you INSPIRE!

Team Plymouth: Umme Alam, Sachi Baviskar, Joya Dutta, Zara Hirji, Rishika Segireddy, Christine Tse

Firstly, I would like to thank you for such an engaging presentation, it was informative and entertaining! How did you as a team find the process of exploring the One Health concept considering how vast it is?

Rishika Segireddy: In our initial planning stages, we prioritised mitigating the human outbreak, with a small focus on zoonotic surveillance. When we came across the concept of One Health during our research, the interconnectedness of humans, animals and the environment, particularly in the context of zoonotic outbreaks, fascinated us greatly. Despite our time constraints in exploring this vast concept, we wanted to include some facets of this approach in our plan. Thinking about the environment, we recognised how loss of biodiversity can increase zoonotic spillover risk1 and wanted to move away from damaging practices like fruit tree deforestation. By adjusting our strategy to minimise environmental impact, we aimed at developing a sustainable and transferable plan in case of future outbreaks.

Christine Tse: As a group, I believe we worked very well together despite the geographical differences of different members being in Plymouth, Torbay and Taunton. It was quite difficult to ensure everyone was on the same page but using a shared Notion allowed everyone to understand what had already been happening. When exploring the case and the health concept, we had to break it up into smaller chunks to evenly distribute between members of the team. We had to delegate tasks surrounding the different domains (planning, epidemiology, global health, stakeholders etc) which made it vastly easier to tackle. This way we could assign each section to different members and explore in greater detail without it being too overwhelming for everyone to investigate everything.

Zara Hirji: The complexity and vastness of the topic was something that I think we all noticed right away. Although it could be overwhelming to consider as a whole, our main priorities were to explore our own curiosities surrounding the topic to start with. I think it helped that we all felt comfortable questioning one another and not dismissing any uncertainties. This meant brainstorming, mind mapping and assigning further research to different groups in our team. In the end I think we found that, instead of trying to dismiss the vastness and complexity of the topic, our approach needed to both acknowledge this and use it to our advantage. It gave us more of an insight into how such a theoretical project may actually translate in the real world. This is how we settled on a One Health approach.

What was something you learned about big data when completing this challenge?

Sachi Baviskar: Using big data has helped us understand the complexity of formulating government-informed interventions for the Nipah outbreak. While big data has been a crucial element in predictive modeling, vaccine rollout strategies and identifying susceptible populations, we've learnt that the inferences we can draw from it are not fully black and white. There are multiple considerations to make regarding the applicability of the data we are using. The role of big data in our strategy extends beyond simply objective measures but also helped us acknowledge the various cultural nuances of the outbreak. This allowed for a more holistic consideration of the implications of our chosen plan of action. For example, communication tools were something we looked at in-depth to enhance public awareness and compliance.

Rishika Segireddy: Looking at big data regarding public health interventions used in previous outbreaks, we realised how successful infographics have been at spreading awareness to large groups of people from varying backgrounds. Making it a key component of our plan, we were able to consider how determinants such as differing sociocultural norms, literacy rates, health beliefs that prevail in a country could be addressed with tailored and evidence-based interventions.

Another big issue we chose to focus on was epidemiological surveillance. Looking at how data was used in previous Nipah virus endemics and the recent COVID-19 pandemic to monitor disease burden and allocate resources efficiently had informed our response strategy in this challenge. This included common approaches such as case-based surveillance for mortality reduction and population-based surveillance for disease control.2

Joya Dutta: An angle of big data that I feel we barely covered in our plan was AI. This was very interesting to me as some of the other groups partaking in the challenge had a great emphasis within this. It makes sense, as AI is something so up and coming within healthcare and the world in general. Truthfully, it was something we glossed over as it felt way outside our scope of understanding and felt like a bit of a mystery. Hearing about all the potential behind utilising AI in the health challenge was amazing, the novel approaches heard were fascinating. One example was using an AI-supported social media screening system to help target transmission and surveillance. I was also amazed by some of the actual data systems and statistical tools that other groups had investigated, it was very inspiring to see the interests and hard work that people put into learning about health challenges and targeting a virus epidemic, exploring in depth epidemiological and statistical measures that are mainly used by specialists.

You mentioned self-disseminating vaccines as a key idea. Please could you explain a little bit more about this novel approach and how you came up with exploring this idea?

