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Clinical Academic Training Programme Showcase 2023

Welcome

To all, a very warm welcome to the 2023 Showcase event of the Nottingham Clinical Academic Training Programme. This event is an opportunity for you to present your work, hear about the work of your peers, and to interact with clinical academics from a wide spectrum of research disciplines. Most of all it is a celebration of all you have achieved over the past year of your clinical academic training.

We have a variety of sessions today covering different areas of the training programme, including oral presentation sessions for selected work from our current Clinical Lecturers (CL) and Academic Clinical Fellows (ACF), poster sessions for clinical academic trainees at all levels, and breakout sessions with experienced researchers covering topics relevant to different stages of training.

As in previous years, prizes will be awarded for oral presentations at CL and ACF level, and for the foundation programme posters. This year we have also included time in the programme for poster viewing, rather than combining this with lunch. If you are presenting a poster, please be ready to talk about your work to the judges and your peers during the poster session!

The breakout sessions have been tailored to different stages of training. We have a session aimed at those looking to apply for ACF posts, a session looking at how to get the most out of your ACF post with a focus on PhD funding applications, and a session on further career development aimed at Clinical Lecturers. More information will be given about the content and venue of the breakout sessions during the day.

As well as taking part in the various scheduled sessions, we hope you also take the opportunity to chat with your colleagues and senior academics during the lunch and coffee breaks. This is a great place to share your work, hear about the experience of others, and to grow your academic networks. We hope that you find the programme interesting, stimulating and enjoyable.

Professor Rob Dineen
Deputy Director of Clinical Academic Training Programme

Dr Shalini Ojha
Deputy Director of Clinical Academic Training Programme

Professor Helen Budge
Director of Clinical Academic Training Programme

Clinical Lecturers' Presentations

Developing an approach for boosting the effects of transcranial magnetic stimulation for major depressive disorder using synchronised transcranial alternating current stimulation

Paul M Briley, Clement Boutry, Lucy Webster, Domenica Veniero, JeYoung Jung, Peter F Liddle, Richard Morriss.

Background

Major depressive disorder (MDD) affects 1 in 7 people during their lifetime[1]. Transcranial magnetic stimulation (TMS) is a NICE-approved neuromodulation treatment for MDD that delivers magnetic pulses over the scalp. It modifies the activity of a target brain area and areas connected with it. TMS is performed whilst a person is awake and alert and is typically well-tolerated. However, clinical response remains highly variable, with some people improving quickly over a few treatment sessions, but most improving gradually over weeks and not achieving remission[2]. We are developing a low-intensity approach for making TMS more effective, more quickly, for more patients, by combining it with a second, low-cost, neuromodulation treatment called transcranial alternating current stimulation (tACS).

Methods

Regularly repeating brain activity patterns – "oscillations" – govern brain excitability and connectivity[3]. Greater "theta" (4-8 Hz) oscillatory activity at the time of TMS predicts clinical response[4]. tACS mimics oscillatory activity and can lead to sustained enhancement of brain oscillations at the applied frequency[5]. In an initial mechanistic study, we are delivering single sessions of tACS in synchrony with TMS to non-patients and measuring post-stimulation changes in theta (using electroencephalography, EEG), as well as in "emotional bias" (measure of potential antidepressant efficacy). The combination is compared to either stimulation technique alone, or double sham.

Results

Initial results (N=15) indicate a single session of "tACS-synchronised TMS" (tsTMS), leads to substantial increases in theta activity measured post-stimulation. Single techniques lead to smaller or less-sustained increases. When viewing ambiguous facial expressions in the emotional bias task, participants who had received tsTMS are more likely to perceive a positive emotion than are those that received other stimulation types. tsTMS appears equally well-tolerated to TMS alone.

Conclusion

We will shortly commence a pilot, multi-session, study, in people with moderate-severity MDD, to further examine mechanism of action, acceptability, and obtain estimates of clinical effect size.

References

1 Kessler RC & Bromet EJ (2013). doi: 10.1146/annurev-publhealth-031912-114409

2 Kaster TS et al. (2019). doi: 10.1176/appi.ajp.2018.18091096

3 Von Stein A & Sarnthein J (2000). doi: 10.1016/S0167-8760(00)00172-0

4 Bailey NW et al. (2018). doi: 10.1016/j.brs.2017.10.015

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The Post-Foundation Training Break ("F3"): Evaluating its Impact on Postgraduate Medical Training

Helen Church, Clinical Assistant Professor/CL in Medical Education
Steven Agius, Associate Professor in Medical Education
Liam Jenkins, Research Assistant in Medical Education

Background

An increasing number of doctors take a break during post-graduate training, the most popular in the UK being the 'Post-Foundation Training Break' (PFTB) (known as 'Foundation 3 (F3) Year'). [1] Since 2017, more doctors have undertaken PFTB rather than immediately enter a Specialty Training Programme (STP) but this trend is poorly understood. Our initial scoping review[2] mapped the existing evidence on PFTBs and led to the development of the following research questions: (1) How do PFTBs affect career progression? (2) What are Medical Educators' perceptions of the PFTB? (3) Is the increasing popularity of PFTBs affecting STP applications?

Methods

A national, GMC and ASME-funded, mixed-methods study was designed to address the research questions. Methods included an online survey of doctors who had undertaken a PFTB in the past 10 years; semi-structured interviews (SSIs) of FP educators; and SSIs of STP recruiters. Survey data were statistically analysed, with thematic coding of qualitative responses. SSIs were thematically analysed.

Results

4,046 doctors completed our survey. Over 80% agreed that the PFTB had impacted their career progression; mainly through confirming career choice (70%) or developing their CV (60%). Our data confirmed that certain demographic characteristics were associated with increased likelihood of completing a PFTB (male, white, undergraduate entrant).

Educators (n=16) found providing guidance to trainees challenging and many do not formally address the 'PFTB option' with trainees, but had confidence in the advice offered by trainee's peers.

Recruiters (n=21) identified that PFTB doctors might more easily fulfil STP application criteria than their FP peers. Despite these potential advantages, whether the candidate has completed a PFTB is not considered.

Conclusion

PFTBs are increasingly popular with doctors striving for more autonomy over their careers, therefore more guidance at FP level is advised. Given the demographic association with PFTBs and its EDI implications, transparency around potential bias at STP recruitment is required.

References

1. GMC. Training pathways: analysis of the transition from the foundation programme to the next stage of training. General Medical Council; 2017.

2. Church HR, Agius S. The F3 phenomenon: Early-career training breaks in medical training. A scoping review. Medical education. 2021.

The association of pain and anxiety and depression, with quality of life in people living in care homes: a secondary analysis of the Falls in Care Homes (FinCH) randomised controlled trial dataset

Collins JT, Irvine L, Gordon AL, Logan PA, and the Falls in Care Homes (FinCH) authors

Background

Pain is a common symptom and is more prevalent with age, and especially prevalent in care home residents. In older people, pain is under-recognised and undertreated [1]. Indeed, pain may be a modifiable target for improving quality of life. In people living with dementia, pain assessment and management is challenging due to impairments in communication and cognition [2]. Further, pain may be expressed as emotional and psychological symptoms in people living with dementia. A better understanding of how these symptoms are linked in people living in care homes, both with and without a diagnosis of dementia, will enable important associations to be made and provide data to pump prime future studies.

Our main aim in this study was to evaluate the association between pain, anxiety and depression, and quality of life, in people living in care homes, with a particular interest in people living with dementia.

Methods

This was a secondary analysis of data from the Falls in Care Homes (FinCH) randomised controlled trial study, the main outcomes and protocol have been published [3,4]. Permission to use this data was obtained from the FinCH Chief Investigator (PAL) and the study Sponsor. Data on age, gender, diagnosis of dementia, pain, anxiety, depression, and Quality of Life scores by DEMQOL and EQ5D-5L were collected at baseline and every 3 months thereafter for a total of 12 months. Falls frequency data was also collected as the FinCH primary outcome measure of interest. Data was statistically analysed using SPSS v28. The chi square test was used to test associations between categorical variables, and binary logistic regression was used to assess the association between pain, anxiety and depression, and quality of life.

Results

The prevalence of people living with dementia in this care homes cohort was 67%. The overall prevalence of pain at baseline in people with dementia was 51.1% and 60.6% in people without a diagnosis of dementia ($p<0.001$).

In the whole cohort, pain at baseline as well as throughout the study timepoints (3,6,9, and 12 months) was associated with anxiety and depression (all $p<0.001$). This association was significant for both people with dementia and people without dementia ($p<0.001$).

QoL was not significantly associated with pain for either dementia or no dementia participants. However, QoL was significantly associated with anxiety and depression in the overall cohort ($p=0.003$), and after controlling for the presence of dementia, this was only significant in people without dementia ($p<0.001$). In regression analysis, the presence of anxiety and depression at baseline was significantly associated with a poorer quality of life (95% CI 1.16-3.06, $p=0.01$), whereas gender, diagnosis of dementia, and pain were not associated (p=NS).

Falls in the first 3, 6, and 12 months were not significantly associated with the presence of anxiety and depression, nor with pain.

Discussion:

- Pain was significantly associated with anxiety and depression in people living in care homes irrespective of diagnosis of dementia and at all study assessment timepoints.

- QoL data was gained from only 21.8% of participants, therefore it is likely that this result was underpowered.
- The prevalence of pain in people living with dementia may be an underestimate. Possible reasons for pain prevalence being higher in the group with no dementia are:

i) The self-report tool EQ5D-5L and EQ5D-5L-proxy was used to gain pain data, therefore there may be under-recognition of pain in PwD given communication and cognitive impairments in people living with dementia and consequent challenges with reporting pain.

ii) A higher proportion of people without dementia residing in care homes due to cancer or other long term conditions associated with pain.

iii) Dementia is often undiagnosed for months to years prior to a formal diagnosis; it is likely that some people in the no dementia group in fact did have a form of cognitive impairment.

Conclusion

Pain is prevalent in people living in care homes, and is higher in people without a diagnosis of dementia compared to those with dementia. Pain is significantly associated with anxiety and depression in people living in care homes. Anxiety and depression at baseline is associated with a poorer self-reported quality of life. Future work should focus on the characteristics of associated features of pain, in people living with dementia, in order to better recognise pain and deliver more targeted care.

References

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2. Achterberg WP, Erdal A, Husebo BS, Kunz M, Lautenbacher S. Are Chronic Pain Patients with Dementia Being Undermedicated? J Pain Res. 2021 Feb 15;14:431-439. doi: 10.2147/JPR.S239321. PMID: 33623425; PMCID: PMC7894836.

3. Logan PA, Horne JC, Gladman JRF, et al. Multifactorial falls prevention programme compared with usual care in UK care homes for older people: multicentre cluster randomised controlled trial with economic evaluation. BMJ. 2021 Dec 7;375:e066991. doi: 10.1136/bmj-2021-066991. PMID: 34876412; PMCID: PMC8649897.

4. Logan PA, McCartney K, Armstrong S, Clark A, Darby J, Conroy S et al (2019) Evaluation of the guide to action care home fall prevention programme in care homes for older people: protocol for a multi-centre, single blinded, cluster randomised controlled trial (FinCH). East Midlands Research into Ageing Network (EMRAN) Discussion Paper Series, vol 25, no. 1, pp. 1–44.

List of publications and achievements

Publications:

Adam Lee Gordon, Jemima T Collins, More data can help us better understand COVID-19 outbreaks but nuanced and critical reflection is required, Age and Ageing, Volume 52, Issue 3, March 2023, afad028, https://doi.org/10.1093/ageing/afad028

Jemima T Collins, Rowan H Harwood, Alison Cowley, et al. Chronic pain in people living with dementia: challenges to recognising and managing pain, and personalising intervention by phenotype, Age and Ageing 2023; 52(1): afac306, https://doi.org/10.1093/ageing/afac306

Ogliari G, Ryg J, Andersen-Ranberg K, Scheel-Hincke LL, Collins JT, Cowley A, Di Lorito C, Howe L, Robinson KR, Booth V, Walsh DA, Gladman JRF, Harwood RH, Masud T. Association of pain and risk of falls in community-dwelling adults: a prospective study in the Survey of Health, Ageing and Retirement in Europe (SHARE). Eur Geriatr Med. 2022 Dec;13(6):1441-1454.

Presentations:

Invited Speaker at British Geriatrics Society annual meeting, May 2023

Grant progress:

Lead applicant on NIHR RfPB grant which has successfully passed through to Stage 2.

Fibroblast $G_{\alpha q/11}$ regulates key extracellular matrix properties to control lung repair

Amanda T Goodwin[1,2], Thomas Owens[1,2], Dominic Taffs[1,2], Amanda L Tatler[1,2].

1) Respiratory Medicine, School of Medicine, University of Nottingham, Nottingham, UK

2) Nottingham NIHR Biomedical Research Centre, University of Nottingham, Nottingham, UK

Background

Lung repair requires controlled extracellular matrix (ECM) generation. We previously demonstrated that mesenchymal Gαq/11 knockout causes abnormal lung development and emphysema with altered lung ECM and transforming growth factor-β2 (TGFβ2) content[1]. However, the role of the ECM in driving these phenotypes is unknown.

Methods

Wild-type (WT) and $Gnaq^{-/-}$;$Gna11^{-/-}$ ($G_{\alpha q/11}^{-/-}$) murine embryonic fibroblasts (MEFs), and A549 lung epithelial cells, were cultured on ECM generated by WT or $G_{\alpha q/11}^{-/-}$ MEFs. Wound healing and TGFβ signalling were assessed using scratch wound and transformed mink lung cell (TMLC) assays.

MEFs were stimulated with TGFβ2 or PDGFBB, and wound healing and ECM component expression assessed.

