INSPIRE

SUMMER RESEARCH SCHOLARSHIPS SYMPOSIUM

1 MARCH 2023

1495 UNIVERSITY OF ABERDEEN

PROGRAMME

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ACKNOWLEDGEMENT

This abstract booklet contains an inspiring collection of abstracts from a diverse range of research projects carried out by summer research scholarship students both at the University of Aberdeen and at prestigious external Universities.

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PROF COLIN J LUMSDEN

INSPIRE LEAD

LEAD OF THE MBCHB

BLOOD MARKERS OF CEREBRAL VASOSPASM AFTER ANEURYSMAL SUBARACHNOID HAEMORRHAGE: A NARRATIVE REVIEW OF CURRENT LITERATURE

RABII ABOULHOSN

BACKGROUND

Cerebral vasospasm (CV) describes the delayed, transitory narrowing of cerebral arteries beginning after subarachnoid haemorrhage. It is a frequent manifestation following aneurysmal SAH (aSAH), identified in up to 70% of patients. Commonly, CV develops 3-4 days post-aneurysmal rupture and contributes to neurological decline by causing delayed cerebral ischemia and subsequently cerebral infarction, producing irreversible brain damage. Given its delayed onset and opportunities for prophylaxis, blood markers of CV have been sought to minimise neurological decline and associated morbidity. This review is aimed at understanding the blood markers of aSAH-induced CV and their implications in disease prognosis.

RECENT FINDINGS

Sodium, glucose, leukocytes, and CRP have been discussed in relation to aSAH-induced CV.

SODIUM

Hyponatremia represents the most common electrolyte disturbance following aSAH, emanating from a cerebral salt wasting syndrome and a syndrome of inappropriate anti-diuretic hormone secretion. In the setting of aSAH, there is an association between hyponatremia and occurrence of CV.

GLYCAEMIC INDICES

While hyperglycaemia predicts poor outcome after SAH, there is inconsistent results on the predictive hypo- and hyperglycaemia and the development and occurrence of CV post-aSAH.

LEUKOCYTES AND CRP

The post-aSAH course is associated with a robust systemic inflammatory response which contributes to neurological deterioration. Fundamentally, leucocytosis and elevated CRP are associated with CV occurrence. Regular monitoring of the inflammatory process could facilitate earlier diagnosis of CV.

CONCLUSION

CV post-aSAH continues to develop and contribute to morbidity and mortality. To date, there is no established panel of blood markers to predict CV. The studies exploring blood markers have utilised a retrospective approach of defined cohorts. Prospective studies are required to further explore the causality and temporal relations between blood markers and CV, in attempts of prompt diagnosis and intervention for CV.

SUPERVISOR: Mr Peter Bodkin

FUNDED BY: Innes Will Scholarship Programme

DISEASE ACTIVITY, COMORBIDITIES AND FUNCTIONAL STATUS PREDICT TREATMENT RESPONSE TO BIOLOGIC AND TARGETED SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN PSORIATIC ARTHRITIS

CHRISTINE ADDAE-KYEREME

BACKGROUND

Much discussion surrounds optimising treatment with biologic and targeted synthetic disease modifying anti-rheumatic drugs (bDMARDs/tsDMARDs) when treating psoriatic arthritis (PsA). This study aims to identify predictors of treatment response among PsA patients initiating bDMARD/tsDMARD treatment, focusing on disease activity, functional status (Health Assessment Questionnaire, HAQ), and comorbidities.

METHODS

Systematic review of clinical trials and observational studies used Medline, Embase and Cochrane databases. Eligible studies included full text papers with quantitative estimates of effect (or data to allow these to be computed). Papers also required a validated assessment of treatment response i.e., Minimal Disease Activity (MDA), or another marker of treatment response like treatment continuation.

RESULTS

From 2824 articles identified, 27 were included. These contained >15 different outcomes, measured at >10 different timepoints. There was consistent evidence to suggest that high disease activity, poor functional status, and the presence of comorbidities was associated with a reduction in treatment response.

For example, some demonstrated that patients with a high disease activity (DAS28 >3.2) experienced over a 90% reduction in the odds of MDA at 12 weeks. Each 1 unit increase in the HAQ disability index (a measure of poor function) decreased the odds of a good European League Against Rheumatism (EULAR) response at 3 months by up to 66%. The presence of baseline comorbidities lessened the odds of MDA at 6 months by up to 80%. Others reported that comorbidities were associated with a reduction in the odds of 5yr treatment persistence by up to 40%.

CONCLUSIONS

This review shows clear evidence of reduced bDMARD/tsDMARD response among PsA patients with higher disease activity, poorer function, and comorbidities. Clinicians should be aware of the reduced chances of treatment success and should consider early review of therapy, to consider whether treatment escalation or switching is required.

SUPERVISORS: Stephanie Lembke, Professor Gary J. Macfarlane, and Professor Gareth T. Jones

FUNDED BY: Institute of Applied Health Sciences under the Aberdeen Summer Research Scholarship (ASRS) Programme for medical students

EVALUATING STROKE CARE DURING THE COVID-19 PANDEMIC

AHMED HUSSAIN

BACKGROUND

The COVID-19 pandemic has impacted the delivery of healthcare in Scotland, as services rapidly adapted to face the additional challenges. This study aimed to evaluate how the pandemic impacted the patterns of stroke admission and severity in Grampian.

METHODS

This is a retrospective observational cohort study using data from the Scottish Stroke Care Audit (SSCA), hospital admissions from the Scottish Morbidity Record 01 (SMR01) and COVID-19 laboratory results from the 1st April 2015 to 31st October 2021. Patterns of stroke admission were evaluated during the height of the pandemic (April 2020 to March 2021) and compared to the previous year (April 2019 to March 2020). Chi-squared tests were used to compare categorical variables. Statistical significance was set at $p<0.05$. Data analysis was done using R version 4.2.1.

RESULTS

A total of 4,872 stroke events were examined. During the pandemic, stroke admissions from care homes decreased (6.2% to 3.6%, $p=0.032$) while admissions from acute hospitals increased (1.6% to 6.9%, $p<0.001$). In addition, more stroke patients during he pandemic were unable to walk unaided (43.6% to 62.1%, $p<0.001$) and unable to talk at initial stroke assessment (20.1% to 33.0%, $p<0.001$) than patients admitted pre-pandemic. Furthermore, stroke patients during the pandemic were more likely to present with a major loss of functionality (56.1% to 74.9%, $p<0.001$).

CONCLUSIONS

The decrease in care home admissions throughout the pandemic may be a result of early pandemic measures, such as social distancing and lockdown, lowering the detection of stroke symptoms. The increased severity of stroke presentation suggests patients may have waited for their symptoms to get worse before accessing health services.

FUTURE GOALS

Further analysis of patterns of stroke care during the pandemic will also be performed, examining variables related to acute stroke care, as well as the impact of the pandemic on mortality outcomes.