Zara Hirji: Self-disseminating vaccines are a more proactive prevention method for reducing the spread of zoonotic diseases by targeting the spillover of zoonotic diseases from animal vectors to humans. High risk for spillover pathogens may be identified targeted within their animal reservoir before a human outbreak even begins to emerge via the use of an animal vaccination.3 In the case of our presentation we thought theoretically of a Nipah virus vaccine to give to the pig and bat vectors rather than sole reliance on human vaccination. A couple of challenges to vaccinating animal populations is firstly the potential high turnover of those animal reservoirs and secondly inaccessible animal populations. Self-disseminating vaccines overcome these challenges as they are actually capable of transferring from one animal to another without needing to vaccinate the entire population.3,4 This also improves the possibility of eradication of the pathogen before it even reaches and causes harm to human populations is much greater than through human vaccinations.

We enjoyed researching into different primary prevention tactics which included the concept of self-disseminating vaccines. We then explored it further with our collaborators who had more expertise

in the area and so were able to direct us towards further reading in this interesting topic, which we knew little about to begin with, and helped us to apply it better to the case of our own project.

Joya Dutta: We were lucky to have discovered a Plymouth university researcher, Michael Jarvis, and his work that has revolutionised disseminating vaccines in general.5 This made a big difference for our plan and the outcomes suggested for the Nipah virus outbreak.

Umme Alam: The concept of self-disseminating vaccines is a fascinating and innovative approach that aligns well with the One Health framework. We wanted to implement this approach throughout our presentation, and exploring self-disseminating vaccines allowed us to do just that. Since Nipah virus is zoonotic, targeting the wildlife reservoir with a self-disseminating vaccine can help break the cycle of transmission and reduce the risk of spillover into human populations. The novelty of this approach lies in its ability to address infectious diseases at their source, taking advantage of natural ecological processes to achieve widespread vaccination. It's a collaborative and interdisciplinary approach that requires expertise in virology, ecology and public health.

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The evening concluded with an open discussion and panel where students had the opportunity to ask questions on how to be more involved with research and the ways to take any research they had conducted further. This was a great opportunity to hear what the different panel leads had to say in response to the questions as everyone had different expertise.

Following this, there was a tribute to INSPIRE Lead for Exeter Professor **Jo Tarr**, who sadly passed away in Summer 2023. All attendees were able to take some time to discuss her wonderful accomplishments and her contributions to both Exeter University and INSPIRE, allowing her colleagues to share some anecdotes about their time with her. In attendance were Professor Tarr's parents, brother and partner who presented the prizes to the winning students in honour of **Professor Tarr**.

The conference was extremely valuable to undergraduate students, introducing them to a variety of professions within the three healthcare fields introduced – medicine, dentistry and veterinary science. It also helped provide insight into the different topics of research that are being undertaken by students – giving a motivational and impressive undertone to the whole event. From the Hackathon presentations, it was clear to see that the students were able to come together and collaborate on perhaps unfamiliar territory regarding subjects outside of their merit, such as more computational approaches, to present a comprehensive answer to the challenge they were faced with. Based off the answers to my questions, it is clear to see the sheer effort that the students have put into this challenge and for this, I commend them. The skills that can be picked up from attending conferences such as this one and participating in events such as 'Hackathons' that stretch you outside of your comfort zone have great implications for future careers that these students might venture into, such as exercising the ability to think on the spot, present in front of large audiences, research and learn skills outside your scope and most importantly, the need to participate as a team.

I would like to extend my gratitude to everyone for their time in answering my interview questions and thank the participants of the conference for their presentations from which I learned a lot. I would also like to thank the INSPIRE leads for coordinating such a successful event.