Results

WT MEFs activated less TGFβ (0.53 relative TMLC luciferase activity (RLA)) when cultured on $G_{\alpha q/11}^{-/-}$ ECM compared with WT ECM. Conversely, $G_{\alpha q/11}^{-/-}$ MEFs increased TGFβ activation (1.8 RLA) and Pai-1, a TGFβ-downstream gene, expression (1.5-fold) on WT ECM. TGFβ signalling was reduced on $G_{\alpha q/11}^{-/-}$ when TMLCs were cultured on ECM alone (0.44 RLA).

WT MEFs and A549s healed wounds more slowly on $G_{\alpha q/11}^{-/-}$ ECM compared with WT ECM (31.7% vs 46.4% 8-hour healing (WT MEFs); 2.0% vs 6.9% 8-hour healing (A549s)).

$G_{\alpha q/11}^{-/-}$ MEFs had lower ECM component (Col3a1, Col1a1, Eln, Pdgfa, Pdgfb, Pdgfd) mRNA expression than WT MEFs. $G_{\alpha q/11}^{-/-}$ MEFs stimulated with TGFβ2 had a time-dependent increase in Eln and Pdgfa mRNA expression, (15.8- and 3.6-fold, respectively), and elastin protein approached WT levels after 48 hours. Wound healing was slower in $G_{\alpha q/11}^{-/-}$ than WT MEFs, and was enhanced by exogenous TGFβ2 and PDGFBB.

Conclusion

The ECM generated by $G_{\alpha q/11}^{-/-}$ fibroblasts is less supportive of repair than WT ECM. This may be due to reduced growth factor content of $G_{\alpha q/11}^{-/-}$ ECM, however restoration of TGFβ2 of PDGFBB signalling does not fully re-establish repair. Further evaluation of these mechanisms may identify methods of manipulating lung repair to therapeutic potential.

References

1. Goodwin AT, John AE, Joseph C, Habgood A, Tatler AL, Susztak K, Palmer M, Offermanns S, Henderson NC, Jenkins RG. Stretch Regulates Alveologenesis Via Mesenchymal $G_{\alpha q/11}$ Mediated TGFβ2 Activation. Development 2023 In Press (BioRxiv doi: https://doi.org/10.1101/2020.09.06.284778).

List of publications and achievements

Publications

- Goodwin AT, John AE, Joseph C, Habgood A, Tatler AL, Susztak K, Palmer M, Offermanns S, Henderson NC, Jenkins G. Stretch Regulates Alveologenesis Via Mesenchymal $G_{\alpha q/11}$-Mediated TGFβ2 Activation. Development 2023 In Press

- Goodwin AT, Thompson JS, Hall IP. Evaluation of outpatient treatment for non-hospitalised patients with COVID-19: The experience of a regional centre in the UK. PLoS One. 2023 Mar 15;18(3):e0281915. doi: 10.1371/journal.pone.0281915. eCollection 2023.

- Goodwin AT, Noble PW, Tatler AL. Plasma cells: a feasible therapeutic target in pulmonary fibrosis? .Eur Respir J. 2022 Nov 24;60(5):2201748. doi: 10.1183/13993003.01748-2022. Print 2022 Nov.

- Tatler AL, Philp CJ, Hill MR, Cox S, Bullock AM, Habgood A, John A, Middlewick R, Stephenson KE, Goodwin AT, Billington CK, O'Dea RD, Johnson SR, Brook BS Differential remodelling in small and large murine airways revealed by novel whole lung airway analysis. Am J Physiol Lung Cell Mol Physiol. 2023 Jan 3. doi: 10.1152/ajplung.00034.2022. Online ahead of print.

Funding

- Academy of Medical Sciences Starter Grant for Clinical Lecturers – "Understanding how mesenchymal G protein signalling controls lung development and repair" - £30,000 awarded February 2023

- University of Nottingham UNICAS scheme – "Real-time micromechanical sensing and 3D imaging of the cell-matrix interface: A novel in vitro pulmonary fibrosis model" - £15,000 awarded April 2022

“Far Away from Home”: Adolescent inpatient admissions far from home, out-of-area or to adult wards - a national surveillance study

Josephine Holland, Jim Roe, Boliang Guo, Saeed Nazir, Adam Wagner, Bernadka Dubicka, Anne-Marie Burns, Ali Jaffrey, Tamsin Ford, Tony James, Anees Pari, Kapil Sayal

Background

Rising rates of psychiatric hospital admissions in <18-year-olds has placed increased pressure on services. Limited bed availability has resulted in many young people being admitted at-distance or to adult wards. Little empirical research has investigated these types of admissions.

This study aimed to determine the incidence, clinical characteristics and 6-month outcomes of admission to at-distance (>50 miles from home or out of region) general adolescent psychiatric wards or to adult psychiatric wards for 13–17-year-olds.

Methods

Surveillance over 13 months using the Child and Adolescent Psychiatry Surveillance System, including baseline and follow-up questionnaires.

Results

Data for 290 unique cases were collected. Demographics showed the majority were female (73%), aged 16-17 years (63%) and 12% of males were of Black African ethnicity. 38% were admitted >100 miles from home and 8% >200. Depression was the most common diagnosis at referral suicide risk was present in 80% and psychotic symptoms in 22%. 41% waited for over 1 week for an available bed, most commonly waiting in general hospital settings (55%), mainly paediatric wards.

Conclusion

At-distance and adult ward admissions for <18s are ongoing. A significant number of acute hospital bed days are used for patients awaiting beds. The over representation of males of Black African ethnicity needs further investigation.

List of publications and achievements

Publications

1. RCPsych Academic Trainee Small Grant - £3047.97 Awarded February 2023.
2. Holland, J., Sayal, K. & Garralda, E. (in press). Epidemiology and Classification. In Shermin & Theodosiou, Seminars in Child and Adolescent Psychiatry. Cambridge Publishers and RCPsych.
3. Nahman, C. & Holland, J. (2022), Incorporating interventions for unhealthy exercise into eating disorders treatment: a survey of attitudes in those with lived experience of an eating disorder. Sports Psychiatry; 1: 100-6.

Academic Clinical Fellows' Presentations

The Duration and Magnitude of Post-discharge Venous Thromboembolism Following Colectomy

Lewis-Lloyd, Christopher; Humes, David; West, Joe; Peacock, Oliver; Crooks, Colin

Background

Disparity exists between the postoperative thromboprophylaxis duration colectomy patients receive based on surgical indication, where malignant resections routinely receive 28 days extended thromboprophylaxis into the post-discharge period and benign resections do not. The objective was to assess the impact of current guidelines by reporting weekly postoperative post-discharge venous thromboembolism (VTE) rates.

Methods

English national cohort study of colectomy patients between 2010 and 2019 using linked primary (Clinical Practice Research Datalink) and secondary (Hospital Episode Statistics) care data. Stratified by admission type and surgical indication, absolute incidence rates (IRs) per 1,000 person-years and adjusted incidence rate ratios (aIRRs) for post-discharge VTE were calculated for the first 4 weeks following resection and post-discharge VTE IRs for each postoperative week to 12 weeks postoperative (see Figure 1).

Results

Of 104,744 patients, 663 (0.63%) developed post-discharge VTE within 12 weeks after colectomy. Post-discharge VTE IRs per 1,000 person-years for the first 4 weeks postoperative were low following elective resections [benign: 20.66, 95% confidence interval (CI): 13.73–31.08; malignant: 28.95, 95% CI: 23.09–36.31] and higher following emergency resections (benign: 47.31, 95% CI: 34.43–65.02; malignant: 107.18, 95% CI: 78.62–146.12). Compared with elective malignant resections, there was no difference in post-discharge VTE risk within 4 weeks following elective benign colectomy (aIRR=0.92, 95% CI: 0.56–1.50). However, post-discharge VTE risks within 4 weeks following emergency resections were significantly greater for benign (aIRR=1.89, 95% CI: 1.22–2.94) and malignant (aIRR=3.13, 95% CI: 2.06–4.76) indications compared with elective malignant colectomy.

Conclusion

Post-discharge VTE risk within 4 weeks of colectomy is ~2-fold greater following emergency benign compared with elective malignant resections, suggesting emergency benign colectomy patients may benefit from extended VTE prophylaxis.

List of publications and achievements

- Lewis-Lloyd CA, Humes DJ, West J, Peacock O, Crooks CJ. The Duration and Magnitude of Postdischarge Venous Thromboembolism Following Colectomy. Ann Surg. 2022;276(3):e177-e184. doi:10.1097/SLA.0000000000005563

  Featured on the Annals of Surgery “What’s New and Interesting” Home page for 6 months from August 2022 as a selected article considered to be highly impactful to readers.

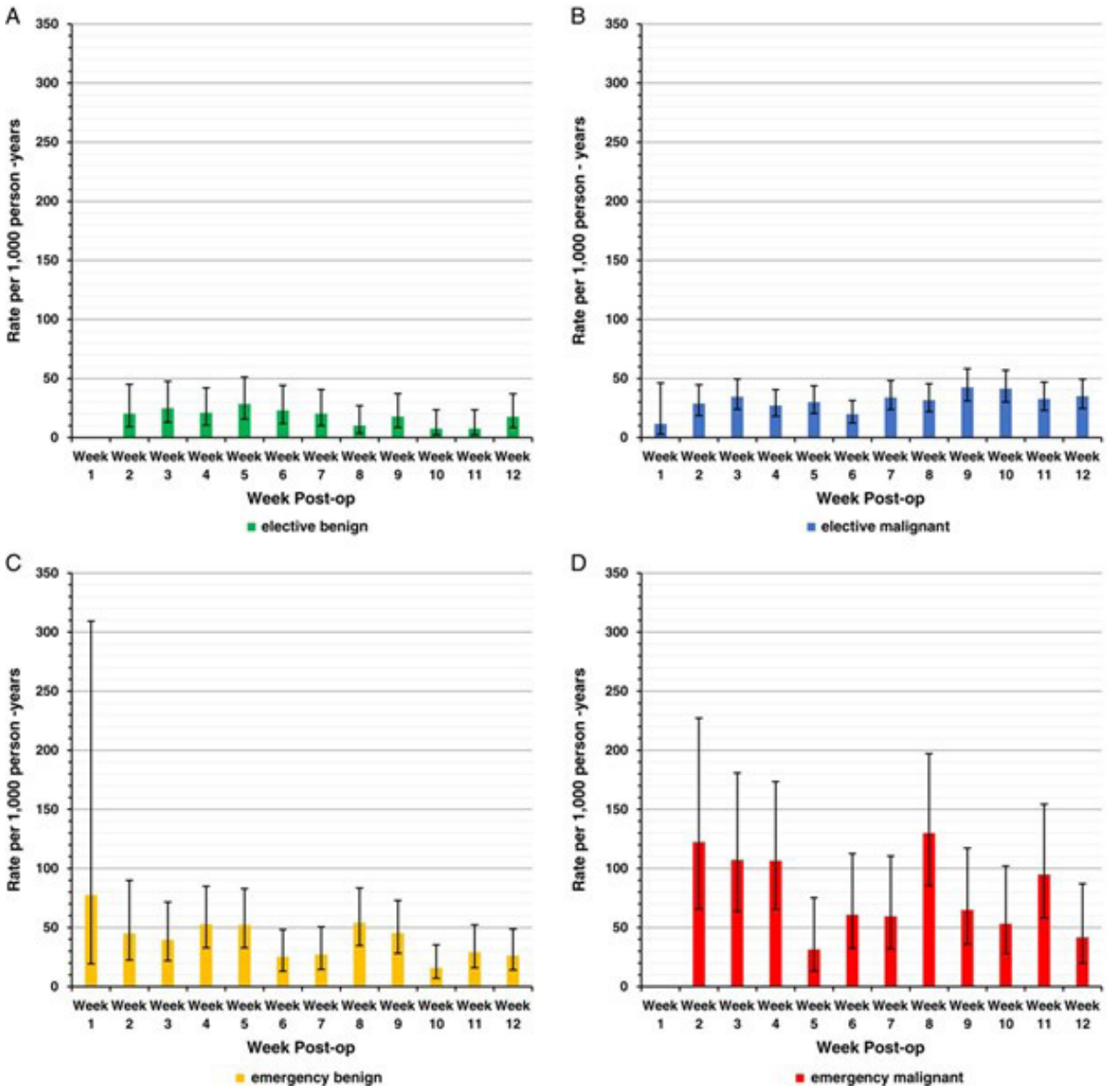

Figure 1: Post-discharge VTE rates by postoperative week stratified by admission type and surgical indication. Elective benign (A), elective malignant (B), emergency benign (C), emergency malignant (D). Data missing within week 1 indicates no post-discharge VTE events occurred within the first postoperative week. Error bars indicate 95% CIs.

Influence of relative age on the symptoms, diagnosis or management of attention deficit hyperactivity disorder and autism spectrum disorder: a systematic review

Eleni Frisira, Josephine Holland, Kapil Sayal

Background

Youngest students in their class, with birthdates just before the school entry cut-off date, are overrepresented among children receiving an Attention Deficit Hyperactivity Disorder (ADHD) diagnosis or medications. This is known as a 'relative age' effect (RAE). The magnitude of this association varies and whether data reflect teachers' or parents' ratings of children's behaviours may be important. This systematic review summarises the evidence on how relative age influences rating of ADHD symptoms, diagnosis and medication prescribing. As no review to date has investigated the association with autism spectrum disorder (ASD), a different neurodevelopmental disorder usually diagnosed in childhood, this is also examined.

Methods

After prospective registration with PROSPERO, a systematic review was conducted according to the PRISMA guidelines. The databases searched were Medline, Embase, Psychinfo, Wed of Science Core Collection, ERIC, Psychology and Behavioural Sciences Collection, and Cochrane Library. Additional references were identified from manual search of retrieved reviews. A meta-analysis of quantitative data was performed.