SUPERVISORS: Dr Mary-Joan Macleod, Professor Lesley Anderson and Dr Clarisse De Vries

FUNDED BY: INSPIRE national scholarship and the Industrial Centre for Artificial Intelligence Research in Digital Diagnostics (iCAIRD)

ADVERSE DRUG REACTIONS IN HOSPITALISED MULTIMORBID OLDER PEOPLE WITH AND WITHOUT DIABETES: FINDINGS FROM THE SENATOR TRIAL

ANAGHA CHINMAYEE

BACKGROUND

Adverse drug reactions (ADRs) are a major cause of morbidity and mortality, especially in older people. Older people with diabetes mellitus may be especially at higher risk of ADRs, however, this risk has not been well studied. This study aimed to compare the severity and type of ADRs in hospitalised, multimorbid older people with and without diabetes and secondly to assess the impact of ADRs on mortality, rehospitalisation and length of stay.

METHODS

Participants in the SENATOR (Software Engine for the Assessment and optimization of drug and non-drug Therapy in Older peRsons) trial were assessed for 12 common and 'other' prevalent and incident adverse drug reactions using a blinded end-point adjudication process. Descriptive analyses, logistic regression and mediation analyses were undertaken using SPSS.

RESULTS

Of 1537 people in the SENATOR trial, 540 (35.1%) had diabetes mellitus (mean age 77.4 ffl 7.3 years, 58.5% male). The median number of medications was significantly greater in people with diabetes (10 [8, 12] vs 9 [6, 11]; p<0.001), as was the number of co-morbidities (12 [8, 16] vs 9 [7, 13], p<0.001).

In the total population, 773 prevalent and 828 incident ADRs were reported. Both prevalent and incident symptomatic hypoglycaemia and incident acute kidney injury (AKI) were significantly more common in people with diabetes ($p<0.05$). People with diabetes had higher all-cause mortality at 12 weeks than those without (9.1% vs 6.3%, $p=0.04$). Mediation analysis revealed that mortality was significantly higher (OR = 1.43, Sobel test $p=0.048$) in people with diabetes and ADRs causing AKI.

CONCLUSIONS

Older multimorbid people with diabetes presenting to hospital with acute illness have significantly higher mortality that is mediated by medication-associated AKI and poorer renal function. Hence, exercising caution when prescribing nephrotoxic medication and deprescribing may provide an opportunity to reduce potentially fatal ADRs.

SUPERVISORS: Selvarani Subbarayan, Phyo Kyaw Myint and Roy L. Soiza

FUNDED BY: Innes Will scholarship, University of Aberdeen

ORAL HEALTH RELATED QUALITY OF LIFE IN HEAD AND NECK CANCER PATIENTS: A SYSTEMATIC REVIEW

CHELSEA COOK

BACKGROUND

Head and neck cancer (HNC) is the 6th most common cancer in the world. It includes cancers of the oral cavity, nasal cavity, larynx and pharynx. Treatment involves surgical resection, chemotherapy and/or radiotherapy and often includes a combination of therapies. The disease and its treatment can lead to devastating oral side effects, such as dry mouth, taste loss, discomfort whilst eating, difficulty swallowing, physical pain and psychological disability. The impact of the disease on the quality of life is such that HNC patient population has the highest suicide incidence compared to all other cancers. Oral health related quality of life (OHRQoL) evaluates a person's oral health well-being. Oral Health Impact Profile (OHIP) and Oral Impacts of Daily Performances (OIDP) are the most common questionnaires used to measure OHRQoL. Understanding a patient's OHRQoL can help clinicians to understand the impact of HNC therapy.

METHODS

A systematic search was conducted using the databases: Psych Info, Embase, Ovid Medline, Scopus and Web of Science. A well-defined search strategy and inclusion/exclusion criteria were used to identify relevant publications and a pre-defined data extraction form was used to gather information from the included studies.

RESULTS

Following the systematic screening process, 67 relevant articles were included in the study: 39 were identified during an initial search from the database inception until 2019. A more recent identical search (2020-2022) found 28 extra articles. The main themes identified included the relationship between OHRQoL and: 1. Risk factors, patient and tumour characteristics; 2. Treatment; 3. Side effects of HNC treatment and 4. General patient quality of life.

CONCLUSION

Our findings suggest that OHRQoL is a growing interest for HNC and is affected by a multitude of variables. Understanding the impact of HNC and its treatment, can result in treatment modification and facilitation of appropriate aftercare for patients.

SUPERVISORS: Dr Rasha Abu Eid, Dr Ekta Gupta & Dr Serena Sinclair

Funded by: Institute of Dentistry, INSPIRE scheme,
Academy of Medical Sciences

DO PATIENTS WITH RHEUMATIC DISEASES LIVING IN RURAL SETTINGS HAVE POORER OUTCOMES? RESULTS FROM AN EXTENDED SYSTEMATIC REVIEW OF THE LITERATURE

NAYAN DEY

BACKGROUND

Rheumatic disease is a major global health burden and refers to arthritis and other conditions that affect joints and tendons. Geographical access to healthcare is a significant factor in health outcomes and so the aim of this study is to update a previous review and assess whether rural location is associated with poorer patient outcomes for those living with rheumatic diseases.

METHODS

We conducted a search on MEDLINE, EMBASE, CINAHL, PsycINFO, Web of Science and Cochrane Library databases and looked for papers that were primary peer-reviewed, published in English or German, 20192022, focused on selected rheumatic diseases (rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (axSpA) or osteoarthritis (OA)), and quantified outcomes by a measure of rurality. All selected articles were synthesised narratively.

RESULTS

4 publications were eligible, including 4047 rural and 6063 urban patients. They reported outcomes in RA (2 studies) and axSpA (2 studies). The studies suggested that there was no significant difference in axSpA disease activity between rural and urban dwellers, however rural dwellers using biologics reported greater work impairment.

Rurality was also suggested to be associated with the development of adverse cardiovascular events (1.32 OR, 95% Cl: (1.03, 1.69)). In RA, the studies suggested no significant difference in mortality rates between rural and urban dwellers. However, educational attainment and income were potential confounders, but weren't considered by the studies.

CONCLUSION

Uncertainty remains on whether outcomes differ for patients with rheumatic disease in rural areas. Future studies should adjust for local area deprivation and consider the impact of contextual factors on healthcare resource uptake. This would allow the true extent of rural-urban health inequity to be observed and determine whether rurality is a surrogate marker for socioeconomic factors, as previously suggested.

SUPERVISORS: Dr. Rosemary J Hollick, Prof. Gary J Macfarlane

FUNDED BY: INSPIRE Aberdeen

EPIDEMIOLOGY AND MANAGEMENT OF EXTRACAPSULAR HIP FRACTURES: RESULTS FROM THE SCOTTISH HIP FRACTURE AUDIT

THOMAS DIFFLEY

BACKGROUND

Extracapsular Hip Fractures are a cause of considerable mortality and morbidity worldwide. Higher blood loss is associated with extracapsular hip fractures and there is still uncertainty in the optimum management of extracapsular hip fractures.

METHODS

Inclusion Criteria was all patients with an extracapsular hip fracture that presented to Aberdeen Royal Infirmary during 2017-2019. Ultimately only 500 of these cases were fully collected and analysed with a further 6 being excluded due to missing data. Descriptive Variables were recorded. Non-parametric statistical tests were used to determine the significance between variables. For ranked variables the Cochran-Armitage Test and ρ were used. If sample sizes were small Fisher's Exact Test was used.