Interview

Andy Gibson, Mission Rabies

by Phoebe Sussman

Year 4, Veterinary Sciences, University of Bristol

Rabies is a lethal viral infection characterised by an acute encephalomyelitis, causing roughly 59,000 human deaths each year.[1] It is caused by an ancient group of viruses, the Lyssaviruses, which are thought to have originated in Old World bats before spilling into human, dog and other wildlife populations.[2] The earliest record of rabies infection in humans dates back to the 18th or 19th century BC on Eshnunna law scrolls from Ancient Mesopotamia.[2] Over many years, we have gained a greater understanding of rabies infection and transmission, with many countries, such as the UK, achieving a rabies-free status. However, the rabies virus still greatly impacts many countries, with the virus being endemic in many areas. Rabies has been categorised as a 'neglected zoonosis' by the World Health Organization (WHO), acknowledging that the disease mainly affects poor, vulnerable and marginalised populations.[1,3] Within these communities, education surrounding rabies infection and access to medical care is very limited. For this reason, it is thought that the number of rabies-related deaths are widely under-reported each year, due to a lack of awareness of the symptoms which occur during rabies infection and under-diagnosis.[3] However, many of the deaths due to rabies are preventable; for the last 138 years we have had access to an effective vaccine.[3] Additionally, 99% of all rabies-related deaths occur due to rabid dog bites.[3,4] For this reason, many organisations believe that it will be possible to eliminate rabies infection from human populations, and the WHO hopes to achieve 0 rabies-related deaths in people by 2030.[5] Due to the zoonotic nature of the rabies virus and stray dogs acting as the main reservoir population of the disease, vets and medics will need to work together to implement control strategies within these vulnerable populations.[3,5] Mass vaccination campaigns within stray dog populations, improving education surrounding rabies infection and ensuring there is greater medical care and access to vaccinations within these vulnerable populations will be crucial to prevent rabies infections within humans.[5]

Many organisations have been working towards the goal of eliminating rabies infection in humans by working to establish many of these strategies to reduce rabies infection. One of the large contributors working to prevent rabies infection in humans and dogs is Mission Rabies. Mission Rabies is a charity which was set up in September 2013 to work towards saving both human and canine lives in rabies hotspots around the world, working alongside local governments and its sister organisation the Worldwide Veterinary Service. The charity has set up mass vaccination projects across many countries, vaccinating over 2 million dogs and educating 5 million children globally. It is headed by a team of vets and supported by many volunteers helping to implement these campaigns. Andy Gibson, one of the vets working on the vaccination campaigns with Mission Rabies, very kindly chatted with me about his work with the charity and how vet students and medics can get involved in working towards the goal of preventing rabies-related deaths in human populations.

How did you end up working for the charity and what inspired you to work on this issue?

To give you a bit of background about myself, I studied as a vet and then went up to the RSPCA, working in Manchester for a bit. I then went back and did an internship in London and after that I didn't really know what to do career wise. I was quite into clinical medicine, and I went out and volunteered with the charity [Mission Rabies]. When I was out there, Luke the CEO really set out the premise that it's on vets to sort out the issue of rabies. There are children dying of rabies being bitten by dogs and no matter how much the human medical sector vaccinates people against rabies, they will still be bitten by dogs, and there will still be deaths due to rabies. It's always treating the symptom of the problem. So, I went out to India and began leading vaccination campaigns. It's a really simple problem to fix; compared to other diseases it is a simple epidemiological situation. There are no insect intermediary vectors and it [rabies] passes from dog to dog before spilling into the human population. The typical rabid dog is often not what you'd expect. They're often not foaming at the mouth or charging around the streets. They often look subdued or completely normal. But seeing the impact rabies had through meeting the families of children who had been really badly bitten drew me to this issue. As vets we can make a difference. And so, I got involved with the vaccination campaigns, working on the development of technology to try and improve the coordination of vaccination teams, making it more efficient to direct them in the

field. This has become a real foundation of our work, and I've gone on to do a PhD at Edinburgh University, which has allowed me to dive deep into the issue of rabies and technology development within this area.

That's so interesting and I completely agree; with the majority of human deaths from rabies being caused by rabid dog bites, it seems that mass dog vaccination is really important in preventing human deaths caused by rabies. What are the main considerations of your team when starting the various mass vaccination projects you currently run and what are the aims of your projects going forward?

There are three main pillars of any project we run: mass dog vaccination, which involves understanding the dog population and its composition, such as owned dogs versus strays, how to access the dogs, and how to plan the campaign to achieve herd immunity; surveillance, which involves establishing good surveillance systems to see the true situation; and education, where we are trying to get rabies included in the school curriculum so that children who are in high risk groups are being made aware of rabies and what to do when they get bitten. In all of our projects we try to engage the government and try to form a partnership, particularly on our larger projects. Our two largest projects are in Goa, where we work as the implementing party under the government's leadership, and Malawi, where we are working alongside the government in the south to implement mass dog vaccination campaigns. We also have other projects that we run and, recently, we ran a campaign in Cambodia where we vaccinated 75,000 dogs in 10 days, working alongside local NGOs and the government as an implementing partner. Our aim at Mission Rabies is to set up huge campaigns to vaccinate hundreds of thousands of dogs in just a few days, working alongside local governments and NGOs to better control rabies.

Wow, that's a lot of dogs vaccinated! Could you explain a little bit about the problem of rabies and how it circulates within the dog population?