Results

Thirty-two studies were included. Thirty measured the RAE on ADHD and two on ASD. Four studies investigating parent-rated symptoms showed no association with relative age, whereas six of seven studies investigating teacher-rated symptoms did. Youngest children in their schoolyear were more likely to receive an ADHD diagnosis in fifteen of seventeen studies and more likely to receive ADHD medication in fourteen of seventeen. Risk ratios for diagnosis were higher in more recently published papers, ranging from 1.37 to 1.72. Both studies on ASD showed that youngest children in their schoolyear had higher rates of ASD diagnosis.

Conclusion

Relative age continues to be associated with clinical diagnosis and management of ADHD. Teachers are more likely to be influenced by relative age than parents when rating children's ADHD symptoms. It is important for clinicians to be aware of how this may contribute to the diagnostic process. More research is needed into the strength of the evidence for ASD.

References

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2. Whitely, M., et al., Attention deficit hyperactivity disorder late birthdate effect common in both high and low prescribing international jurisdictions: a systematic review. J Child Psychol Psychiatry, 2019. 60(4): p. 380-391.

3. Brault, M.C., et al., Relative Age Effect in Attention Deficit/Hyperactivity Disorder at Various Stages of the Medicalization Process. Children (Basel), 2022. 9(6)

Clinical characteristics and outcomes of consecutive patients with functional dyspepsia taking opioids referred to a UK tertiary care hospital

Mohsin F. Butt, Arkadeep Dhali, Grace Isherwood, Tilly Lewis-Lawson, Debbie Bush, Tim Card, Maura Corsetti

Background

Functional dyspepsia (FD) is one of the commonest disorders of gut-brain interaction (DGBIs) in the general population and is frequently encountered by gastroenterologists (1). Opioids have no therapeutic role in the management of non-malignant pain. Opioids have been associated with dysfunction of the entire gastrointestinal (GI) tract, from mouth to anus, and are commonly encountered by gastroenterologists in the context of esophageal dysmotility, chronic nausea, gastroparesis, constipation, and narcotic bowel syndrome (2).

The primary aim of this study is to determine the proportion of patients with ROME IV FD presenting to a UK tertiary care neurogastroenterology service taking opioids. Secondary aims related to the differences in phenotype and clinical outcomes between FD patients taking opioids compared to those not taking opioids.

Methods

Results from 157 consecutive patients with FD who presented to a tertiary care neurogastroenterology clinic between January 2016 – December 2021 were analysed. Phenotype and clinical outcomes were compared between FD patients taking opioids versus those not taking opioids.

Results

One in five (21.7%) patients diagnosed with FD in a tertiary care UK neurogastroenterology setting are prescribed opioids. Nausea (n=28, 82.4% versus n=75, 61%; p=0.02), vomiting (n=19, 55.9% versus n=34, 27.6%; p=0.002), and constipation (n=18, 52.9% versus n=21, 23.6%; p=0.001) were more common in the opioid group. The frequency of hospital admission for both gastrointestinal (p=0.002) and non-gastrointestinal factors (p=0.02) were higher in the opioid group. Only 15/32 (46.8%) of FD patients who took opioids followed opioid cessation advice.

Conclusion

This is the first study to explore the phenotype and clinical outcomes of patients with clinically confirmed ROME IV FD who take opioids in the UK. Opioid intake in FD is associated with more nausea and vomiting, and a higher number of gastrointestinal and non-gastrointestinal-related hospitalisations compared to patients who are not prescribed opioids.

References

1. Aziz I, Palsson OS, Tornblom H, Sperber AD, Whitehead WE, Simren M. Epidemiology, clinical characteristics, and associations for symptom-based Rome IV functional dyspepsia in adults in the USA, Canada, and the UK: a cross-sectional population-based study. Lancet Gastroenterol Hepatol. 2018;3(4):252-62.

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Novel Technologies for Improved Safety and Comfort in Neonatal Inter-Hospital Transport

R B Simpson, D Harvey, A Mistry, A Leslie, D McNally, D Sharkey

Background

16,000 neonatal inter-hospital transfers take place in the UK each year. These expose fragile infants to excessive noise and vibration[1]. Premature infants who are transferred in their first 72 hours of life experience higher rates of severe intra-ventricular haemorrhage[2]. Current methods of restraining infants inside transport incubators carry a risk of severe injury or death in the event of a road traffic collision[3]. A medical device is being developed that will comprise a vibration-dampening mattress, miniaturised active noise-cancelling headphones and a novel restraint system. This academic clinical fellowship has focussed primarily on noise cancellation to date.

Methods

Sound measurement was undertaken during simulated inter-hospital transfers. The acoustic environment is described by its' component frequencies.

Several iterations of prototype passive noise-cancelling and active noise-cancelling headphones were developed. Prototypes were tested on a mannequin in a sound laboratory and during actual ambulance journeys.

Results

Frequencies below 250Hz are predominant during interhospital transfer. When corrected for audibility, frequencies between 80 and 1000Hz are most important.

Prototype active noise-cancelling headphones provide up to 9 dBA of attenuation in laboratory settings and negligible attenuation in ambulance settings. Further iterations of the passive and active noise-cancelling headphones have been produced and are awaiting testing.

Conclusion

There are challenges to passive noise cancellation during neonatal inter-hospital transfer. Low frequencies are predominant. These are not readily absorbed. Scaling down noise cancelling equipment in size reduces efficacy. Active noise cancellation may be necessary to effectively reduce sound exposure in this setting.

The active noise-cancelling prototype requires further refinement to improve its performance in a transport setting. We plan to explore developing bespoke active noise cancellation which would allow those frequencies that are of greatest concern to be targeted and generate cancelling sound waves of the correct amplitude.

The headphones will need to interface with the other components of the device which are being developed in parallel. A prototype mattress with restraint configuration is in design.

References

1. Prehn et al, 2014
2. Shipley et al, 2019
3. Melvin et al, 2016

List of publications and achievements

European Association of Paediatric Societies 2022 Congress - E Poster and discussion

Crowdsourcing vibration and noise exposure during inter-hospital transport using smartphone technology: improving safety with intelligent routing.

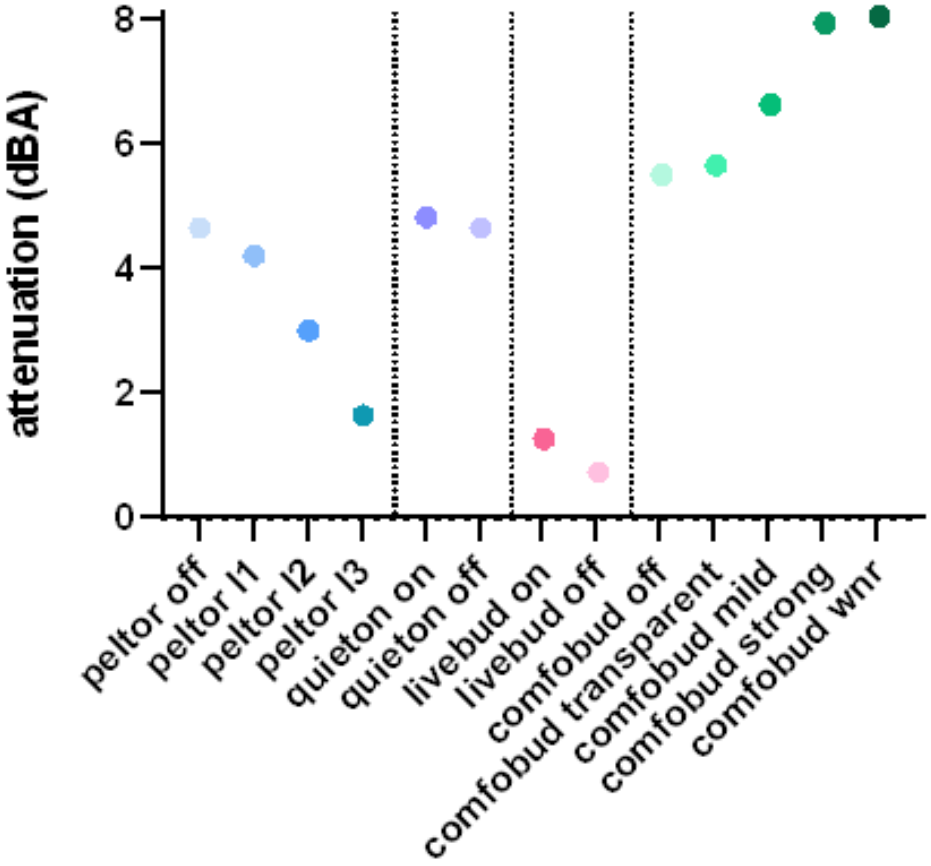

Figure 1: Mean performance of prototype active noise cancelling headphones in sound laboratory testing (pink noise challenge). Four commercially available active noise-cancelling earbuds are integrated in the prototypes. Prototypes are tested with active noise cancellation turned off, turned on, and where there are multiple possible modes, in each mode.

m6A RNA modification and a driver of cellular plasticity and intra-tumoral heterogeneity in Glioblastom

S Deacon, Masar Radhi, Jonathan Rowlinson, Helen Knight, Dong-Hyun Kim, Stuart Smith

Background

The immense cellular plasticity of glioblastoma is a key barrier to successful therapy. N6-methyladenosine (m6A) methylation of RNA is increasingly recognised as a key driver of cellular differentiation [1]. Crucially, it is a reversible and dynamic modification that alters cellular phenotype via the regulation of mRNA metabolism [2]. We hypothesise that m6A methylation may mediate GBM plasticity, regulating transcriptional networks and thus influencing cellular adaptation under different microenvironmental conditions[3]. Our aims are to assess whether total m6A levels and m6A regulatory gene expression are responsive to change in oxygen levels and cellular confluency. Furthermore, we aim to characterise the spatial distribution of m6A in 3D cell culture models.

Methods

We have investigated m6A levels in patient-derived cell lines from the invasive region of adult glioblastoma. Mass spectrometry and anti-m6A immunofluorescence confocal microscopy was used to quantify total m6A levels. We have compared total m6A levels in normoxic versus hypoxic conditions, using a hypoxic chamber, low versus high confluency 2D cell culture, and cell migration using a scratch assay. We have measured expression levels of key m6A RNA regulatory gene using rtPCR.

Results

Total m6A levels and regulatory gene expression were not significantly different in normoxic versus hypoxic conditions. However, m6A levels were decreased in high confluency versus low confluency culture conditions. We will further characterise the spatial distribution of m6A in 3D cell culture models using immunofluorescence confocal microscopy.

Conclusion

We demonstrate a degree of variability in m6A levels in response to micro-environmental conditions, such as cellular confluency. These findings indicate a role for m6A in tumoural heterogeneity and cellular adaptation.

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List of publications and achievements

Funded by Jean Shanks/Pathological Society Pre-doctoral research bursary.

Clinical Lecturers' Posters

Addressing social determinants in the management of asthma: A systematic review of the literature

I Adejumo, TM McKeever, DE Shaw

Background

Asthma is a condition in which both pulmonary and extra-pulmonary factors mediate adverse outcomes such as asthma attacks and death (1). A 2014 review of asthma deaths highlighted the role of psychosocial and behavioural factors in adverse outcomes (2) and a more recent survey has highlighted the role of socioeconomic disparities in access to good care (3). Whilst it has long been accepted that social inequalities lead to poor outcomes in asthma (4), this is not addressed in routine care. This review seeks to provide clarity on the role of socioeconomic disadvantage and race/ethnicity on asthma outcomes and asthma care in the UK. It is expected that such an understanding will inform the development of effective interventions.

Aims and objectives

1. To determine the role of socioeconomic disadvantage in asthma in a UK context
2. To determine the role of ethnicity in asthma in a UK context
3. To determine what (if any) interventions have been conducted to directly address the impact of socioeconomic and/or ethnicity disadvantage in asthma

Methods

Studies from the last 20 years will be identified from the MEDLINE group of databases, Web of Science and Scopus. Two independent reviewers will inspect retrieved citations and identify relevant publications for inclusion. Citations will be managed using an online application (https://rayyan.ai/).

Data will be extracted onto pre-designed forms. Outcome measures will include a narrative description, including broad identification of mediating factors for adverse asthma outcomes. A quality assessment will be undertaken, including assessment of heterogeneity should a meta-analysis be possible and assessment of risk of bias.

Conclusion

This systematic review will assess the roles of two key societal inequalities on asthma outcomes. It is hoped that this will inform future work to incorporate ways of directly addressing the effect of inequity in routine asthma care.

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A systematic review of the association of Tobacco 21 policies on cigarette smoking in children and young adults

Nathan Davies, Ilze Bogdanovica, Shaun McGill, Rachael Murray

Background

Tobacco use remains the leading cause of morbidity and mortality for many countries. Reducing uptake of smoking is a key way to reduce this harm. Raising the minimum legal age of sale of tobacco (MLSA) to 20 or above might reduce tobacco smoking compared to the traditional MLSA of 18.

Methods

We searched 6 electronic databases from 1 January 2015 – 29 September 2022 for studies reporting the association of raising the MLSA to 20 or above and tobacco use. There were no language restrictions. Studies that reported quantitative measures of association were included. The primary outcome was cigarette smoking prevalence amongst the target age group (11-20 year olds), with secondary outcomes including cigarette sales and smoking initiation rates. Random-effects meta-analyses are planned for studies meeting Cochrane Effective Practice and Organisation of Care criteria. The PROSPERO registration is CRD42022347604.

Results

We identified 2771 records and assessed 27 full texts for eligibility. 19 studies met the inclusion criteria. All studies were based in the US and included local, state and national-level Tobacco 21 policies, with outcomes on cigarette smoking amongst 13-20 year olds and cigarette sales. Independent pairs of reviewers extracted data and assessed risk of bias. Risk of bias was moderate in 7 studies, serious in 8, critical in 3 and 1 had insufficient information for judgement. 9 studies reported an association with decreased current cigarette smoking or cigarette sales, 8 reported no association and 2 provided insufficient information for judgement.