RESULTS

494 patients were included, 68% Female, 336/158. 177 (36%) received an Intramedullary Nail and 317 (64%) a Dynamic Hip Screw.

There was a significant difference in 30-day mortality between Intramedullary Nails and Dynamic Hip Screws (Chi Squared Test – $\chi 2$ = 4.852, p = 0.0276, 95%CI 0.001-5.024). However, we found that was no longer significant at 60 days post-operatively ($\chi 2$ = 0.9237, p=0.3364).

We found that there was no trend associated between age group and increasing 30-day mortality risk (Cochran-Armitage Test: β – 9.48199, p=0.30328) or at 60-days (p=0.36784). There was also no Significant difference in 30-day mortality between fracture Types (p=0.7723)
We found that all Scottish Hip Care Standards reduced 30-day and 60-Day mortality except when patients were delayed to surgery past 36 hours (Chi Squared: $\chi 2 = 2.635$, p=0.10), ($\chi 2 = 3.080$, p=0.079). We also identified a significant trend between Age and Acute Length of Stay ($\rho = 0.9667$, $p<<0.001$).

CONCLUSIONS

The identified association of a higher 30-day mortality for intramedullary nail compared to DHS constructs is in keeping with other U.K. research. We provide further evidence that, where feasible, utilising DHS constructs likely provides a relative mortality benefit for hip fracture patients. Interestingly we found that patients delayed over 36 hours to surgery had no significant increase in mortality. As Such Discussions and further research must be done to evaluate the risk-benefit ratio of these patients.

SUPERVISORS: Luke Farrow

FUNDED BY: Inne's Will

OUTCOME DIFFERENCES BETWEEN PATIENTS WITH OR WITHOUT SEPSIS UNDERGOING EMERGENCY SURGERY ARE ATTENUATED BY FASTER TIME TO CARE MEASURES

NATTHAYA EIAMAMPAI

BACKGROUND

Emergency general surgery (laparotomy and laparoscopy; EmLap) is amongst the commonest surgeries with high sepsis prevalence and hence, poor outcomes. However, whether outcomes in patients requiring antibiotics for suspected infection are influenced by time taken to receive care is largely unexplored. This project aims to determine whether time to care influences the outcome differences (1) between EmLap patients with suspected infection versus those without and (2) only amongst those with suspected infection.

METHODS

Clinical information was obtained from the 2017-2018 Emergency Laparotomy and Laparoscopic Scottish Audit (ELLSA). Time to care referred to six temporal variables related to radiological investigation, anaesthetics triage, and surgical management. Outcome measures (mortality, readmission, hospital death, post-operative destination, length of stay (LoS)) were compared using adjusted and unadjusted regression analyses to determine whether the differences in outcomes could be explained by the faster or slower time to care for each of the six temporal variables.

RESULTS

Amongst 2243 EmLap patients (median age 65 years [IQR 51-75], sex 51.1% female), 892 (39.77%) received antibiotics for suspected infection. Although patients with suspected infection had faster time to care ($p \leq 0.001$ for all) and higher mortality rate (10.9%) compared to those who did not (6.5%), outcome differences were not statistically significant when the analysis accounted for time ($p > 0.05$ for all). Amongst those who received antibiotics only, every slower-than-median time to care contributed to increased LoS except time from computed tomography request to scan ($p < 0.05$ for all).

CONCLUSIONS

Worse outcomes associated with infection in EmLap patients were attenuated by faster time to care amongst patients with suspected infection and this may also provide additional benefit of shorter LOS in the same patient group.

SUPERVISORS: Professor Phyo K Myint and Dr Roy L Soiza

FUNDED BY: University of Aberdeen Innes Will Endowed Research Scholarship 2022

RECORDING OF DENTAL IMPLANTS PROVIDED IN NHS GRAMPIAN, FROM 1996 TO 2022

CHLOE HORSFALL

BACKGROUND

Dental Implants have been provided by NHS Grampian since 1996. Patient and dental implant details are recorded on a hard copy proforma and stored in a binder. The study aimed to ev aluate the current method of implant recording and create a more accessible electronic database for future implant dentistry recording which can serve as a core tool for service evaluation and clinical effectiveness trials. Such an electronic database is expected to increase comprehensiveness, resilience, and accessibility of clinical data in compliance with current clinical information governance standards.

METHODS

Following a literature review aimed at researching data recording within implant dentistry, and guidance from Restorative Dentistry consultants, the electronic database was developed in Microsoft Excel. Subsequently, all the information from the written records was entered into the electronic database. Results from the data collection were analysed and presented, highlighting any missing data before further investigation into complete clinical records to fill the gaps. The database contained the following information: patient details, date of pre-operative augmentation, implant placement date, implant model specifics, any augmentation at placement, final restoration & status if known.

RESULTS

In this study, 646 implants were identified placed from 1996 to 2022. An average of 17 implants were placed per year until 2016. The results showed an increasing number of implants placed in 2017 onwards, with the average increasing to 54 implants per annum. In 91% of cases, the consultant for the procedure was recorded. Findings showed that in 29% of cases, the site of the implant was not recorded. Site of implant placement was the detail most omitted. Lastly, in 2.5% of cases, no implant details were given.

CONCLUSIONS & IMPACT

This project disclosed the need for a computerised method of implant recording, which provided a more structured, comprehensive, and accessible record-keeping system. Although the written records were of a good standard, a small percentage of data was missing. It is recommended that there is staff training to introduce the electronic database and ensure consistent data entry. The electronic database will be a critical tool to enable clinical effectiveness programmes for evaluating failure rates, material usage and more. Through this study, we show how the electronic database will serve as a foundation for continuous quality improvement by making the implant placement recording process more streamlined. It will continue to positively impact patient care, improving the ability to check any implant details as needed.

SUPERVISORS: Dr Dean Barker and Dr Karolin Hijazi

FUNDED BY: INSPIRE Summer Scholarship Fund

THE ASSOCIATION OF CUMULATIVE BLOOD PRESSURE TRAJECTORIES WITH COGNITIVE DECLINE AND DEMENTIA USING THE ENGLISH LONGITUDINAL STUDY OF AGEING (ELSA) PROSPECTIVE COHORT

ISHA IQBAL

BACKGROUND

Due to the shortage of efficacious treatments for dementia, identifying modifiable risk factors which can potentially delay the onset of incident dementia is critical. Evidence has shown an association between elevated blood pressure (BP) and cognitive decline and incident dementia, however few studies have explored long-term effects of BP measurements, and their trajectories on these outcomes. Thus we aimed to investigate whether long-term BP trajectories are independently associated with subsequent cognitive decline and incident dementia diagnosis amongst cognitively healthy adults aged ≥50 years.

METHODS

This cohort study utilised data from the English Longitudinal Study of Ageing (ELSA), a large prospective cohort including participants aged ≥50 years in England. Data were used from wave 0 (1998) to wave 9 (2018). Cognitive decline and dementia were assessed from wave 4 (2008) to wave 9 (2018). Exclusion criteria was applied. Descriptive statistics considering baseline measurements were calculated. Work is currently in progress to determine BP trajectories and the link to dementia.