To give some context, from the time of exposure, dogs will get the virus from a dog bite and there's a long incubation period while the virus is tracking through the peripheral nerves and the central nervous system. This typically takes three weeks in dogs depending on where they receive the bites. Once the virus enters the brain, the virus then replicates and disseminates back to other parts of the body. From that point, death is inevitable, and typically progresses in three days, so the infectious period is quite short. The reproduction number for the rabies virus is between one and two. This means that each rabies-infected dog generally passes on the virus to one or two dogs before it dies. So, the virus slowly propagates through the population and is not very transmissible. Because of the long incubation period you never get a surge in infection. When you start mapping those dogs and surveilling infections, you begin to see that it's everywhere, but as the infection is not very apparent, it flies under the radar. So, it's [rabies] hugely under-reported and therefore the public and political awareness of this issue isn't there.

How do you decide on in which regions to vaccinate dogs?

Some recent work we've been doing is high resolution mapping of dog populations, trying to get better data before we start working somewhere on the distribution of dogs, the number and the geography. We then use this information to help plan the strategy and help the government to plan a strategy which is likely to succeed. We've also now developed an app which enables us to direct teams in a much more spatially defined way. We want to avoid patchy 'Swiss cheese' coverage; it is important to achieve homogeneous, even coverage of a region. If you have pockets where you don't vaccinate, you have virus present which stays within those regions. The app that we've created tries to direct teams region by region. Each day, teams will get assigned a new area where they need to vaccinate, and we have black GPS points on the map which represent the dogs we've vaccinated. You can see the teams moving across the area week by week, comprehensively vaccinating every community. This helps us to see if we've missed a patch, and so we can assign those areas and send the teams back to those regions to vaccinate and continue. You get nice repeat coverage, and this helps us to prevent the virus from continuing to circulate in these areas.

That sounds really effici t and important to ensure you vaccinate enough dogs! How many dogs do you aim to vaccinate in a campaign to achieve herd immunity?

When it comes to achieving herd immunity, we actually only need 40% coverage to interrupt transmission. So, the vaccine number needed is really low. And for this reason, when it comes to rabies elimination, it is actually very achievable. We can vaccinate 40% of the population and interrupt that cycle so the virus disappears. But the problem is we usually vaccinate the population once a year. However, there's not a common veterinary practice vaccinating puppies, especially strays, between our campaigns. As more puppies are born and some of the vaccinated population die, the number of unvaccinated dogs increases in between our campaigns. Although our threshold is 40%, if we only vaccinate 40% each year, we could drop below that threshold in between our vaccination campaigns and the virus will circulate between these periods. So, the current recommendation is 70% to maintain the high coverage throughout the period and disrupt transmission even if the coverage depletes between your campaigns. However, the coverage we need may vary between regions, and we are currently beginning to carry out research into what factors may affect this.

How do you estimate the number of dogs you need to vaccinate in each specific egion before carrying out your campaigns?

Currently, we are looking at existing data and using this to predict the dog population in that area. There's a balance between putting resources into running lots of surveys and running campaigns where you also get data about the population. We know that dog populations are very closely related to human populations; where there are people there is a predictable relationship with the dog

population. So, we have created maps of human populations which we can then apply a human dog population ratio to which we can extrapolate from other study sites. And we've done this for many countries. We can then start to prioritise areas. We're really trying to use technology and data to guide what we are doing.

It does seem like technology and data will play a crucial role in controlling rabies. How important do you think research will be in tackling this problem and forming your campaigns?

There's been 100 years of research into rabies. We've known that vaccination has been effective for over 100 years, so the question now is, how do we actually do it and get into the nuts and bolts of vaccinating a large number of dogs efficiently through local infrastructure and capacity? So that's where our research is really focused: on the applied aspect of it and the operations of campaigns, planning campaigns and evaluating them. That is probably where there is the greatest need; how do we run these programs, as well as understanding dog populations and how we can make accessing dogs more efficient. Some of the work we've done recently is looking at how oral vaccines could play a role in dogs which are harder to vaccinate. We've shown that for dogs which are difficult to catch, it is much more efficient to drop a bait and allow them to receive a vaccine that way. But then for dogs which are community dogs or have a guardian, we want to encourage that guardian to handle that dog for parenteral vaccination. That's the best and most efficient way of vaccinating, and we want to encourage responsible ownership so that the majority of dogs can be brought for vaccination or held for it when the teams come round. It also builds trust in the communities. If you are vaccinating everywhere ideally, through the animal husbandry department, it's gaining that engagement with dog owners to encourage them to sterilise their dog as well as vaccinate, reducing the issue of stray dogs.