Conclusion

Preliminary review of the data suggests that there may be a potential association between Tobacco 21 policies and reduced current cigarette smoking in 13-20 year olds, although there was serious or critical risk of bias for more than half of included studies. The planned meta-analysis of eligible studies will provide further evidence.

References

Nathan Davies, Rachael Murray, Ilze Bogdanovica. Effects on smoking of raising the age of sale of tobacco to 20 or above: a systematic review. PROSPERO 2022 CRD42022347604

List of publications and achievements

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Richard Madeley Prize for highest MPH mark, University of Nottingham, 2018/2019

Phenotypic and functional characterization of the immune cell compartment in Cholangiocarcinoma tumours using novel in vitro and ex vivo methodologies

Isioma U. Egbuniwe, Mireia Sueca-Comes, Anna M. Grabowska, David O. Bates, Kevin Gaston, Sheela Jayaraman

Background

Cholangiocarcinoma (CCA) is an aggressive cancer arising from the epithelial lining of bile ducts within and outside the liver. It's dismal prognosis (5 year survival <10%), and rising incidence make this an urgent clinical problem to be addressed[1].

Using conventional immunohistochemistry analysis on human tumour samples, we have previously demonstrated preferential accumulation of CD3+ T cells and CD68+ macrophages within CCA tumours compared to adjacent non-tumour bile duct tissue, highlighting the potential importance of an immune component to interactions within the CCA microenvironment. However, we sought to develop novel analytical methods in order to better characterise the immune tumour microenvironment in CCA – specifically focusing on the CD3+ T cell and CD68+ macrophage compartments.

Methods

We first established a physiologically representative 3-dimensional in vitro tumour culture system involving co-culture of CCA tumour spheroids with human peripheral blood lymphocytes, for the assessment of cellular interactions between tumour and immune cells.

Using NanoString™ Digital Spatial Profiling (DSP), we next developed a pipeline to undertake spatially-resolved analysis of immune protein signatures within human CCA tumours.

Results

From our 3D in vitro modelling experiments, we demonstrated production of the IL-17 cytokine from human CD3+ T cells (n=4 donors) co-cultured with CCA tumour cells. Furthermore, increased IL-17 production from CD3+ T cells was shown to be linked to expression of the Proline-Rich Homeodomain (PRH) transcription factor in CCA tumour cells, as non-PRH expressing cells were unable to generate increased IL-17 production from CD3+ T cells.

Our preliminary results from digital pathology analysis and spatial profiling (n=2) has revealed differential accumulation of different immune cell populations, including CD68+ macrophages within distinct tumour regions. In addition, distinct clustering patterns between CD68+ macrophages and the immune checkpoint molecule B7-H3 have been highlighted.

Conclusion

Using a combination of in vitro modelling and ex vivo spatial analysis, we have been able to functionally and phenotypically characterise the CD3+ T cell and CD68+ macrophage compartment in CCA tumours.

With further funding secured to extend the characterization of the CCA immune tumour microenvironment, as well as to investigate tumour-immune cell interactions via the PRH/ IL-17 axis in CCA, we hope to uncover translationally relevant pathways that could be potentially targeted for better outcome in patients diagnosed with CCA.

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Can we improve access & outcomes for patients with cirrhosis who require surgery?

Scott R, Aithal G, Humes D, Ollivere B, Bains M, Rowe I, Hammond J, Sreedharan A, Hutchinson J, Hardy T, Smith I, Stocken D

Background

Half of patients with cirrhosis are undiagnosed, most have normal blood tests. By using risk factors (alcohol, diabetes, obesity) & non-invasive tests (eg Fibroscan) you can screen patients for cirrhosis [1]. Non-invasive tests (eg MRI) can detect clinically significant portal hypertension [1,2], the only evidence-based predictor of peri-operative risk [3]. Patients with cirrhosis (particularly alcohol) are more likely to get fractures. Mortality after surgery is 3x higher in orthopaedic surgery [4] & 8x higher in colorectal surgery [5]. This need can be addressed by high-quality research which requires multi-disciplinary & cross-speciality collaboration. Using non-invasive tests in targeted populations to identify high risk patients & develop a multi-disciplinary approach to mitigate peri-operative risk.

Aim: establish & grow a research partnership across diverse areas (established hubs in Nottingham, Newcastle & Leeds to support under-served high prevalence spokes in Lincolnshire, Yorkshire & Tees valley) to tackle inequalities of access, research and national variability in surgery provision to patients with cirrhosis

Objectives:

- Develop a sustainable multi-disciplinary, cross-speciality, research partnership
- Share topic & methodological expertise
- Identify high-priority unanswered research questions with stakeholders
- Co-design & submit high-quality competitive research proposals to NIHR
- Build capacity & capability to deliver nationally generalisable studies

Methods

1. Mapping & building skills: Electronic surveys of staff & public to map elective, emergency & cancer surgery, existing services & barriers to research. We will use the NIHR & Clinical Research Network portfolio to map research activity across these services to identify & engage new members (including offering structured training sessions, mentorship, skill-sharing opportunities, & protected time for proposal development).

2. Analyse existing datasets: Perform preliminary analysis on existing datasets (colorectal operations, fracture admissions) to provide crucial feasibility data & strengthen stage 2 grant proposals.

3. Identifying important, unanswered research questions: Lead a research question generation exercise, through a modified Child Health and Nutrition Research Initiative (CHNRI) methodology to identify & prioritise important unanswered research questions about screening, risk assessment & peri-operative care of patients with cirrhosis who require surgery.

4. Developing high-quality research proposals: Proposals addressing high-priority research questions will be developed, & supported through three structured workshops with input from the Leeds Clinical Trials Research Unit (CTRU). The workshops will focus on shaping the proposal, strengthening the methodology, refining the proposals, providing space for constructive discussion & feedback from expert researchers & public members.

Results

Our NIHR-funded national liver partnership will establish high-priority research questions, submit collaborative proposals to the NIHR to answer them, & ensure that diverse teams across the country are well-prepared to deliver high-quality research to address inequalities, improve access & outcomes from surgery in patients with cirrhosis.

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Academic
Clinical
Fellows'
Posters

Risk of osteopaenia, osteoporosis and osteoporotic fractures in patients with chronic pancreatitis: a systematic review and meta-analysis

Amanda Koh, Olamide Oyende, David J Humes, Dileep N Lobo

Background

Chronic pancreatitis results in irreversible pancreatic dysfunction and malnutrition, which, alongside excess alcohol intake, can increase the risk of low bone density. Osteoporosis increases the risk of fractures and chronic bone pain, reduces quality of life, and poses considerable costs to healthcare. Despite this, there remains a paucity in literature evaluating bone health in this patient population. This systematic review and meta-analysis evaluated the prevalence of osteopaenia, osteoporosis and fractures in patients with chronic pancreatitis.

Methods

A comprehensive search of Medline, Embase, ClinicalTrials.gov, and CENTRAL databases was undertaken to identify eligible studies from January 2000 to May 2022. The prevalence of osteopenia, osteoporosis and fragility fractures were extracted from the included studies. Where available, a subgroup analysis was performed to compare the likelihood of developing osteoporosis in patients with chronic pancreatitis compared with control.

Results

Nineteen studies reporting on 2,027,767 participants were included (20,463 with chronic pancreatitis and 2,007,304 controls). The pooled prevalence of osteoporosis was 19% (95% CI 13-26%; I2=94%). Patients with chronic pancreatitis were more likely to have osteoporosis when compared with the control group (OR 2.80, 95% CI 1.86-4.21). The prevalence of osteopaenia and overall fractures were 37% (95% CI 31-44%; I2=81%) and 14% (95% CI 7-22%; I2=99%) respectively.

Conclusion

The prevalence of osteopenia and osteoporosis is significant in patients with chronic pancreatitis, and can increase the risk of developing fractures. Further population-based studies are required to evaluate the disease burden of osteoporotic fractures and associated morbidity and mortality in chronic pancreatitis.

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Investigating the effects of anti-diabetic medications on the gut microbiome in non-alcoholic fatty liver disease

Ammar Ahmed

Background

Non-alcoholic fatty liver disease (NAFLD), a chronic liver disease (CLD), is increasingly becoming common worldwide. NAFLD occurs in patients independent of their alcohol consumption, the leading lifestyle-associated cause of CLD. NAFLD initially involves fatty deposits in the liver, having minimal impact on function; however, it can progress to liver fibrosis, and even permanent damage (cirrhosis) requiring transplantation. NAFLD is closely associated with type 2 diabetes (T2DM), and is linked to lifestyle factors, particularly diet. It is estimated that over 50% of patients with T2DM will have NAFLD [1]. Although there is currently no medication licensed for treating NAFLD, various anti-diabetic medications (ADMs) have shown to improve clinical outcomes in NAFLD [2, 3]. The gut comprises bacterial communities, i.e. the microbiome; as the portal circulation links the gut to the liver, the microbiome and metabolites are thought to affect the liver [4]. Alterations in the microbiome (dysbiosis) have shown to play a role in the disease processes of NAFLD and T2DM. This project thus seeks to explore how ADMs have an impact on the gut microbiome in NAFLD patients.

Methods

As part of an ongoing study, NAFLD patients provided stool samples, which underwent DNA extraction. Two cohorts of patients were chosen: those taking (n = 10) and not taking ADMs (n = 10), the latter being the control group. Data obtained from 16S rRNA amplification and sequencing is being analysed using QIIME 2 (a bioinformatic tool) to characterise bacterial taxonomy and diversity analyses.

Results

This is an ongoing project, and investigations are still underway. Preliminary results seem to indicate lower microbiome diversity in patients not taking ADMs, however further data purification and statistical analyses will need to be carried out.

Conclusion

Although increased microbiome diversity indicates a protective role of ADMs, prospective interventional studies will be needed to determine true causal relationships. It is hoped that this project will contribute to improved understanding of the pathophysiological role of the gut microbiome in NAFLD, and better promote the use of ADMs in the clinical management of NAFLD.

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Baseline risk as a violation to the transitivity assumption in network meta-analysis

Brett Doleman, Ole Mathiesen, Alex Sutton, Nicola Cooper, Jon Lund, John Williams

Background

Transitivity is a central assumption of network meta-analysis (NMA), which states that important effect modifiers in trials are equally distributed between different treatment comparisons. We have previously demonstrated that analgesic agents are more effective when the severity of baseline risk in the control group (pain) increases [1]. Therefore, if average baseline risk (effect modifier) varies between different treatment comparisons, then the assumption of transitivity is violated, making NMA invalid.

Methods

We conducted a Bayesian network meta-regression of randomised controlled trials evaluating non-opioid analgesics in reducing the incidence and severity of chronic post-surgical pain (CPSP). We also repeated the analysis taking into account the uncertainty in baseline risk to exclude regression to the mean. Estimates are presented as b coefficients with 95% credible intervals (CrIs). Plots of baseline risk for each trial were plotted in covariate plots to identify baseline risk imbalance. All analyses were conducted in R and WinBUGS software.

Results

We included 88 (incidence) and 65 (severity) randomised controlled trials. As baseline risk increased (increased pain severity) in a trial, the greater the pain reduction in the trial (Figure 1). This was the case for incidence (b -0.58, 95% CrIs -1.00 to -0.12) and severity of CPSP (b -0.59, 95% CrIs -0.87 to -0.29), as well as when analysed excluding regression to the mean. Covariate plots showed unequal distribution of baseline risk between treatment comparisons, indicating potential violations to the transitivity assumption.

Conclusion

We have identified baseline risk as a major threat to the transitivity assumption in NMAs in pain. This finding calls into question the validity of the entire evidence base in this area, which requires urgent action and solutions such as the use of alternative methods [2] to improve the validity of NMAs in pain.

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List of publications and achievements

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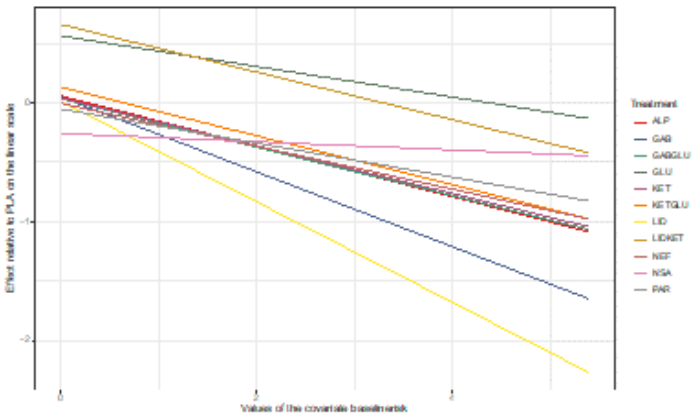

Figure 1: Network meta-regression plot of pain reductions with analgesic agents (Y-axis) which is greater as baseline risk increases (X-axis). Abbreviations to the right of the plot indicate different analgesic interventions and their corresponding colour on the plot.

The degree of lymphopenia with siponimod

Christopher Gilmartin, Terri Worthington, Nikos Evangelou

Background

Siponimod is a sphingosine 1-phosphate (S1P1,5) receptor modulator licenced for secondary progressive multiple sclerosis (SPMS). Its mechanism of action includes the reduction of lymphocyte egress from secondary lymphoid organs, and therefore has an adverse effect of lymphopenia. The degree of lymphopenia has not been previously categorised, and this has implications for clinical practice including the potential risk of infection for patients.

Objective

To characterise the degree of lymphopenia experienced by SPMS patients receiving siponimod

Methods

This is a retrospective cohort analysis of all SPMS patients receiving siponimod at a tertiary centre in the United Kingdom.

Results

45 patients with a median age of 53 (IQR 46-59) were evaluated. 1 month after receiving siponimod, 44 out of 45 patients (97.8%) experienced lymphopenia, and 35 out of 45 patients (77.8%) experienced Grade 3 or 4 lymphopenia. At 6 months after receiving siponimod, 36 out of 36 patients experienced lymphopenia (100%), and 29 out of 36 patients (80.6%) experienced Grade 3 or 4 lymphopenia. A multiple linear regression model did not identify baseline lymphocyte count, age, sex or previous use of other disease modifying therapy associated with lymphopenia as being significant predictors of lymphocyte count 6 months after commencing siponimod.