PROGRESS TO DATE

26,716 participants formed the total cohort. Following exclusion criteria, 2,418 cognitively healthy participants remained.

Participants without dementia had median age 58.0 years (IQR: 47.0–69.0 years), compared to 62.0 years (IQR: 50.0–74.0 years) for those with dementia (p=0.167). Men accounted for 42.5% of participants without dementia, compared to 23.8% of participants who did (p=0.085). Average systolic BP was 6.98mmHg lower for participants who had dementia compared to those without (95% CI -20.23, 6.27; p=0.302). Average diastolic BP was 3.74mmHg lower for those who had dementia compared to those without (95% CI -12.62, 5.14; p=0.408). The mean blood glycated haemoglobin level was 0.4% lower for participants without dementia, compared to those with (95% CI 4.9, 6.3; p=0.077).

EXPECTED OUTCOME

We hypothesise that BP trajectories are associated with risk of incident cognitive decline and dementia.

SUPERVISORS: Professor Phyo Myint, Dr Ben Carter, Dr Tiberiu Pana and Miss Zahra Pasdar

FUNDED BY: Flora Gow Murray Neuroscience Scholarship

PRESENCE OF TRANSCRIPTS CODING FOR PROTEINS TARGETED BY AECAS IN SYSTEMIC VASCULITIDES IN THE HCMEC/D3 CELL LINE

SONA JESENAKOVA

BACKGROUND

The presence of anti-endothelial cell antibodies (AECAs) has been documented in a wide variety of systemic vasculitides. Furthermore, many different antigenic molecules targeted by AECAs in these diseases have been identified. AECAs could bind to endothelial cells (ECs) lining blood vessels and potentially trigger pathophysiological processes. However, this remains controversial. Thus, our aim is to establish the presence or absence of transcripts of these different antigenic molecules, which were identified in previous literature, in an immortalised human brain microvascular endothelial cell line (hCMEC/d3), with a view to establish an assay for AECAs in patient samples.

METHODS

First, hCMEC/d3 were cultured in the endothelial cell growth medium (ECGM2) at 37°C in 5% CO2. Subsequently, ECs were either harvested for RNA purification or split and grown until confluence to undergo cell treatments with recombinant human cytokines or heat followed by RNA purification. The purified RNA was utilised for cDNA synthesis which was used as a template for the reverse transcription polymerase chain reaction (rtPCR), where 15 different previously designed primer pairs were used. The amplicons were visualised by agarose gel electrophoresis.

PROGRESS TO DATE

To date, we have successfully designed 15 primer pairs and optimised their rtPCR conditions. Furthermore, we determined which of the transcripts encoding the sought-after AECA targets were present in the untreated hCMEC/d3. Once the cell cultures are treated with their respective cytokine/heat treatments, it will be determined if the amplification of the investigated transcripts differs from the untreated cells.

EXPECTED RESULTS

Establishing the presence or absence of investigated transcripts in the hCMEC/d3 cell line will contribute to the development of an assay for AECAs in vasculitis patients in a reproducible manner. Furthermore, establishing the differences in transcription induced by different treatments administered to cells might potentially unveil the roles different cytokines play in vasculitides.

SUPERVISORS: Dr Euan W. Baxter, Dr James I. Robinson, Professor Ann W. Morgan

FUNDED BY: INSPIRE Centre of Excellence Scholarship

THE PREVALENCE OF ENT SYMPTOMS FOLLOWING COVID-19 INFECTION – A SYSTEMATIC REVIEW

NADA JODEH

BACKGROUND

It has already been 3 years since SARS CoV-2 appeared, and though the numbers and case severities have reduced, its impacts still remain. There is growing evidence of symptoms persisting weeks or even months after an acute infection. The persistence of symptoms 12 weeks after an infection is defined as Long Covid by the NHS. This systematic review sets out to collate and bring forward the most prevalent ENT symptoms people may experience following COVID-19 Infection. It also aims to present the reader with mentioned interventions that could treat or even prevent these symptoms.

METHOD

Systematic review searches, following the PRISMA protocol, were performed from inception up to the 1st of September 2022 in the following databases: Medline, PubMed, Cochrane Library and Embase. Search terms included 'COVID-19' or 'Long COVID' or 'Post Covid' combined with 'ENT' or 'ENT symptoms'. Articles were screened against the inclusion and exclusion criteria which were that the articles must be following a COVID-19 infection and be about ENT symptoms. All types of articles were accepted including systematic reviews, randomised controlled trials and case reports.

PROGRESS TO DATE

Systematic searches returned 330 studies and 97 remained after abstract screening. Full text screening resulted in a pool of 43 included articles which were data extracted and analysed. The analysis showed that the most frequently occurring symptom following COVID-19 infection, amongst the articles, was olfactory disturbance which could be partial or complete. Other symptoms include taste disturbance, sensorineural hearing loss, fatigue, psychological disorders namely depression and cognitive disorders like poor memory and mental clouding.

EXPECTED OUTCOME

This project is in the process of being further expanded; I am searching additional databases like CINAHL, Scopus, Web of Science and I am also extracting and analysing further criteria from the articles. It is expected the study will conclude that the major ENT symptom people with Long Covid experience is olfactory disturbance. Currently, there is no consensus regarding the most effective treatment. The combination of Olfactory Training, systemic steroids and nasal irrigation with a mixture of different substances (Betamethasone, Ambroxol and Rinazina) seem to cause the most significant improvement in olfactory disturbance. However more work is needed in the form of randomised trials to deem the most appropriate treatment.

SUPERVISOR: Professor Ah-See

FUNDED BY: Innes Will Scholarship, Development Trust

GROWING FOREBRAIN ASSEMBLOIDS WITH INTEGRATED MICROGLIA

MOHAMMAD MOIZ KHAN

BACKGROUND

An organoid is a small three-dimensional tissue culture that replicates the specialized tissue of an organ. They are grown using induced pluripotent stem cells. They are useful research tools as they could be controlled to replicate organ pathology. Assembloids are the term for when organoids unite and interact with one another. For this research, forebrain organoids are grown.

There are microglia in the brain which can contribute to many pathologies; especially those involving neuroinflammation. When growing organoids however, microglia are not present. This is because microglia are mesodermal in origin whereas the brain is ectodermal in origin. This makes it difficult to accurately replicate the brain and its pathophysiology.

This research project aims to use different techniques to introduce microglia to forebrain organoids. Fully understanding microglia framework in the brain could lead to a new understanding of the neuroinflammatory component in many diseases and disorders, such as Alzheimer's disease.

METHODS

One technique is to grow the microglia and the organoids in parallel and then introduce the microglia to the organoids for coculture. While this has seen some success, it is difficult and expensive to replicate. Instead, we have tried to grow microglia progenitors, and integrate them into the organoids.

The progenitors would eventually differentiate into microglia, allowing the creation of an assembloid with an accurate microglia framework that is easy to replicate. After growth, the organoids are frozen, sectioned, and immunostained using microglia markers such as IBA1. They are then imaged, examined, and analysed.

PROGRESS TO DATE

The introduction of microglia progenitors in forebrain organoids has been encouraging. With histochemical analysis, there has been some evidence of microglia within the forebrain organoids.