Running these campaigns must come with many different costs, what are your main sources of funding for campaigns?

There is a global community trying to support the elimination effort across the world. We're very lucky to have Dogs Trust funding us for the last 10 years and MSD Animal Health (a veterinary pharmaceutical and technology company) is donating large numbers of dog vaccines. Another benefit of this partnership is the thermostability of those vaccines; the cold chain is less of a concern, so the hotter temperatures are less of a concern when we are out in the field, and we don't have to be quite so worried. Most of the cost of running a campaign is in the staff salaries, the transport, the logistics and only 10% of the cost is in the vaccine itself (it costs around £2 per dog vaccinated and only 20p of that is in the vaccine) and so after having gone to all that effort, the last thing you want is to inject something which doesn't work. We always advocate for using good quality vaccines. So, we're very fortunate to get support from MSD. Volunteers and fundraisers help us to expand our work, provide more education and more vaccination campaigns. We also have a partnership with the CDC (Centers for Disease Control) and they've been supporting our app development and technology.

There seems to be many parties working on this issue and a large amount of success being achieved. What do you think the likelihood of eliminating the virus will be?

It's a big undertaking eliminating the virus and that's one of the major concerns of these big corporations supporting these efforts, but in the modern world it's terrible that we've got this ancient virus which we've known how to eliminate for so long. We've got modern technologies which make it easier and more efficient and yet it's still rampant and not even under control. As human populations increase there will be more dogs, and if we don't act now the issue will be worse. We can take a step towards combating the disease and reducing the burden in many places and protecting people who already have such a difficult circumstance. The virus mostly impacts on people at the fringes of society; whether you are geographically isolated or socioeconomically isolated, you are far more likely to die from rabies as you either have to travel a long way to get vaccinated or you can't afford the vaccine which is available. It's not the wealthy people who die of rabies, therefore, the prioritisation and big push to address this problem isn't there. Of all issues it's of huge humanitarian benefit starting to get on top of this. It will be a long journey, it is incredibly complicated to run campaigns of that scale but with oral vaccination especially, that will be a game changer in increasing the ease of vaccinating those types of dogs. If that comes through, certainly India would be able to mount a very comprehensive vaccination program. Beyond India, I believe it could scale out in Asia. In Africa, it's a slightly different situation with dog availability. But if governments get on board with this, it is certainly possible.

I completely agree, it really is an issue which we need to work on globally, especially with its humanitarian impact. With rabies being a zoonotic disease, how have vets and medics been working together to prevent rabies infection and what improvements do you think we will need to have to work towards elimination of human infection?

There's been so much push on the medical side. The medics have done so much work on the efficiency of vaccinating people, for example intradermal vaccination decreases the dose required tenfold and they're looking at dermal patches to improve the accessibility of vaccination. They have also improved the accessibility to monoclonal antibodies. Instead of the old school immunoglobulins, they've developed new ways to develop stable immunoglobulins. But if we continue with that approach of just improving access to post exposure treatment, there's still going to be people bitten by rabid dogs and rabid dogs in communities, so I feel that the veterinary sector needs to step up and address our area of the problem too. Access to post exposure treatment depends on where you are; if you are in a city, hospitals will have access to the vaccination, but there are still shortages across Africa and India. Globally there are always shortages. In rural areas access is typically poor. As I've said, they are trying to make it easier to get vaccine to different places and make it cheaper and so that is an improvement and will save people's lives but that doesn't get to the root of the problem. No matter how

easy we make it for people to get access to the vaccine, there are still people getting bitten. The bites alone are a horrible thing to go through. That's the bit we [Mission Rabies] want to address.

How can vet and medical students begin to get involved in this issue?

We have volunteer opportunities all over the place. Recently in Cambodia we had around 100 volunteers come out and get involved in that project. We have volunteer programs in Tanzania, Uganda and Ghana, and this really expands our capacity. Volunteers really help to bring additional training capacity especially with the use of technology. It makes a huge difference. Coming out and seeing the work is how I got involved! You just get a totally different experience of a place than visiting as a tourist; you're working alongside people from the country, going through every nook and cranny of a community to find dogs to vaccinate and speaking to people in the community. You just get such an exposure to that culture. A lot of our volunteers find it a very formative experience and a great thing to be a part of. Otherwise, just being a part of the conversation is important. We need more vets and medics to take an interest in this issue. For me, I see it as a generational opportunity to try and influence this problem. Obviously, there are loads of problems in the world, but as vets and medics this is an issue which affects people where we can make a difference. Even if you are working in the UK, just supporting campaigns through liking and sharing stories about rabies can help. Increasing the discussion on this issue is a really important thing. Also, getting into research and carrying out research will be important. I hope that the next generation of vets and medics will be inspired to work on this issue, improving our control of the disease and preventing human deaths.