Conclusion

Lymphopenia is a very common adverse effect, with a high proportion of patients experiencing this to a significant degree. This ought to inform discussions with patients when deciding whether to commence siponimod, and a close level of monitoring is advised.

Association between modifiable risk factors for dementia and neuroimaging-based brain-predicted age

Dewen Meng

Background

According to the 2020 Lancet Commission on dementia prevention, intervention, and care, 40% of dementia cases could be prevented or delayed by targeting twelve modifiable risk factors throughout life [1]. Brain structure and function among individuals can be substantially different, suggesting that they change at different rates as a consequence of heterogeneity in genotype, environment, lifestyle and disease [2]. Brain-predicted age, which is the estimation of the brain biological age by applying machine learning algorithms to MRI data, has recently emerged as a reliable imaging-based biomarker of brain health [3]. The difference between brain-predicted age and chronological age (brain age gap) signifies a deviation from the normal ageing trajectory and has the potential to identify risk factors that are beneficial or detrimental to brain health and thus detect potential targets for interventions [4]. The aim of this study is to investigate if the brain age gap can serve as a mediating indicator in the associations between risk factors for dementia and cognition.

Significance of the study

Understanding the impact of modifiable risk factors on brain ageing represents a window of opportunity wherein interventions targeting modifiable risk factors may delay and even prevent pathological brain changes.

Future research plans

1. Literature review to identify and synthesise the evidence for an association between brain age gap and twelve dementia-related modifiable risk factors.
2. Collaboration with researchers from the NIHR Nottingham BRC to use the established brain age prediction training model that developed using UK Biobank data.
3. Using UK biobank data to investigate the association between modifiable risk factors, brain age gap and cognition.

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Predictors of quit attempts and successful smoking cessation in pregnancy: An Exploratory Analysis

Hannah Igoe; Jo Emery; Felix Naughton; Jaspal Taggar; Jo Leonardi-Bee; Tim Coleman

Background

Smoking in pregnancy has negative outcomes, including miscarriage, still birth, and pre-term labour. In the UK 11-20% of pregnant women smoke.[i]

Previous studies have investigated predictors of smoking cessation, but most have not distinguished between factors influencing quit attempt and abstinence. [ii] This is potentially important as the processes of initiating cessation and maintaining abstinence are likely to have different predictors. A study by Emery et al. found that smoking beliefs predicted quit attempt, but not cessation, and nicotine dependence was inversely associated with quitting but not with trying to quit, but analyses was possibly underpowered (N=207). [iii]

Using a larger dataset (N=1,409), we will replicate the Emery et al. study and may detect associations not apparent previously.

Methods

This secondary analysis of pooled data from the MiQuit2 [iv] and MiQuit3 [v] RCTs of a pregnancy smoking cessation intervention will investigate which variables (demographic; smoking behaviours; beliefs) predict each of two binary smoking outcomes – making a quit attempt, and abstinence in women who made a quit attempt.

We used logistic regression analyses (univariate and multivariate), using the same potential predictor variables for both outcomes.

Results

In the final multivariate models:

Quit Attempt: 'MiQuit Condition'; 'increasing intention to quit'; and 'increasing self-efficacy' were the only significant predictors of quit attempt.

Abstinence: 'Decrease in number of cigarettes in early pregnancy' & 'length of longest Previous quit attempt' were the only two significant predictors of abstinence.
These are emergent results and sensitivity analyses are ongoing.

Conclusion

Self-efficacy and intention to quit were significant predictors of a quit attempt, but not abstinence.

Decrease in number of cigarettes early in pregnancy, and having made a previous quit attempt > 6 weeks, were significant predictors of abstinence.

Findings from this study could help inform intervention development for smoking cessation in pregnancy.

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Potential synthetic lethality approaches in breast cancer cells with XRCC1 deficiency

Brownlie, J., Algethami, M., Madhusudan, S

Background

Synthetically lethal pairs are identified where impairment or inhibition of a specific gene leads to cell death only in the context of a pre-existing distinct genetic mutation [1]. Current clinical application of this concept is the pharmacological inhibition of PARP (poly (ADP-ribose) polymerase) in the treatment of breast and ovarian cancers with BRCA mutation. BRCA deficiency affects each cell's ability to repair DNA damage and can leave them more vulnerable to PARP inhibition with resultant accumulation of DNA damage and then cell death [2].

XRCC1 (x-ray repair cross-complementing protein 1) is a scaffolding protein involved in DNA damage repair. Loss of XRCC1 expression, identified in 16% of breast cancers, is associated with an aggressive tumour phenotype [3]. Our hypothesis is that XRCC1-/- triple negative breast cancer cells will be addicted to certain protein kinase (PK) signalling for survival and their blockade will induce selective cell kill.

Methods

Breast adenocarcinoma cells from the MDA-MD-231 cell line with XRCC1 knockout (using a CRISPR-Cas9 system) were treated in triplicate with compounds from the Published Kinase Inhibitor Sets 1 and 2 (PKIS)(total 884 inhibitors) [4,5]. Cell survival was then compared with that of control MDA-MD-231 cells using an MTS assay (Promega, UK). Results for the 100 most promising compounds were validated in HeLa XRCC1-/- vs HeLa XRCC1+/+ cells.

Results/Next steps

Several protein kinase inhibitors, including chemical probes that block cyclin dependent kinases (CDK2, CDK4 and CDK6) were found to be selectively toxic in XRCC1-/- compared to XRCC1+/+ cells. The next steps will be to conduct detailed in vitro and in vivo studies with the aim of selecting a drug candidate for future clinical study.

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Accepted manuscript:

1. Targeting DNA damage repair precision medicine strategies in cancer. Brownlie J, Kulkarni S, Algethami M, Jeyapalan J, Mongan N, Rakha E, Madhusudan S. Current Opinion in Pharmacology

Publications as contributing author:

1. Evolving DNA repair synthetic lethality targets in cancer. Kulkarni S, Brownlie J, Jeyapalan JN, Mongan NP,Rakha EA, Madhusudan S. Biosci Rep. 2022;42(12).

2. Towards Personalized Management of Ovarian Cancer. Algethami M, Kulkarni S, Sadiq MT, Tang HKC, Brownlie J, Jeyapalan JN, et al. Cancer Manag Res. 2022;14:3469-83

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Case report and literature review of overdose of intravenous lipid emulsions in infancy

Melissa-Sue Ryan[1], John McIntyre[2], Lizzie and Dave Bramwell[3], Shalini Ojha[1,2]

[1.]Academic Unit of Lifespan and Population Health, School of Medicine, University of Nottingham, [2]Neonatal Unit, Derby Children's Hospital, University Hospitals of Derby and Burton NHS Foundation Trust, [3]Parent authors, Derby

Background

Intravenous lipid emulsions (ILE), a component of parenteral nutrition (PN), are frequently administered to preterm infants and infants with gastrointestinal problems while they establish milk feeding[1].

ILE is often infused separately from other components of PN and accidental overdoses can occur. Reports of such overdoses cite serious adverse effects, such as respiratory distress, fat overload syndrome, metabolic acidosis, and death[2-4].

We report an accidental overdose in a preterm infant.

Methods

On Day 2 of life, a 29-week gestational age (GA) twin was accidentally given 47.5mL of Intralipid 20% (≈3x daily amount) in 50-minutes. This equated to 5.85g of triglycerides instead of ~0.07g of his total 1.6g/kg/day, giving a large volume of fluids (54.8 ml/hour) over this short time.

Results

The infusion was immediately stopped and it was noted that the pump was incorrectly set. No apparent clinical deterioration occurred, although blood samples were initially grossly lipaemic.

Outcomes at 2 years corrected gestational age were similar to that of his twin (see Table 1.).

Learning from this mistake, and published research on medication errors in neonates, service changes were made to infusion packaging and lipid administration to avoid similar errors.

Conclusion

Medication errors in neonates are unfortunately common[5]. Published literature usually focus on poor outcomes, which can increase the distress for parents of children where errors have occurred.

Publishing the full spectrum of outcomes instead allows parents and professionals to be aware of all possibilities and lessons learnt, even if serious harm was avoided.

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Infant parameters	Twin 1	Twin 2
Gestational age at birth	29 weeks and 5 days	29 weeks and 6 days*
Birth weight (g)	1329	1273
Apgar score at 1min	6	3
Apgar score at 5min	9	8
Resuscitation breaths	Yes	Yes
Respiratory support received		
Initial support	CPAP	Mechanical ventilation
Days of mechanical ventilation	0	6
Days of CPAP	16	30
Days on supplemental oxygen	19	29
Oxygen at discharge	none	Low flow oxygen (0.1 L/min)
Cranial ultrasound	Small cyst at right caudothalamic notch	Grade 1 left-sided GMH
Weight at discharge (g)	2920	2920
Feeding at discharge	Full milk feeds via breast/NG tube	Full milk feeds via NG tube
Length of hospital stay (days)	70	70
Clinical course after discharge home		
Hospital admissions	0	0
Medications	None	None
Follow up at 2 years CGA		
Weight (kg)	13.4	12.5
Height (cm)	91.0	89.1
Head circumference (cm)	51	49
PARCA-R (percentile)		
Language score	79 (7.6)	71 (2.8)
Non-verbal cognition score	90 (26.3)	84 (13.6)
BSID-III (percentiles)		
Cognition score	100 (50)	95 (37)
Motor score	94 (34)	82 (12)
Language score	83 (13)	76 (8)
Social emotional score	85 (16)	85 (16)
Adaptive behaviour score	85 (16)	70 (2)

*born at 00:25hours the following day
CGA, corrected gestational age; CPAP, continuous positive pressure ventilation; GMH, germinal matrix haemorrhage

Table 1. Neonatal course and two-year corrected age follow-up of the case and his twin brother

Characterisation of myeloid-derived suppressor cells (MDSCs) as a therapeutic target in glioblastoma multiforme (GBM)

Daniele Scotto, Hester Franks, Andrew Jackson, Poulam Patel

Background

GBM is the most aggressive adult brain tumour with a high mortality rate and poor response to immunotherapy. The immunosuppressive microenvironment of GBM presents a major barrier to effective implementation of immune-based approaches. Improving our understanding of this tumour's microenvironment is key to the development of novel immunotherapies. GBM tumours contain a substantial proportion of myeloid cells and amongst these, MDSCs correlate with disease grade, recurrence, and adverse clinical outcomes (1,2). Our understanding of the role of MDSCs in GBM remains inadequate.

Aim

The aim of our study is to determine the location and activity of MDSCs within the microenvironment of GBM. We will map the immune landscape of GBM with a particular focus on MDSCs and T-lymphocytes (a major target of MDSC suppressive activity).

Methods

Characterisation of leucocyte phenotypes: During surgery, the fluorescent metabolic dye 5-ALA is used to identify tumour cells and allow more complete excision of GBM tissue. Leucocytes can be enriched from surgical samples by flow-sorting 5-ALA-fluorescent tumour cells from other cell components and identifying immune cells in the 5-ALA-negative fraction using antibody panels to major leucocyte subsets (figure 1) (3). Leucocyte cytokine profiles will be characterised by multiplex cytokine assay and transcriptomic analysis.

Determination of the functional potency of MDSCs: Myeloid cells will be isolated by flow-sorting the 5ALA-negative fraction of GBM tumours and the immunosuppressive activity of MDSCs determined by studying their ability to inhibit T-cell responses in a mixed-lymphocyte reaction.

Mapping the distribution of T-lymphocytes and myeloid cells: The relative location and abundance of T-cell and myeloid subsets across tumour tissue will be determined by multiplex staining of different tumour regions using a panel of myeloid-cell and T-cell-specific markers.

Significance

Our results will provide insight into the contribution of MDSCs to the microenvironment of GBM, highlighting potential therapeutic targets for immunotherapies that seek to overcome the tumour's immunosuppressive network.

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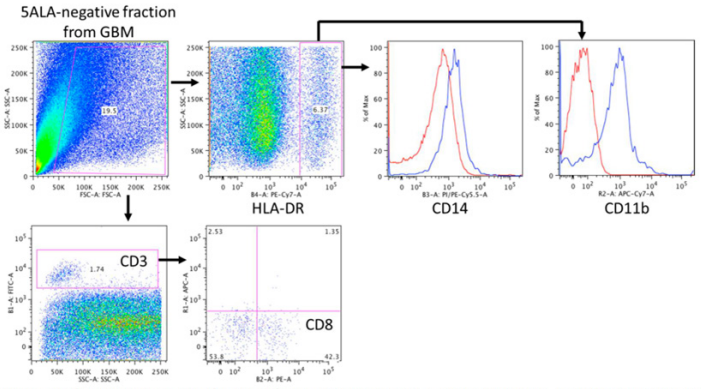

Figure 1 The 5ALA-negative fraction from GBM tumours contains HLADR+ positive immune cells which express CD14 or CD11b as well as CD3+CD8+ cells

Academic Foundation Programme Doctors' Posters

Factors influencing General Practice capacity for medical students: A Literature Review

Lucy Adams, Jaspal Taggar

Background

As medical school expansion continues, there will need to be increasing capacity on the part of general practices to take on medical students. It is unclear what influences this capacity and to this end there will be a larger research project to investigate this. As part of this, a literature review is necessary in order to understand what the current understanding is.

Methods

To use a formal PICO search method on Embase, Medline, and PubMed in order to create a collection of the relevant literature on this topic. I will then read, analyse, and summarise the literature into a literature review. This will hopefully create a better understanding of where to gaps in research are, and areas that need further understanding.