EXPECTED OUTCOME

We expect to grow forebrain assembloids with an extensive and accurate microglia framework. These can then be used for testing and experimentation.

SUPERVISORS: Dr. Daniel Berg, Muhammad Zaman Assir

FUNDED BY: Aberdeen Summer Research Scholarship

CADAVERIC STUDY OF THE MEDIAL BRANCHES OF THE LUMBAR DORSAL RAMI AND THEIR RETRIEVAL FOR FURTHER HISTOLOGY STUDY IN THE CONTEXT OF LOWER BACK PAIN AND RADIOFREQUENCY THERMAL ABLATION

MONIKA MIKALAUSKAITE

BACKGROUND

Facet joint degeneration is a major source of lower back pain. These joints receive dual innervation from the medial branches (MBs) of the dorsal rami. Proximal part of the MBs is targeted for thermal ablation by the radiofrequency (RF) treatment for pain relief. This procedure usually gives only a temporary relief (9-18 months). The morphology of MBs have not been described. Establishment of morphology and course is essential to evaluate whether adequate thermal RF has been used in therapy.

METHODS

Twelfth thoracic and all lumbar dorsal rami were dissected in two phenol-embalmed male cadavers. Note was taken of the number of branches, pattern and course of the primary dorsal rami with particular attention to MBs. Each MB was traced to the origin of facet joints and multifidus muscle. Proximal roots of the MBs were excised and preserved for histological studies.

RESULTS

T12-L5 dorsal rami gave off MBs within intervertebral foramen. MBs then followed the lateral neck of superior articular process. They travelled deep to the intertransversarii mediales muscle. MBs reached mamillo-accessory notch by following the anterior half of the neck laterally.

Branches passed under the mamillo-accessory ligament (MAL) on the posterior margin of the superior articular process. The average length of the proximal MB root – between intervertebral foramen and MAL - was 15 mm. MBs branched into small nerves carrying sensory and motor fibers to supply superior and inferior facet joints and multifidus muscle. The origin of MB branching varied – occurring either before or after the MAL, though they all travelled under MAL in one bundle. The excised MB samples were the middle 5mm of the proximal root.

CONCLUSIONS

Anatomical course of MBs observed in this study is consistent with published literature. We aim to proceed with histological study of MBs to describe their size, a number of nerve fibers and myelination.

SUPERVISORS: Regius Professor Simon Parson

FUNDED BY: SurgAnat Scholarship

IMPACT OF COVID-19 ON THE WAITING TIME INTERVAL BETWEEN MULTIDISCIPLINARY TEAM MEETING AND TREATMENT IN NEURO-ONCOLOGY PATIENTS

KAI NEWTON

BACKGROUND

Brain tumours are the second leading cause of death from neurological disease in the UK. Multidisciplinary team (MDT) meetings is an important part of many neuro-oncology patient care. There is limited evidence regarding the effect that waiting times between MDT meetings in neuro-oncology patients and the commencement of treatment has on survival rate of patients. The objective of this study was to compare the waiting times between MDT meetings and 1-year survival before the COVID-19 pandemic lockdown in the UK and after.

METHODS

The data that was used to conduct this study was a database on Microsoft Access containing 1174 neurooncology patients offered by Barts Health NHS Trust on the diagnosis, treatment and follow up of neurooncology patients.

RESULTS

Waiting times for surgical intervention after MDT meetings before COVID-19 lockdowns versus during and after COVID-19 lockdowns was 24 days versus -10 days, respectively ($p<0.001$). The 1-year survival rate for patients that had surgical intervention before COVID-19 lockdowns versus during and after COVID-19 lockdowns was 47% versus 92%, respectively ($p<0.001$).

Waiting times for radiotherapy intervention after MDT meetings before COVID-19 lockdowns versus during and after COVID-19 lockdowns was 144 days versus 1 day, respectively ($p<0.001$). The 1-year survival rate for patients that had radiotherapy intervention before COVID-19 lockdowns versus during and after COVID-19 lockdowns was 51% versus 87%, respectively ($p<0.001$). Waiting times for chemotherapy intervention after MDT meetings before COVID-19 lockdowns versus during and after COVID-19 lockdowns was 75 days versus 0 days, respectively ($p<0.001$). The 1-year survival rate for patients that had chemotherapy intervention before COVID-19 lockdowns versus during and after COVID-19 lockdowns was 41% versus 89%, respectively ($p<0.001$).

CONCLUSIONS

The results of this study illustrates that to improve patient survival for neuro-oncology patients requiring treatment that the waiting times between MDT meeting and treatment should be reduced into improve patient outcomes.

SUPERVISORS: Professor Edward McKintosh & Mr Paolo Jose Deluna

FUNDED BY: INSPIRE

TRENDS IN DIETARY FIBRE INTAKE IN A US POPULATION OVER 10 YEARS (2011-2020)

ERIN O'BREE

BACKGROUND

Fibre is an essential component of our diets, contributing to metabolic health, appetite regulation and risk reduction in cardiovascular disease, gastrointestinal pathologies, and cancerous pathways. Data on current dietary intake is important to support policy making. The Dietary Guidelines for Americans recommend adults eat 28 to 34 g of fibre per day. Data was collated from the National Health and Nutrition Examination Survey, a longitudinal study that assesses the health and nutrition status of adults and children in the United States.

METHODS

45.4% (20633/45462) of the participants surveyed in NHANES were over the age of 18 and had valid data (figures for day 1 and day 2 of the food diary) for dietary fibre intake. Analysis was carried out using SPSS software version 28.

RESULTS

Over the 10-year period, one-way ANOVA revealed that there was a statistically significant difference in fibre intake between the years the survey was performed ($F(3,20629)=19.919$, $p<0.001$). Analysis of mean and median values for fibre intake shows a decline in fibre intake. Men consume a mean fibre intake of 18.4 g (95% CI 18.20-18.60) and women consume a mean fibre intake of 15.25 g (95% CI 15.10-15.40). There is a statistically significant difference in fibre intake between men and women ($F(1, 5621) = 68.784$, $p<0.001$).

When comparing ethnicity, non-Hispanic black individuals consume the lowest amount of fibre at 14.25 g/day (95% CI 14.03-14.47) and Mexican American individuals consume the highest amount of fibre at 20.16 g/day (95% CI 19.77 to 20.56).

CONCLUSIONS

From 2011 to 2020, adults in the US did not meet the daily fibre dietary recommendations and intake is decreasing.

SUPERVISORS: Professor Phyo Myint and Professor Alexandra Johnstone

FUNDED BY: INSPIRE National Summer Research Scholarship Programme

RESEARCH AND CLINICAL APPLICATIONS OF RAMAN SPECTROSCOPY IN LUNG CANCER

SAOIRSE PAGEL

BACKGROUND

Lung cancer is one of the most commonly diagnosed malignancies and leading causes of cancerrelated deaths worldwide. An estimated 2.2 million new cases and 1.8 million deaths were recorded in 2020. The five-year survival rate is poor for all stages of lung cancer at 17%. This is linked to two-thirds of patients being diagnosed at a late stage that is currently not amenable to curative treatment. Poor prognostics and diagnostic challenges have prompted researchers to explore alternative approaches for diagnosing and treating lung malignancies with high sensitivity, specificity and accuracy. Raman spectroscopy is a powerful analytical methodology that can characterise biological specimens at high spatial resolution in a non-invasive manner. It is one of the most promising alternative approaches as the spectra are sensitive to subtle biochemical changes. These can be seen in the very early stages of malignant transformation, facilitating the classification and staging of tumours to guide precision medicine and improve prognostics. This review aims to synthesise the current research carried out on ex-vivo models and identify the potential for in-vivo use in clinical settings.