For more information about Mission Rabies, go to missionrabies.com or find the charity on social media. Photographs kindly reproduced with permission from Mission Rabies and Andy Gibson.

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Interview

Fatma Sabet, Research fellow in school food system transformation, social activist and Shillingford Organics Farm School creator

by Mimi Mostefai

Year 5, Medicine, University of Exeter

Fatma Sabet is a postdoctoral knowledge exchange research fellow at the University of Exeter, collaborating with Sustainable Food Cornwall and the Cornwall Council Public Health team to develop a sustainable school food landscape for Cornwall. I first met Fatma when she delivered a lecture during the Planetary Health module as part of my Public Health Master's degree.

Planetary health underscores how human health is contingent on the health of our planet and the ecosystem services it provides. Thus, there is a need for us to cherish and conscientiously safeguard our planet. Food systems constitute just one facet of planetary health with the potential to be harnessed and ameliorated. Globally, our food system is a key driver of greenhouse gas emissions contributing to global warming, biodiversity loss through land conversion and loss of regulatory services that the environment, particularly forests. Yet, large quantities of our global population remain malnourished, accentuating how unsustainable our current food systems are.

Fatma's passion for food education for health and sustainability along with her drive to address policy challenges and solutions was evident in her lecture where she discussed her research journey and experiences at the 2022 United Nations Climate Change Conference or Conference of the Parties of the UNFCCC, known as COP27, held in Egypt. To me, Fatma appeared to be the ideal candidate to foreground the importance of planetary health. Indeed, it behoves all allied health professionals to be more cognisant of it.

Tell us about yourself and your academic background.

I embarked on an MSc in educational research at Exeter University in 2018 with a keen interest in research methods and academic inquiry. Throughout my MSc journey, I conducted various research studies for each module assignment, allowing me to gain hands-on experience and fuel my passion for rigorous academic research. Graduating with distinction, I was honoured to receive an ESRC scholarship to pursue a PhD focused on theorising sustainable school food in England.

What was it that first inspired you towards the subject area of planetary health and the specific area of "Food Education for Health and Sustainability"?

In 2016, I started the Shillingford Organics Farm School, a social educational enterprise located on an organic farm near Exeter.[1] The purpose of this initiative was to educate the public about the food system, where food comes from and the importance of healthy and sustainable eating. Witnessing the transformative changes in children and adults eating behaviours alike was truly eye-opening. It became evident to me that educating the public about sustainable food systems through experiential and authentic food education was not only possible but essential. While the Farm School was successful, I wanted to reach a broader audience, particularly families who faced barriers such as lack of transportation or limited educational opportunities. This motivated me to focus my PhD research on sustainable food provision and food education in schools.[2]

Please could you give us an overview of your current research work.

During my PhD, I conducted the first sustainable school meal and food education evaluation study in three schools in England. Through realist evaluation, I developed a theoretical and practical framework for sustainable school food, elucidating what works, for whom and how.[3] Subsequently, I started a postdoctoral research fellow position, collaborating closely with Cornwall Council and Sustainable Food Cornwall to develop a strategy for sustainable school food in Cornwall. Additionally, I am involved in a climate science communication project at the University of Exeter, utilising

artistic mediums to amplify the voices of indigenous communities in sharing their climate stories.[4] This interdisciplinary work bridges facts and emotions, generating a profound impact.

Having attended COP27 in Cairo, Egypt, what were the key lessons/challenges you drew from this that you would like to share with us?

Attending COP27 was a profoundly enlightening experience, highlighting the stark divide between politicians and activists all over the world. I had the privilege of meeting senior academics in the field as well as passionate activists from around the world advocating for climate justice, indigenous rights and food and water security. One key observation was the inclination of politicians and governments to rely on technology as a solution and a means to perpetuate the status quo rather than embracing necessary changes.

What would you consider to be the most pressing planetary health issue of the 21st century?

In my view, the most pressing planetary health issue of the 21st century revolves around the food system. As a major contributor to greenhouse gas emissions and soil degradation, our current food system fails to meet the nutritional needs of the population while exacerbating climate change. Urgent action is required to transition to a more sustainable and equitable food system.