Results

Although the literature review is not yet completed, it will likely show factors such as financial considerations, location in comparison to a local medical school, and adequate staffing.

Conclusion

By understanding the factors that influence general practice capacity to take on medical students, this can then create a good starting point for further research and understanding into how to these can be mitigated. This is important for creating adequate clinical teaching and supervision for increasing numbers of medical students.

Antihypertensive drug treatments in older adults with multimorbidity: a scoping review protocol

Amir Reza Akbari, Barbara Iyen, Jo Leonardi-Bee, and Tony Avery

Background

A scoping review will be conducted to examine the benefits and harms of using antihypertensive medications in older adults with multimorbidity. The primary review question is “What is the available evidence on benefits and harms of antihypertensive drug treatments in older adults with multimorbidity?” Secondary review questions include examining the reported benefits and harms of antihypertensive drug treatments in older adults aged 65-80 years and those aged 80 years and over, and identifying the disease burden and treatment burden, including the presence or absence of polypharmacy, reported in this population.

Methods

The scoping review will adhere to PRISMA-ScR guidelines and the methodology described by Arksey and O’Malley (1). The protocol has been registered on Open Science Framework (2). Studies including individuals aged 65 years and older with multimorbidity who are prescribed one or more regular antihypertensive medication at the beginning of the study will be considered. The search strategy will consist of a three-step process, including a preliminary search of two relevant online databases (MEDLINE and Embase), a secondary comprehensive search of MEDLINE, Embase and PubMed databases, and a search of the reference lists of identified articles.

Results

The source of information will include primary and secondary sources of evidence, such as primary research studies, systematic reviews, meta-analyses, case-reports, and conference abstracts. A charting table will provide a descriptive summary of key characteristics of the included studies. The findings extracted from the studies will be descriptively mapped. Drug benefits and harms will be identified and classified in different subgroups of individuals, and these subgroups of patients will be characterised. The occurrence of outcomes in different populations will be presented as summary statistics including frequency counts and proportions as appropriate.

Conclusion

This scoping review will provide an overview of the existing evidence on the benefits and harms of using antihypertensive medications in older adults with multimorbidity. The review will identify gaps and inconsistencies in the research and highlight areas for future research, with the aim of improving the safety and efficacy of antihypertensive medication use in this population.

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The role of the autonomic nervous system in cerebral blood flow regulation in stroke: A review

Alex Mankoo, Sankanika Roy, Aaron Davies, Ronney B. Panerai, Thompson G.Robinson, Patrice Brassard, Lucy C.Beishon, Jatinder S.Minhas

Background

Stroke is a pathophysiological condition which results in alterations in cerebral blood flow (CBF). The mechanism by which the brain maintains adequate CBF in presence of fluctuating cerebral perfusion pressure (CPP) is known as cerebral autoregulation (CA). Disturbances in CA may be influenced by a number of physiological pathways including the autonomic nervous system (ANS). The cerebrovascular system is innervated by adrenergic and cholinergic nerve fibers. The role of the ANS in regulating CBF is widely disputed owing to several factors including the complexity of the ANS and cerebrovascular interactions, limitations to measurements, variation in methods to assess the ANS in relation to CBF as well as experimental approaches that can or cannot provide insight into the sympathetic control of CBF. CA is known to be impaired in stroke however the number of studies investigating the mechanisms by which this occurs are limited. This literature review focused on highlighting the assessment of the ANS and CBF via indices derived from the analyses of heart rate variability (HRV), and baroreflex sensitivity (BRS), and providing a summary of both clinical and animal model studies investigating the role of the ANS in influencing CA in stroke. Understanding the mechanisms by which the ANS influences CBF in stroke patients may provide the foundation for novel therapeutic approaches to improve functional outcomes in stroke patients.

Methods

Literature review was conducted following pre-defined protocol.

Results

Current research suggests stroke pathophysiology involves impaired autonomic function as indicated most frequently by a reduced HRV. However, the validity of HRV as a measure of autonomic function in a stroke population is uncertain. The most common limiting factor for interpretation of ANS function in a stroke population is the heterogeneity between studies investigating ANS function in stroke. The ARS and CASS are potential measures of autonomic function that could be used to standardise assessments between centers and overcome some of these limitations. Further investigation is required to assess the validity of combining HRV and beat-to-beat BPV to assess ANS function in stroke patients as suggested by Tang et al. (2020).

Conclusion

In conclusion, autonomic dysfunction is common in stroke. ANS dysfunction alone is a risk factor for as well as a result of stroke. The markers of autonomic dysfunction (HRV, BRS) are reduced in stroke. The ANS is also responsible for regulating CBF up to a certain extent, hence a stroke causing ANS dysfunction can result in CBF dysregulation. However, a key area for future research remains the harmonization of autonomic assessment between centers. The development of standard autonomic assessments such as ARS and CASS need exploring in stroke, and may address some of the heterogeneity identified by this review. Finally, this review identified a paucity of studies specifically investigating the role of the ANS in control of CBF in stroke, and research in this area should be prioritized to facilitate the identification of novel biomarkers and therapeutic targets.

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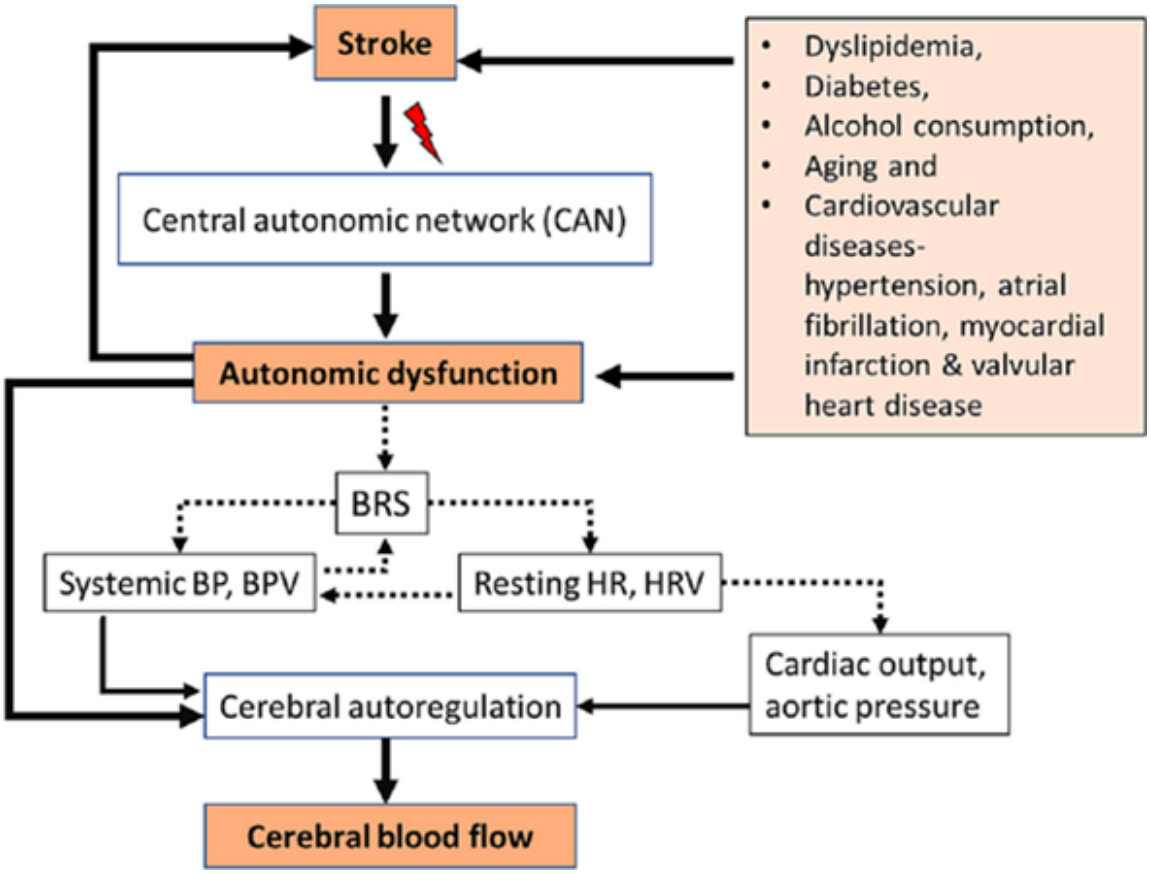

Relationship between stroke, autonomic dysfunction and cerebral blood flow. Thick arrow –direct effect and broken arrow – indirect effect, BRS – baroreceptor sensitivity, BP – blood pressure, HR – heart rate, HRV – hear rate variability

Evaluating the efficacy and safety of single agent etoposide intra-CSF chemotherapy in children and young people with relapsed/refractory central nervous system tumours

Anna Butler, Lisethe Meijer, Jo-Fen Liu, Manjit Chohan, Ibrahim Jalloh, Donald Macarthur, Margaret Parr, Sophie Wilne, Shaun Wilson, David Walker, Richard Grundy, Madhumita Dandapani

Background

The aim of the project was to evaluate intra-CSF etoposide administration in a palliative setting for children and young people with relapsed/refractory central nervous system (CNS) tumours, with the primary endpoints being overall survival and progression-free survival time. A safety endpoint was to assess the side effect profile and complications of intra-CSF etoposide.

Methods

35 patients under the age of 30 years (median age 5.33 years) were enrolled onto the project. The cross-centre study was a service evaluation, with a data collection spreadsheet being completed by the Nottingham centre and sent to the Oxford centre. Data was analysed using SPSS, assessing the overall survival and progression-free survival times, as well as the 6-month and 1-year survival rates.

Results

The median overall survival and progression free survival times were 10.97 and 5.91 months respectively. The 6-month and 1-year overall survival rates were 67% and 48%, and the progression-free survival rates were 50% and 22%. Age at the start of intra-CSF therapy was significantly associated with overall survival (P=0.046), with the 6+ age group having improved overall survival. Treatment type was significantly associated with overall survival (P=0.012), with etoposide intra-CSF treatment being associated with improved overall survival. Treatment duration was significantly associated with both overall survival (P<0.001) and progression-free survival (P<0.001).

Conclusion

Intra-CSF etoposide treatment has shown to increase both overall and progression-free survival significantly, whilst having few side effects and maintaining a good quality of life for patients, reflecting it as a beneficial therapy in the palliative setting.

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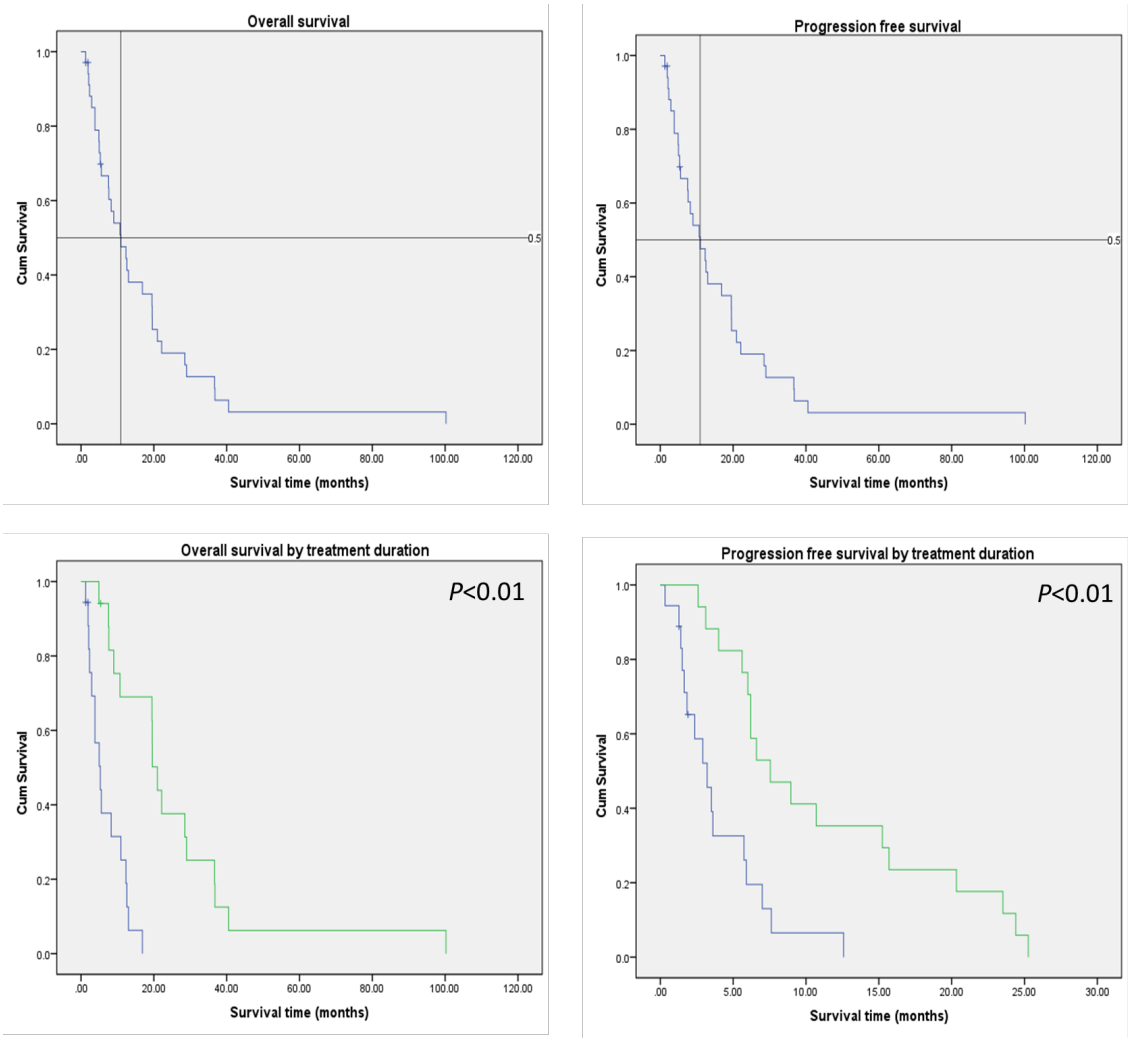

Fig. 1 Kaplan-Meier curves of overall survival of all patients (A) and progression free survival of all patients (B). The overall survival (C) and progression free survival (D) by treatment duration, with 0-3 months of treatment (blue) and 3+ months of treatment (green) groups.