METHODS

Using PubMed Central and ResearchGate, 78 original research papers were compiled and reviewed by two authors. Thematic analysis identified four potential areas of interest from these papers as follows: 1) detection and diagnosis of lung cancer, 2) subtypes and predicting patient outcomes, 3) monitoring treatment response and 4) clinical applications.

PROGRESS TO DATE

Using the themes identified, the research and clinical applications of Raman spectroscopy and imaging in lung cancer have been compiled. All papers have been included to date focusing particularly on how exvivo studies in research can be brought in-vivo in clinical settings. At the time of submission, the synthesis of these papers is still in progress.

EXPCTED OUTCOME

Synthesis of research and data from papers are ongoing and intended for publication in a scientific journal. The target journal identified is the Journal of Thoracic Oncology.

SUPERVISOR: Professor Valerie Speirs

FUNDED BY: Cyril & Margaret Gates Trust

MAPPING THE METABOLIC EVENTS THAT ACCOMPANY THE PROGRESSION OF COLON CANCER

NAIN TARA RAJA

BACKGROUND

Colorectal cancer is the third most common cancer in the world. There are three major pathways in genetic instability of colorectal cancer - microsatellite instability (CIN), chromosomal instability (MSI) and CpG island methylator phenotype (CIMP) pathways. The risk of developing colorectal cancer is also associated with increased obesity and metabolic disease. This project investigated the metabolic events that accompany the progression of colon cancer, and in particular how diet may interact with colon cancer.

METHODS

Publicly available repositories including Metabolites and Metabolomics Workbench were used. Studies were split into animal, in vitro (cell culture) and human studies (separated into analysis of tumor itself or biofluids). The metabolites found across the literature search were mapped onto metabolic pathways using MetaboAnalyst and the pathway mapping tool within the software. The following metabolites with $p<0.05$ following the false discovery rate correction were identified: Aminoacyl-tRNA biosynthesis (p= 1.05E-06), Arginine biosynthesis (p=7.12E-05), Alanine, aspartate and glutamate metabolism (p=0.001625), Glutathione metabolism (p=0.006816), Taurine and hypotaurine metabolism (p=0.009028), Glyoxylate and dicarboxylate metabolism (p=0.015083), Arginine and proline metabolism (p=0.015083), Glycerophospholipids metabolism (p=0.031011), beta-Alanine metabolism (p=0.038887),

Glycine, serine and threonine metabolism (p=0.038887), Cysteine and methionine metabolism (p=0.038887), Valine, leucine and isoleucine biosynthesis (p=0.038887) and Ascorbate and aldarate metabolism (p=0.038887).

RESULTS

There were 16 studies, of these 9 were human studies, 2 were animal studies and 5 in vitro studies. For the human studies, 1 analyzed tumor samples, 1 analyzed biofluids, 8 analyzed fecal, serum and colonic mucosal samples and for the rest, data was not available.

CONCLUSIONS

These results emphasize the utility of using untargeted metabolomics to reveal susceptibility and resistance and integrated analysis reveals pathways that are likely to be universal targets for intervention.

SUPERVISOR: Professor Jules Griffin

FUNDED BY: Rowett Institute under the Aberdeen Summer Research Scholarship (ASRS) Programme

SCOPING REVIEW: STORYTELLING, ETHNIC MINORITIES, AND POSTCOLONIAL EQUITY IN CANCER CARE

MX LOUIS J RUDDY, MA (OXON)

BACKGROUND

Ethnic minorities experience a greater burden of disease from cancer versus non-Hispanic Whites. This situation is exacerbated by clinical trials, in their design and outreach, historically failing to recruit underserved populations. Consequently, one theory for creating equity in cancer care is to modify the method of communicating with ethnic minorities. A common medium is "storytelling", whereby a narrative referencing cultural nuance and social hierarchy is utilised to communicate the importance of cancer care.

METHODS

We used grounded theory from a starting question of "What are the effects of storytelling on the cancer care journey for ethnic minorities as determined by changes in attitudes, knowledge, and behaviour (AKB)?". For the review, we conducted a systematic search of literature through Scopus in Embase (1974 to 2022/Aug/04), Ovid Medline (1946 to July Week 5 2022), and APA PsychInfo (1806 to July Week 4 2022) databases. After deduplication, 1182 articles were screened in titles and abstracts for inclusion in the review, 56 papers were identified based on inclusion criteria (English language and intervention type), and 53 of those articles were retrieved for analysis with a SPIDER framework for data extraction.

RESULTS

Typically, studies had small sample sizes which impacted statistical power. Data was mostly qualitative even if the process of aggregation was quantitative and systematic. There were problems of selection bias, lack of control groups, and Western-dominant research. However, there was a trend of benefit from storytelling interventions for participants as determined by modification to AKB regarding cancer.

CONCLUSIONS

For the effect of encouraging engagement with healthcare, storytelling offers the opportunity to implement interventions for ethnic minorities delivered by representatives of their respective communities. Thus, a pathway for decolonising Western medicine has been instantiated.

SUPERVISORS: Dr Sara MacLennan & Sheela Tripathee

FUNDED BY: ASRS

ASSESSING THE RISK OF PRETERM BIRTHS FOLLOWING UPTAKE OF THE HUMAN PAPILLOMAVIRUS VACCINE

ANSU MARI SAJI

BACKGROUND

Cervical cancer rates in England decreased by 87% in women in their 20s; offered the vaccine aged 12-13 years. The risk reduction for cervical intraepithelial neoplasia (CIN) grade 3 was 97% in the same cohort. CIN is associated with a greater risk of preterm birth. Our objective was to assess the risk of preterm birth following the uptake of the human papillomavirus (HPV) vaccine by linking routinely recorded perinatal data with HPV vaccination data.

METHOD

Web searches of National Ministries of Health and Department of Public Health were conducted for World Health Organization's (WHO) 194 member states. HPV vaccination data was extracted. Extracted data was validated against WHO's database on Status of HPV Vaccine Introduction. Estimated preterm birth rates from 2000 and 2014 were extracted from WHO's Global Preterm Birth Estimates. Extracted data was coded and analysed using Excel.

RESULTS

Countries with a gender-neutral complete national immunisation programme included mainly developed North American and European nations. Average predicted preterm birth rate in 2014 decreased by 0.3% with a national immunisation programme compared to those without. No conclusions could be drawn on the overall change in predicted preterm birth rate from 2000 to 2014.

Since 2010, Sub-Saharan Africa, Northern Africa and North America has had the highest preterm birth rates which may correlate with the lack of immunisation programmes. The lowest rates were seen in Europe. Preterm birth rate remained high in North America implying the contribution of confounding factors.