Do you have any suggestions for how readers of this journal might individually take a step towards helping to achieve planetary health/attempting to overcome the aforementioned issue?

Addressing the most pressing planetary health issues depends on individuals' roles within society. As a parent, for example, my responsibility lies in educating my children about healthy and sustainable food choices, minimising food waste, and supporting local food sources. As an academic, my aim is to provide compelling evidence for innovative and sustainable approaches to food production and consumption. Overall, it is essential for everyone to engage in education and activism. Education is a powerful force for positive change, and each person can make a difference within their sphere of influence. Maintaining a philosophy of active hope, fostering a positive outlook and driving change are vital for a sustainable future.

Do you have any advice for students who wish to take up a career in your area?

In the field of sustainable food systems and sustainable school food, interdisciplinary approaches are crucial. I would advise students interested in this field to embrace the complexity and interdisciplinarity it entails. Navigating such a multifaceted topic requires in-depth knowledge across different disciplines, avoiding working within disciplinary silos. While it may not be feasible to master every discipline, maintaining a certain level of expertise in one's field while also gaining knowledge from other disciplines enables a comprehensive understanding of this complex subject. Building networks with colleagues from diverse backgrounds and shared interests fosters collaboration and facilitates the production of transformative knowledge.

Are there any additional points or issues that you would like to address, or that you believe would be of interest to our journal audience?

One important aspect to address is the interconnectedness of planetary health and human well-being. It is crucial to recognise that our actions and choices regarding food, environment, and sustainability have far-reaching implications for both people and planetary health. By promoting sustainable food systems, embracing local and agroecological food sources, reducing food waste, and advocating for policies that prioritise health and sustainability, individuals can contribute to achieving planetary health goals. Additionally, stakeholder involvement and fostering collaborations between different sectors, including academia, government and civil society, is essential for creating holistic approaches that address the complex challenges we face. Through knowledge exchange, we can drive meaningful change and promote a more sustainable and healthier future for all.

Images provided by the interviewee.

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Senior Editors, Winter 2023/2024

Moyowa Arenyeka

Year 4, Medicine, University of Plymouth

The INSPIRE scheme has given me multiple opportunities to pursue my interest in medical research. Through this scheme, I became a trained peer reviewer, attended taster days, participated in a residential summer school for research and more. These experiences, as well as becoming an editor for this journal, have exposed me to the different facets of research and have reaffirmed my interest in the field.

I am glad to have been given the opportunity to be on the INSPIRE journal's editorial team. It has been a great learning experience, which has broadened my perspective and has built upon my skillset in different ways. Thank you.

Thomas Butler

Year 4, Medicine, University of Plymouth

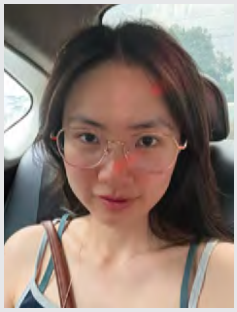
I'm a keen rugby player for our medical school and am interested in anaesthetics. Next year I am looking forward to intercalating in psychology and going on my elective to Sri Lanka. I've really enjoyed not only reading all the articles that have been sent my way as an editor but being involved in the process of refining the excellent work that is submitted to us.

Sanay Goyal

Year 4, Medicine, Cardiff University

Hey, I am a fourth-year medical student with an interest in digital health and medical devices. I am currently intercalating at Imperial College London to further my interests in medical management and working in the digital health industry. I am thrilled to have been on the editorial team for the INSPIRE Student Journal this year. It has been a pleasure to read all the submissions and curate another brilliant edition for our readers. Being a part of the editorial team has provided me with the chance to gain academic skills and appreciate how a medical journal functions which will serve me well in my pursuit of a surgical career. I look forward to reading more of your submissions and helping you publish your research!

Caroline Gu



Medicine, University of Exeter

Hi! I am an Exeter medic currently doing an BSc intercalation on Molecular Biology with Translational Haematology at Imperial College London. I am interested in an academic career in surgery and oncology. Working as an editor for INSPIRE, I'm glad to have the opportunity to read your ideas, interact with exciting fellow students and promote research in healthcare.

Kelly Jiayi Gu

Year 2, Medicine, Cardiff University

I feel very honoured to be able to be part of the INSPIRE team during my first and now second year doing medicine as I had the opportunity to read many insightful articles written by my peers about topics I've never linked together or heard about. The journal is filled with good reads! I'm currently interested in neurology and psychiatry, however, I am still exploring! A doubt I had with choosing medicine was the inability to explore niche biological topics in more depth and to write academically, however INSPIRE has given me the chance to do so as well as the chance to critically appraise other's articles. We hope you enjoy the magazine!