Adolescents admitted to psychiatric units far away from home (FAFH) or to adult units and the impact of COVID-19: the clinicians' perspective

Morenike Da-Silva-Ellimah, Josephine Holland, Kapil Sayal

Background

In England, the demand for Child and Adolescent Mental Health Service (CAMHS) inpatient beds outweighs the supply, and the recent COVID-19 pandemic has added to this demand (1). As a result, there are instances where young people have been admitted to adult wards or out-of-area. Whilst it is widely recognised that these admissions are not ideal, few studies have explored these admissions from the perspective of clinicians, or detailed how they perceived COVID-19 to impact the admissions.

Methods

Qualitative study featuring the content analysis of open-ended questions from a questionnaire answered by consultant CAMHS psychiatrists working in England who reported seeing an eligible case. This included adolescents (aged 13-17 years) who were admitted to a General Adolescent Unit out-of-area (over 50 miles from their home address or outside of their NHS commissioning region) or to an adult ward for psychiatric care.

Results

52 consultant psychiatrists in England participated. When asked to comment on anything related to the young person's care and admission, the main themes identified were 'the distance made discharge planning difficult', 'distance made contact with family difficult', 'experience of the transfer/repatriation process', and 'admission outcome'. From the comments related to the impact of COVID-19 on the referral and admission process, the main themes identified were 'COVID-19 delayed admission and transfer', 'COVID disrupted discharge planning' and 'COVID reduced the young person's contact with others'.

Conclusion

Clinician's comments mainly reflected a negative perspective of out-of-area and adult admissions, with COVID-19 adding further delays and disruption to the referral and admission process. Factors attributed to a positive experience were finances, completing the Care Programme Approach before the transfer, and heavy support from social workers.

Further insight into the clinician experience of these admissions can be gained from research that allows respondents to elaborate on their answers such as interviews.

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What is the effect of HRT on OA of the knee, hip and hands?

Charles Hillman, Katie Marino, Oliver O'Sullivan, Stefan Kluzek, Robert Atkinson

Background

Osteoarthritis (OA) is a degenerative disease that can lead to progressive pain, which can ultimately lead to a joint replacement. Hormone replacement therapy (HRT) is widely prescribed to treat menopausal symptoms in women, and its beneficial effect on osteoporosis is well known[1]. We sought to find the effect of HRT on the prevalence, incidence or severity of hip, knee or hand OA in peri- or post-menopausal women.

Methods

A systematic review was performed using PRISMA guidelines and prospectively registered on PROSPERO. A search was conducted on 7/10/22 on Medline for related terms. Two independent reviewers screened results, extracted the data, and conducted a quality assessment with 'ROBINS-E', with a third for arbitration. Studies had to be primary research in humans using validated patient reported outcome measures (PROMs), or objective measures of OA.

Results

1672 results were reduced to 27 studies included. 11 studies assessed the hip, 19 knee, and 8 hand. 16 studies used radiographic measures to assess OA, 9 joint replacement surgery, 1 GP records, and 1 PROMs. Most studies (n=18) were considered to have a 'High Risk of Bias'.

Prospective studies were most at risk of poor study quality. Positive correlations between HRT use and hip or knee replacement were observed across studies. No effect, or a decreased risk in radiological OA with HRT use was found for all joints studied.

Conclusion

There were widespread differences in confounding variables adjusted for, methods of measuring both HRT exposure and presence of OA, impacting the quality of data. Despite this, use of HRT appears to increase the risk of having a knee or hip joint replacement. Duration of HRT use appears to play a role in this effect. Future research should aspire to appropriate confounding analysis, accurate recording of HRT exposure (including formulations) and use PROMs alongside objective measures of disease.

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Shortlisted for Helal and Haries award; Sports and Exercise Medicine section of Royal society of medicine annual award for: 'A fractured Achilles tendon'

Pre-emptive acetaminophen for postoperative pain (PAPP): a randomized control trial and updated meta-analysis

Brett Doleman[1,2] , Daniel Last[1,2,*], Síle Ann Johnson[1,2,*], Nuriyah Ali[1], Zdenek Klezl[1], David Rogerson[1], Jonathan Lund[1,2], John Williams[1,2]

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[2] University of Nottingham, Nottingham, United Kingdom
[*] Presenting authors

Background

Postoperative pain is a common consequence of surgery. Pre-emptive analgesia involves the initiation of analgesics prior to surgical incision and has been proposed as a simple method to help reduce postoperative pain, which may be more effective in higher-risk populations (cervical spine surgery). A previous meta-analysis has demonstrated that pre-emptive paracetamol may be effective in reducing postoperative pain although the certainty of evidence was limited.

Methods

We conducted a randomized, placebo-controlled, double-blind trial of 47 participants undergoing cervical spine surgery. The pre-emptive group received paracetamol at induction of anaesthesia and the control group received paracetamol at the end of surgery. This data was utilised in an up-to-date meta-analysis.

Results

We included 845 participants and 12 studies in the updated meta-analysis. The meta-analysis found reduced 24-hour morphine consumption in the pre-emptive group MD -2.42 (95% CI, -4.26 to -0.59), as well as reduced post-operative vomiting RR -0.57 (95% CI, -1.01 to -0.13). There was no significant difference between pre-emptive paracetamol and control groups for time to analgesia request, pain scores at 6 and 24 hours or post-operative pruritis. The GRADE certainty of evidence found very-low certainty of evidence for all outcomes assessed.

Conclusion

The meta-analysis found pre-emptive paracetamol reduced 24-hour opioid consumption and post-operative vomiting, but trials with greater certainty of evidence are required to consolidate this finding.

Chronic conditions related to nutrition in people living with an ileostomy – a scoping review

Tjun Wei Leow, Georgia Herbert, Alexandra Mitchell, Rachel Perry, Gabrielle Thorpe, Scott Clifford, Charlotte Atkinson, Clare England, David Humes

Background

Ileostomy formation can radically disrupt bodily functions that are acutely relevant to health[1-3]. These effects could lead to chronic conditions and health burdens for patients, and increased costs to the health service. The aim of this scoping review was to explore the extent and type of literature examining the chronic conditions related to nutrition in adults living with an ileostomy.

Methods

Databases including MEDLINE, Embase, CINAHL, AMED and Web of Science were searched for studies on chronic conditions (kidney, bone, metabolic health and anaemia) related to nutrition from any type of ileostomy in adults. Search results were screened against inclusion/exclusion criteria. Data from included studies were extracted by two independent reviewers. Results were summarised narratively.

Results

Twenty-one independent studies (22 articles) met the inclusion criteria. Included studies comprised of thirteen cohorts, five cross-sectional and three case studies. Seven studies reported on chronic kidney health, two studies on cardiovascular health, four studies on bone health and six studies on anaemia in relation to ileostomy formation. Indications for ileostomy formation varies across studies but they were predominantly due to colorectal cancer and inflammatory bowel disease (IBD). Included studies reported that patients with ileostomy have an increased incidence of chronic kidney disease (CKD), osteopenia, osteoporosis and anaemia. However, there is a variation in reporting of ileostomy type, length of ileostomy and data collection timeframe among studies which limits data analysis.

Conclusion

This review found that ileostomy is associated with the development of chronic health conditions (CKD, anaemia, osteoporosis). However, current evidence available in the literature is highly heterogenous in terms of ileostomy characteristics. More robust studies are required to facilitate accurate quantification of the risk of chronic health conditions due to ileostomy formation.

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Adjunctive Intra-Arterial Antithrombotic Therapy during Endovascular Thrombectomy for Acute Ischaemic Stroke: A Systematic Review and Meta-Analysis

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Background

In patients with acute ischaemic strokes (AIS) the role of intraarterial adjunctive antithrombotic therapies (AAT) such as glycoprotein IIb/IIIa therapy (GPIIb/IIIa) and tissue plasminogen activator (tPA) is not well understood1-3. Our aim was to assess whether the use of AAT during EVT improves functional and safety outcomes of patients with acute ischaemic strokes compared to standard therapy (ST) alone.

Methods

Four electronic databases (PubMed, MEDLINE, EMBASE, The Cochrane Library) were searched between 2010 and January 2023, and out of 1705 non-duplicated papers that were screened, 38 fulfilled our eligibility criteria. We compared patients above the age of 18 who had an AIS due to large vessel occlusion (LVO) and were treated with AAT plus EVT (with or without intravenous thrombolysis) against those who received ST only. Primary outcome was good functional outcome (mRS 0-2) at 3 months and secondary outcomes were successful recanalization (TICI ≥2b), symptomatic intracranial haemorrhage (sICH), any ICH and mortality at 3 months.

Results

Overall, 13,106 patients were included; 3,039 patients were treated with AAT during EVT and 9,977 were treated with ST only. Compared to ST, patients treated with AAT demonstrated higher odds of achieving functional independence (47.4% AAT vs 43.4% ST; OR=1.27, 95%CI 1.11 to 1.44, p=0.0003, I2=36%; Figure 1), and a lower likelihood of mortality at 3 months (OR=0.71, 95%CI 0.60 to 0.83, p<0.0001, I2=21%). The rates of sICH (OR=0.99, 95%CI 0.8 to 1.22, p=0.93, I2=18%) and successful recanalisation (OR=1.21, 95%CI 0.94 to 1.55, p=0.14, I2=69%) were not significantly different between each cohort.

Conclusion

The use of AAT during EVT may improve functional outcomes and reduce mortality rates compared to ST alone, without an increased risk of sICH. These findings should be interpreted with caution pending the results from ongoing phase III clinical trials to establish the efficacy and safety of different adjunctive antithrombotic agents during EVT.

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List of publications and achievements

Publications:

- Incidence and Predictors of Poor Functional Outcome Despite Complete Recanalisation Following Endovascular Thrombectomy for Acute Ischaemic Stroke (Journal of Stroke and Cerebrovascular Diseases – PMID 36931092)
- Prescribing costs of hypoglycaemic agents and associations with metabolic control in Wales; a national analysis of primary care data (Diabetic Medicine – PMID 35766972)
- Can an algorithm help in the difficult dilemma of upper gastrointestinal bleed and anticoagulant? (Gut, BMJ)
- XTRA study protocol: eXploring medical sTudents' caReer reAdiness—a cross-sectional study in the UK (Journal of Surgical Protocols and Research Methodologies)
- Acute subdural haematoma in the elderly: to operate or not to operate? A systematic review and meta-analysis of outcomes following surgery (BMJ Open – PMID 34862284)
- Dissociable effects of complement C3 and C3aR on survival and morphology of adult born hippocampal neurons, pattern separation, and cognitive flexibility in male mice. (Brain, Behaviour and Immunity – PMID 34403734)
- Understanding the role of HMGB1 post-traumatic brain injury - the complex interplay between neuro-inflammation and neurogenesis. (Abstract – British Journal of Surgery)
- The effect of the C3 and C3aR on adult hippocampal neurogenesis (Abstract – British Journal of Surgery)
- Neurogenesis after traumatic brain injury – The complex role of HMGB1 and neuroinflammation (Journal of Neuropharmacology - PMID:33189765)

Achievements:

- Alan Trevor Jones Memorial Scholarship (2021)
- Wellcome Inspire Vacation Studentship (2020)
- Certificate of merit – Ranking in top 20% of cohort (2020)
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- Wellcome Inspire Vacation Studentship (2018)
- Most outstanding delegate at Harvard Model Congress Dubai (2016)
- Outstanding performance at IGCSE level (2015)
- Coaches award (2011)
- Distinction award University of Waterloo Mathematics contest (2011-2014)