CONCLUSION

National immunisation programmes were associated with decreased average predicted preterm birth rate. The potential pathophysiological role of HPV infection in preterm birth needs to be explored. Coordinated action across global partners is required to close the vaccine equity gap.

SUPERVISORS: Dr Sohinee Bhattacharya, Professor Margaret Cruickshank, Dr Andrea Woolner

FUNDED BY: Carnegie Trust for the Universities of Scotland

INVESTIGATION OF THE CYTOTOXIC EFFECTS OF THREE COMMENSAL GUT BACTERIA GROWN ON DIFFERENT DIETARY FIBRES

DANIEL SESCU

BACKGROUND

The role of the gut microbiota in improving therapeutic outcomes in pelvic cancer patients is of clinical importance. Gut microbiota supplemented with dietary fibre can result in production of therapeutically advantageous metabolites, with anti-tumoural and radiosensiting properties. In this study, we aimed to investigate the impact of dietary fibre supplementation on the growth of commensal bacteria and the effect of the bacterial extracts on the viability and colony formation in bladder (RT112) and colorectal (Caco-2) cancer cells.

METHODS

Bacterial strains: Eubacterium eligens, Faecalibacterium prausnitzii and Roseburia intestinalis: were grown in YCFA medium supplemented with inulin, apple pectin, psyllium, basal or glucose and their growth measured spectrophotometrically at 600 nm for 48 h. Caco-2 and RT112 cells were treated with extract from E. eligens grown in apple pectin and the effect on cell viability at concentrations of 0 – 50% was measured using the MTT assay. Regarding colony formation, RT112 cells were irradiated with 0 – 8Gy to determine their survival after exposure to radiation. Data were analysed using Excel and GraphPad Prism 5.0

RESULTS

Growth of E. eligens in apple pectin was significantly higher than in psyllium and inulin. No significant growth was seen for F.prausnitzii and R.intestinalis in the five media. Viability of RT112 and Caco-2 cells was inversely proportional to extract concentration. Cell viability was significantly reduced in RT112 ($p=0.0137$) and Caco-2 ($p=0.083$) cells after 24 and 48 h of treatment with bacterial extracts (≥25%) compared to controls. Colony formation in RT112 cells was inhibited significantly by increasing doses of radiation but there was insufficient time to study effects of extracts.

CONCLUSIONS

E.eligens, F.prausnitzii and R.intestinalis grew at different rates in inulin, apple pectin and psyllium media. E.eligens grew better when supplemented with apple pectin and showed cytotoxic effects on colorectal and bladder cancer cells at higher concentrations.

SUPERVISORS: Professor Anne E Kiltie and Dr Aliu Moomin

FUNDED BY: The Innes Will Trust, Endowed Scholarship

DIGITAL ANALYSIS OF THE TUMOUR STROMA RATIO IN ER+ BREAST CANCER AND BRIEF OVERVIEW OF THE IMMUNE MICROENVIRONMENT.

NANNA SIVAMANOHARAN

BACKGROUND

Growing evidence has highlighted the importance of the tumour microenvironment in tumour progression. The tumour stroma has been identified as a key driver in tumour progression, however indicators of tumour stroma ratio have not yet been integrated into routine clinical practice.

METHODS

Haematoxlin & Eosin stained images were provided from the Breast Cancer Now Tissue Bank and the Grampian Biorepository. All images were scanned at 20x magnification and quality checked by another scientist to ensure all regions were in focus prior to analysis. Digital analyses were performed using QuPath, an open source software. Training areas were selected to segment tumour epithelium and stroma whilst adipose tissue was ignored. This algorithm was applied to all the samples and data output provided the area of tumour epithelium and stroma separately in μm^2. In parallel, literature on the stromal microenvironment, in particular the role of immune cells was reviewed.

RESULTS

The optimal cut off tumour stroma ratio value is yet to be calculated as there are a few more samples yet to be analysed. Subsequently, Kaplan-Meier survival curves using each individuals clinical outcomes along with the tumour stroma ratio value will be calculated. The review literature reviewed 48 articles to date and the findings have characterised ER+ breast cancer to have a low tumour infiltrating lymphocytes and an increased recruitment of immunosuppressive cells. The role of tumour associated macrophages has shown to potentially be the culprit for T-cell and neutrophil exclusion in the tumour microenvironment.

CONCLUSIONS

Tumour stroma ratio has previously proven to be a predicator for 5-year disease free survival in breast cancer with worse survival outcome pointing to low tumour stroma ratio. From the literature review it appears that the immune microenvironment of ER+ breast cancer, can be reprogrammed using oncolytic virotherapy or monoclonal antibodies to respond to immune checkpoint inhibitors.

SUPERVISORS: Professor Valerie Speirs

FUNDED BY: INSPIRE

UNDERSTANDING THE CELLULAR CONSEQUENCES OF NEK1 MUTATION IN MOTOR NEURON DISEASE (MND)

DANAH SLEIBI

BACKGROUND

Amyotrophic Lateral Sclerosis (ALS) is a progressive and fatal neurodegenerative disease, leading to muscle weakness and paralysis and eventually death within 2-5 years after diagnosis due to respiratory failure. Many genes have been associated with ALS including a recently associated gene, never in mitosis A (NIMA)related kinase 1 (NEK1), a serine/threonine kinase which plays a key role in several cellular functions, including DNA damage response and regulation of the cell cycle. Whole-exome sequence studies have shown NEK1 loss of function variants, in particular the p.Arg261His missense variant to cause an increased risk and disease susceptibility for ALS. This study aims to understand the resulting neuropathological phenotypes associated with NEK1 mutations in ALS.

METHODS

Our cohort included three Scottish patients with a mutation in the NEK1 gene, including one individual with the p.Arg261His missense variant, who went to develop ALS. We evaluated the distribution and cellular expression of NEK1 and TDP-43, the pathological hallmark seen in most ALS cases at post-mortem, in the Amygdala and Motor Cortex of these NEK1-ALS cases compared to age and sex matched control tissue. Following this, we quantitatively evaluated the spatial distribution of NEK1 mRNA molecules using BaseScope in situ hybridization (ISH).

RESULTS

Using immunohistochemistry, we demonstrated pathological pTDP-43 cytoplasmic aggregates in all three NEK1-ALS cases. Increased pTDP-43 aggregation negatively correlated with survival, albeit in a small sample size. NEK1 immunostaining revealed no immunoreactivity in two of the NEK1-ALS cases, indicating a loss of function, a finding that corresponded to reduction in NEK1 mRNA detected by ISH. However, the p.Arg261His missense mutation increased mRNA molecules and abundant NEK1-positive aggregates, with the same morphologic appearance as the pTDP-43 aggregates in this case.

CONCLUSION

Our results indicate TDP-43 pathology is present in these cases and that the p.Arg261His mutation results in co-aggregation of NEK1 protein with cytoplasmic pTDP-43 aggregates, a novel pathological feature of NEK1-ALS.