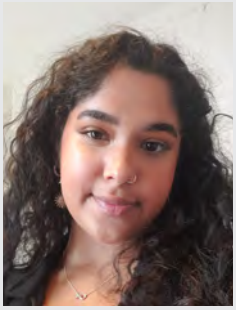
Meg Ireland

Year 4, Medicine, University of Bristol

I spent the last year at the University of Manchester in order to complete an intercalated Masters in Public Health. I am now a research assistant in their Population Health department, working on projects that qualitatively evaluate perceptions of and interactions with existing services and organisations. I am passionate about qualitative research and its ability to uncover the deeper experiences and human stories behind medical conditions, and interactions with healthcare personnel and organisations. My personal interests lie either side of the age spectrum; I care deeply about both dementia care and paediatrics.

This experience has been incredibly enriching, expanding my horizons and teaching me many new skills. I've thoroughly enjoyed every aspect of handling submissions by our talented peers for INSPIRE, and hope that readers find as much delight in reading it as we did in creating it.

Gayathri Kannan



Year 3, BDS, Cardiff University

I have a particular interest in the ever-evolving clinical research world and how it can be incorporated into patient-centered treatment to make life a lot easier for everyone! INSPIRE has helped me hone my critical appraisal skills and has expanded my knowledge of authoring scientific papers, a valuable skill for a profession such as dentistry which involves life-long learning. Aside from INSPIRE, I am involved in DentEazy which is a novel platform aiming to publish free resources for dental students to help them with their education. By being a part of these platforms, I hope to spread the idea of student-led content to others of varying ages, to help young professionals take charge of what they can extract from university life and degrees leading to high levels of self-sufficiency.

Senior Editors, Winter 2023/2024

Nell Marquess

Year 4, Medicine, University of Exeter

Hi! My interests in medicine include women's health, general practice, oncology and medical education. Being part of the INSPIRE editorial team has been incredibly rewarding and it has been great to be able to get to know the other team members. I have loved reading the work of the talented students that have submitted to INSPIRE and I am very proud of the issue we have created! I hope you readers enjoy it just as much as we enjoyed making it.

Mimi Mostefai

Year 5, Medicine, University of Exeter

Hi! I am currently a final year medical student and I recently completed an intercalated Master's degree in Public Health with a specialism in Global Health. My current clinical medicine and research interests span from general internal medicine, geriatrics and palliative care medicine to global health. Indeed, my Master's degree alongside being an editor of the INSPIRE journal have enabled me to explore fascinating topics outside my interest purview, particularly reinforcing the heterogeneous lenses through which one can consider health and strive to improve it, such as taking a 'One Health' approach. I have thoroughly enjoyed working as part of the INSPIRE team to produce this issue. I feel great pride in it as it is accessible and caters for a diverse audience. I hope that you, as readers, can really immerse yourselves in our great reads produced by myriad talented peers (authors and artists) across the UK.

Ethan Randall

Year 5, BDS, University of Bristol

I initially got into research through a paper that me and a fellow student wrote during our elective project in 2022. Since then I have been involved with INSPIRE and enjoyed helping other students work on and finalise their own work for the journal. It is a unique and rewarding experience to be a part of a student research journal and one that has taught me a great deal at the same time.

Phoebe Sussman

Intercalation onto MSc in Global Wildlife Health and Conservation, Veterinary Sciences, 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 provides 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.

Amirali Ziaebrahimi

Year 2, BDS, University of Plymouth

Hi. Beyond my studies, I serve as an editor at this INSPIRE student journal and hold the position of President at Dentsoc, where I foster a sense of community among dental students.

My primary passion is dental public health, with a focus on policy design and implementation. I'm dedicated to researching and improving oral healthcare strategies and policies. Additionally, I have a keen interest in dental technologies, recognising their potential to enhance patient care and treatment outcomes.

In both academics and extracurricular activities, I strive to make a positive impact in dentistry. My goal is to grow as a student, researcher, and leader, advancing the dental profession, promoting oral health, and harnessing the potential of dental technologies to benefit patients and practitioners.

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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

www.cures.cardiff.ac.uk/inspire

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

University of Exeter

www.medicine.exeter.ac.uk/study/ug/medicine/researchopportunities

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

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