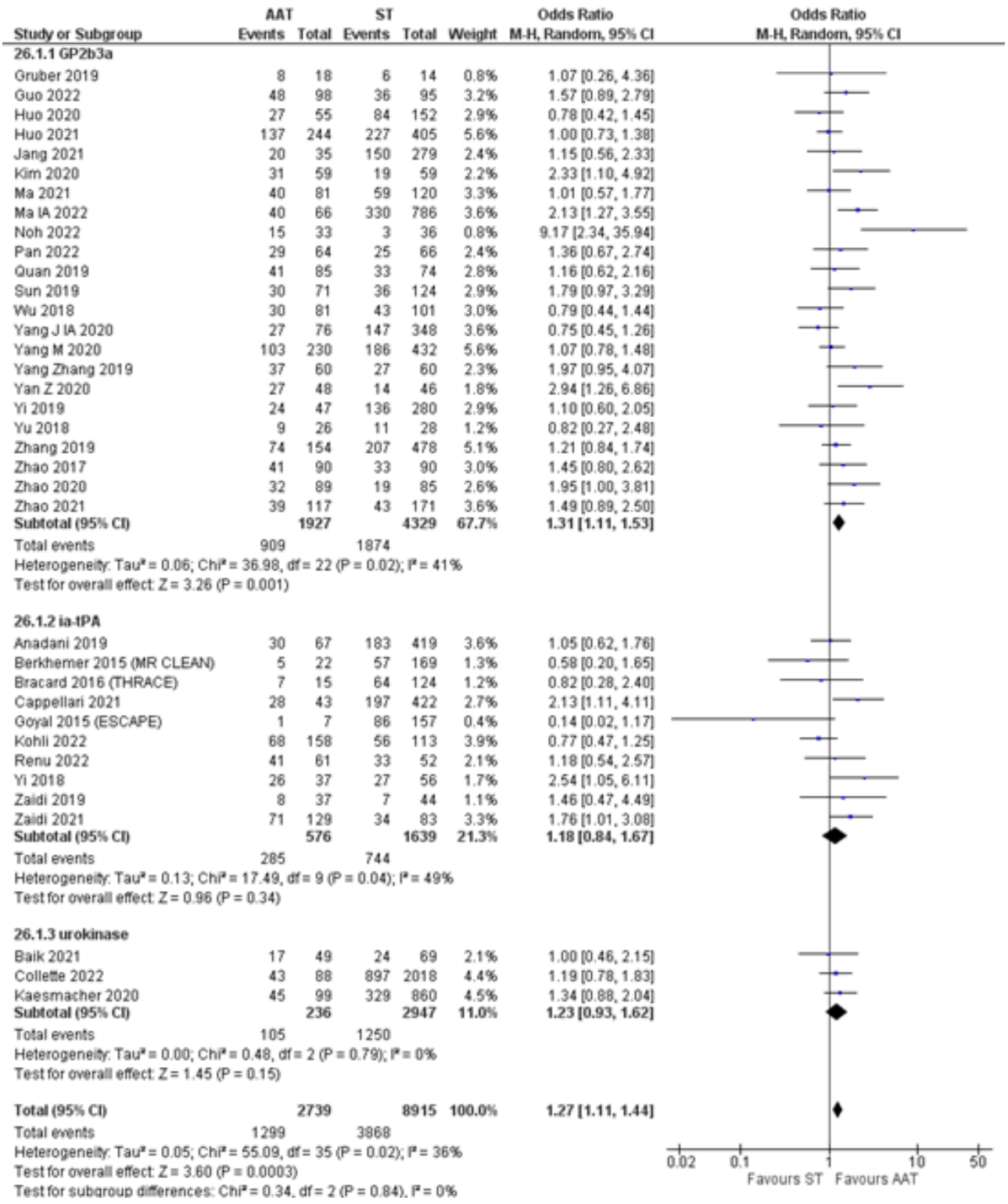

Figure 1. Forest plot demonstrating the odds ratio of functional independence at 90 days between adjunctive intra-arterial antithrombotic therapy (AAT) compared to standard therapy (ST), according to the type of drug used (GPIIb/IIIa inhibitors, Intra-arterial-rtPA or urokinase).

A Scoping Review of LGBTQ+ Education and PrEP Training in the Medical Curriculum

Adrian McGrath, Anthony Gifford, Imogen Hullis, Jatinder Hayre, Joanne Morling

Background

Men-who-have-sex-with-men (MSM) and transwomen are at higher risk of acquiring HIV, and so represent a key group to target with HIV pre-exposure prophylaxis (PrEP). PrEP is a safe and effective tool to reduce HIV transmission, however, a barrier to its uptake is a lack of knowledge and training among healthcare professionals. This scoping review aims to assess the extent to which content on PrEP is embedded and taught within the medical curricula.

Methods

Scoping review: we searched the databases EMBASE, PsychINFO, ERIC and Web of Science to identify articles using a novel search string. Included studies related to medical students' experience with PrEP content within their medical curricula. Relevant data were extracted using standardised forms and thematically analysed with meta-aggregation before narrative synthesis.

Results

From an initial sample of 42 papers, 16 papers were included in this review. No UK studies were identified. Superordinate themes generated from meta-aggregation included: 1) PrEP education and training, 2) sexual health and HIV knowledge, 3) PrEP knowledge, 4) clinical decision-making and 5) social bias. Key findings include a moderate-low level of PrEP knowledge, a high level of HIV knowledge, moderate-high confidence in discussing sexual behaviours with MSM, but less confidence with transgender patients, and social biases (racial bias and heterosexism) that may impact clinical decision-making.

Conclusion

Our review highlighted several important areas to be improved with medical curricula. Medical education should offer more comprehensive training on PrEP, with a focus on improving the identification of PrEP candidates, encouraging confidence in clinical consultation with patients from high-risk groups (including MSM and transgender patients), and raising awareness of the role of social biases with the aim to limit the impact on clinical decision-making. We also highlight a need for further research on PrEP education in the UK, where barriers to PrEP uptake have been demonstrated among MSM.

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Menopausal Hormone Therapy and the association with Ischaemic Stroke and Myocardial Infarction

N Joseph, Y Vinogradova

Background

Menopause is the cessation of menstruation and the completion of a woman's reproductive years (1,2). Eighty per cent of women are post-menopausal by the age of 54 (3). The peri-menopausal and post-menopausal period is associated with challenging symptoms including vasomotor, urinary and vaginal symptoms, as well as metabolic changes (4). Menopausal Hormone Therapy (MHT) is a medicinal preparation containing either oestrogen alone or an oestrogen-progestogen combination for the relief of post-menopausal symptoms. In the 1980s there was a large uptake of HRT as it suggested HRT has cardiovascular benefits. However, in the early 2000s, the World Health Initiative (a large randomised controlled trial) demonstrated that HRT adversely affects cardiovascular health (5).

Objectives

To assess the effects of oral and transdermal MHT on the incidence of coronary heart diseases and Ischaemic Stroke.

Methods

A multitude of search terms were used to identify randomised controlled studies and observational studies, from the databases Pubmed and Scopus.

Results

A meta-analysis of RCTs suggested no statistically significant association between the use of HRT and the incidence of death from cardiovascular causes (Risk Ratio (RR): 0.81 95% CI: 0.47- 1.40), non-fatal MI (RR1.02, 95% CI: 0.80 – 1.31) (4). The use of HRT demonstrated an increase in stroke risk (RR: 1.32 95% CI 1.12 – 1.56) (4). Some variabilities of results were noted in the sub-group analysis of the different preparations.

Conclusion

The use of HRT in the post-menopausal period and the adverse effects associated with this have been an area of interest for over three decades. However, consistent research have yet to be produced. The existing studies have been limited to CEE, Estradiol, MPA and micronized progesterone formulations and have not included all the current prescribed prescriptions. This review of existing research has identified a need for a large-scale population-based case-control study.

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Is Sodium Magnetic Resonance Imaging (MRI) sensitive to pathological processes occurring in generalized epilepsy?

Hari Pai, Nikos Evangelou, Susan Francis, Ben Prestwich, Michael F O'Donoghue

Background

Epilepsy is classified into:

1. focal epilepsies where seizures start in one brain region,

2. generalized epilepsies, where seizures start in networks involving both hemispheres from the start of the seizure. [1]

Focal epilepsy, but not generalized epilepsy, is often associated with brain abnormalities that are easily visible on MRI [2]. Epilepsy that is normal on conventional MRI may have subtle abnormalities detectable using new MRI technique. Recent studies suggest that Sodium MRI can detect such abnormalities in focal epilepsy [3]. Sodium MRI has already revealed that patients with focal epilepsy have higher Total Sodium Concentration (TSC) levels compared to healthy controls and elevated Sodium in areas associated with seizure propagation [4]. TSC has previously been shown to be a marker of cell dysfunction [5]. It is unknown whether such abnormalities in TSC occur in generalized epilepsy. This project represents the first time that brain Sodium MRI will be conducted in patients with generalized epilepsy.

Primary Objective

To compare brain sodium concentration in patients with generalised epilepsy and controls.

Methods

10- 20 patients with generalized epilepsy and healthy controls will be scanned using 3T Sodium and proton MRI. This will generate pilot data on the levels and distribution of TSC within subjects' brains, which we can then be used to compare between the two groups.

Benefits

This study will help us to explore the utility of Sodium MRI as a biomarker for neurological dysfunction. By analysing the distribution of TSC within subjects brains it may also help us to identify an "epileptogenic zone" (where seizures are first propagated) in generalized epilepsy. This study may help explain why some patients with epilepsy respond better to sodium channel antiepileptic medicines compared to others. It could also help plan surgical intervention for patients with drug-resistant epilepsy.

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Does the use of trained lay workers improve Perinatal Mental Health Outcomes? – A mixed methods systematic review

Rachel Hill, Neil Nixon

Background

It is known that around 20% of women will experience mental health difficulties in the perinatal period. Due to demand in mental health services globally, there can be difficulties in women accessing resources. Furthermore, this can disproportionately affect women from disadvantaged backgrounds, resulting in worse outcomes for both mother and infant. Where there are difficulties in accessing mental health services, one solution may be to train lay health workers (often those from the communities they serve), to deliver psychological interventions to attempt to meet the demand for mental health care. This can also include doula support who work to provide practical and emotional support to the birthing person and their family. They provide continuous support throughout pregnancy, birth and the immediate postpartum period. There is a widely recognised impact of continuous support during birth, evidence has shown that those who are supported by a doula are less likely to require a Caesarean section, use pain medication and are more likely to feel satisfied with their birthing experience. This systematic review aims to analyse quantitative and qualitative papers that have investigated whether the use of lay support workers, including doulas, have improved perinatal mental health outcomes.

Methods

We have begun to draft a Medline search strategy using terms such as ‘perinatal’, ‘intrapartum’, ‘antepartum’, ‘postpartum’, ‘lay workers’, ‘peer support’, ‘doulas’

Draft exclusion criteria includes: Studies not written in English, does not address a specific perinatal mental health condition (can include antenatal depression, postpartum depression, OCD, post-partum pscychosis, OCD, PTSD). Has to be specific to the mother/birthing person (not including fathers/partners).

Results

Awaiting results

Conclusion

Awaiting conclusion

Delayed functional improvement may persist beyond 90 days following endovascular thrombectomy

Emma Soo, Permesh Dhillon, Sharron Moorby, Alexina Smalley, Samuel Adetunji, Robert Lenthall, Norman McChonachie, Nair Sujit, Malik Luqman, Robert Dineen

Background

Endovascular thrombectomy (EVT) has become the standard of care for large vessel occlusion in acute ischaemic stroke (AIS) [1]. However, only around 50% of patients achieve functional independence (modified Rankin Scale [mRS] score 0-2) at 90 days, despite successful recanalisation following EVT [2].

We proposed that functional improvement may occur beyond 90 days and aimed to study the incidence of improvement and functional independence at 6 months following EVT in AIS patients.

Methods

We assessed functional and safety outcomes using data collected by the local interventional radiology department. Individuals were dichotomised according to improvement in mRS scores from 90 days to 6 months. A secondary outcome measure was functional independence achieved at 6 months.

Functional independence was defined as mRS of 0 to 2. Those who were not functionally independent at 90 days but became functionally independent at 6 months were defined as having ultra-delayed functional independence. We compared groups using the Chi-squared test for binary variables and student's t-test for continuous variables. STATA software was used for statistical analysis.

Results

Among 329 patients who had a mRS score >0 at 90 days, 59 patients (17.9%) continued to improve at 6 months, while 270 (82.1%) did not improve. Lower age (OR= 0.974, CI [0.956 to 0.993], p=0.007) and having a thrombolysis in cerebral infarction (TICI) score of 2c-3 (OR= 1.96, CI [0.982 to 3.14], p=0.056) were predictors of improvement. Of the 216 individuals with a mRS score >2 at 90 days, 20 (9.26%) achieved functional independence at 6 months.

Conclusion

A lower age and having a TICI score of 2c-3 were predictors of continued improvement. Lower NIHSS on arrival and greater early neurological improvement were predictors of ultra-delayed functional independence. 59 patients had continued improvement, and 20 (33.9%) of these patients achieved ultra-delayed functional independence.

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Deprescribing in older adults with falls using the STOPPFall tool: A Quality Improvement Project

Ella Wooding, Anchal Gupta, Khansaa Talaat, Zareena Sa Khan, Thai Wong, Masud Tahir

Background

One of the most important modifiable risk factors associated with falling is the use of falls-risk inducing drugs (FRIDs). The World Falls Guidelines identified this as a key domain and recommended that a validated tool should be used in medication reviews targeted to falls prevention in older adults (Montero-Odasso et al., 2022).

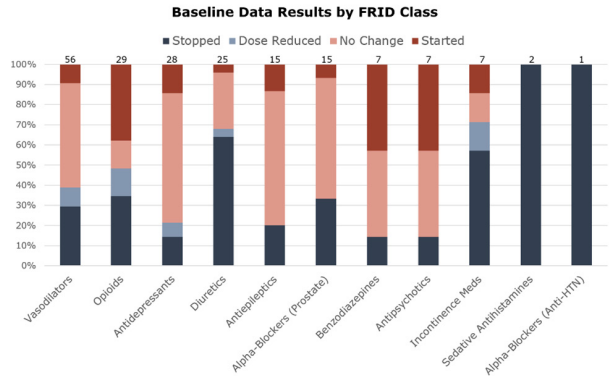
A proforma was created based on the STOPPFall Tool (Seppala, L. et al., 2021) to aid doctors in performing structured medication reviews in patients with falls. The research question was 'in older adults with falls, does use of the STOPPFall screening tool increase deprescribing of FRIDs?'

Methods

The project was carried out on HCOP (health care of older people) wards. Patients were included if they were HCOP inpatients and had been admitted with fall, had a history of recurrent falls or had an inpatient fall. FRID classes were identified using STOPPFall, and FRIDs prescribed on admission and discharge were determined using discharge letters. The primary outcome was the number of FRIDs stopped or dose reduced on discharge. An online survey assessed HCOP doctors confidence in deprescribing.

Results

102 patients were reviewed at baseline. A total of 162 FRIDs were prescribed on admission; 73 (45.1%) of these were stopped and 12 (7.4%) were dose reduced.



19 prescribers responded to the online survey, and self-assessment of confidence in deprescribing averaged at 7.74 (1-10 - 'not confident at all' to 'very confident'). The STOPPFall proforma is awaiting implementation, pending governance approval. Once introduced a further 100 patients will be reviewed to assess if deprescribing of FRIDs increases with use of the proforma.

Conclusion

52.5% of FRIDs prescribed in older adults with falls on HCOP wards were stopped or reduced. Introduction of a STOPPFall proforma is hoped to increase deprescribing of FRIDs in this patient group.

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