SUPERVISOR: Dr Jenna Gregory

FUNDED BY: Institute of Medical Sciences

THE EFFECTS OF BISPHENOL A ON BREAST CARCINOGENESIS

SHREEJA TRIPATHI

BACKGROUND

Breast cancer accounts for around 11,500 deaths per year and is the fourth most common cause of cancer death in the UK. An intricate mix of risk factors leads to breast cancer development, including nonmodifiable factors such as age, genetics, and modifiable factors relating to a person's lifestyle choices. The breast microenvironment is a complex ecosystem containing various cell types, including fibroblasts, adipocytes, and immune cells such as macrophages, mast cells and T cells. Endocrine-disrupting chemicals can disturb the cellular components of the breast microenvironment and contribute to breast carcinogenesis. One of these is Bisphenol A (BPA), a chemical polymer that is found in polycarbonate plastics and epoxy resins and is classified as an Endocrine Disrupting Chemical (EDC). This literature review aimed to collate evidence from studies published from 2000-present date to determine the effects of BPA on each cellular component of the breast stromal microenvironment and how this might contribute to breast carcinogenesis.

METHODS

An initial general review was carried out by studying existing literature, to study the effect of BPA on breast cancer development. Medline, PubMed, and cross-references were searched to identify papers which described the nature and effects of BPA on cells found within the breast stromal microenvironment, namely: epithelial, myoepithelial, fibroblasts, adipocytes and, immune cells. Papers were selected for further analysis based on their editorial quality and presence of scientific rigour with an unbiased manner of presenting results.

PROGRESS TO DATE AND EXPECTED OUTCOME

Eighty papers were reviewed and cross-referenced resulting in an initial draft. BPA altered normal cellular signalling mechanisms of fibroblasts, adipocytes, and epithelial cells within the breast microenvironment, ultimately contributing to tumorigenesis. However, studies investigating the effects of BPA on immune cells were lacking. More edits are planned with the goal of publishing the paper in a peer-reviewed scientific journal.

SUPERVISOR: Professor Valerie Speirs (Chair in Molecular Oncology)

FUNDED BY: Cyril Margaret Gates Charitable Trust

GUIDANCE FOR THE INDEPENDENT ADJUDICATION OF CLINICAL EVENTS

CHRISTOPHER WALKER

BACKGROUND

Independent adjudication is a process whereby clinical trial data are assessed by independent experts. This can reduce bias and preserve clinical trial quality. The Medical Research Council Clinical Trials Unit (MRC CTU) at UCL conducts internationally important studies focussed on infectious diseases and cancer. While adjudication is commonly used in these studies, there is no standard approach. Therefore, this project aimed to provide members of the MRC CTU at UCL with guidance for the independent adjudication of clinical events.

METHODS

The guidance was based on the experience of adjudication in four clinical trials undertaken by the MRC CTU at UCL. Documentation concerning each trial's adjudication process was reviewed and semi-structured interviews were conducted with members of each trial team.

RESULTS

We found that there were five important factors to consider when implementing independent adjudication. These included subjectivity of the clinical event, selection of adjudicators, adjudication meetings, selection of clinical events and blinding. The number of experts selected to conduct the adjudication process would usually depend on the subjectivity of the clinical event and the anticipated resource burden. Meetings can be required when there are multiple experts conducting the adjudication process.

The format and frequency of these meetings would normally depend on the availability of those involved and the level of contention in the adjudicated events. The selection of events for adjudication can influence the allocation of resources and the potential for bias. To protect against detection bias, independent experts should review clinical data blind to treatment allocation when this is possible.

CONCLUSIONS

The process of adjudication can depend on the nature of the clinical event, the potential for bias and the resource requirements. This document will provide guidance to members of the MRC CTU at UCL who are considering the use of independent adjudication in a clinical trial.

SUPERVISORS: Professor Sheena McCormack, Professor Sarah Meredith and Dr Peter Godolphin

FUNDED BY: INSPIRE Centre of Excellence Scholarship

ANTICHOLINERGIC BURDEN FROM MEDICATIONS WORSENS OUTCOMES IN THE SENATOR (SOFTWARE ENGINE FOR THE ASSESSMENT AND OPTIMISATION OF DRUG AND NON-DRUG THERAPY IN OLDER PERSONS) TRIAL

MAN CHUN WONG

BACKGROUND

Whilst the impact of anticholinergic burden (ACB) from medications are well documented, there remains doubt on how best to measure it.

METHODS

Using data from the SENATOR trial (https://clinicaltrials.gov/ct2/show/NCT02097654), ACB was calculated from medications at baseline using 10 most commonly known scales. The primary outcomes were length of stay (LOS), all-cause mortality within 12 weeks of randomisation, and rehospitalisation within 12 weeks of discharge. LOS was dichotomised as short (0-5) and long LOS (≥6) using median LOS (6 days) as cut-off point. ACB scores for each scale were categorised into ACB=0, ACB=1-2, ACB≥3. Logistic regression models for each outcome were constructed. Model 1 adjusted for age and sex. Model 2 as in Model 1 plus Cumulative Illness Rating Scale-Geriatric score, Barthel Index, Mini-Mental State Examination, and fall(s) in the previous 12 months. Model 3 adjusted as in Model 2 plus number of medications. Model 4 adjusted as in Model 3 plus smoking status, and alcohol use.

RESULTS

N = 1537 (47.2% women), mean (SD) 78.2ff17.4 years. Their mean (SD) co-morbidity was 11.2ff15.0. Highest ACB score calculated using Anticholinergic Cognitive Burden scale was 15. In Model 1, Anticholinergic Impregnation Scale (OR 1.24, 1.06-1.46) and Anticholinergic Activity Scale (OR 1.36, 1.03-1.81) were most strongly associated with mortality for ACB ≥3 compared to ACB=0. Modified Anticholinergic Risk Scale (mARS) was most strongly associated with mortality for ACB=1-2 relative to ACB=0: OR 2.41 (1.06, 5.5), OR 2.48 (1.08, 5.69), OR 2.51 (1.1, 5.77) respectively for Models 2, 3 and 4. In Model 2, mARS (OR 1.45, 1-2.1) was most strongly associated with long LOS relative to ACB=0. No significant association was found for rehospitalisation with any scale.

CONCLUSIONS

Our findings suggest ACB measured across a range of scales is associated with mortality and long LOS in multi-morbid older hospitalised patients.

SUPERVISORS: Professor Phyo Kyaw Myint, Dr Selvarani Subbarayan and Dr Roy Soiza

FUNDED BY: ASRS Programme, Department of Medicine for the Elderly (Gwyn Seymour Scholarship)

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FURTHER YOUR ACADEMIC INTEREST

Below is a selection of useful organisations and websites to help further your interest in academic medicine as a student.

ABERDEEN STUDENT SOCIETY FOR ACADEMIC MEDICINE (ASSAM)

The Aberdeen Student Society for Academic Medicine (ASSAM) was established in 2012 with the hope to encourage undergraduate interest in medical research. Even though their primary aim is to inspire medical students to pursue a career in academia, they also try to highlight the importance of basic research skills and critical appraisal in normal clinical practice.

Email: **assam@nsamr.ac.uk**
Facebook: **AberdeenASSAM**
Instagram: **assam_aberdeen**

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