Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

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School of Medicine Research News

We hope you enjoy our Trinity School of Medicine November 2023 Newsletter, showcasing selected research highlights and developments generated by our 800+ strong community of researchers and academic clinicians over the past year.

HEALTH POLICY IMPACT

The PRESTO Report: An analysis of resilience and sustainability in the Irish health system

The impact of Covid-19 on the Irish health system, the Government's response to the pandemic and the ways in which the HSE can prepare for the next crisis are evaluated in a report launched by Trinity's Centre for Health Policy and Management on 29 March 2023.

The PRESTO report suggests that Covid-19 provided a profound stress test for the Irish health system. Going into the pandemic, the Irish system had low capacity, with very long waiting lists for acute and community care. The pandemic itself then created unprecedented demands on services and the workforce, placing huge strain on a system already under pressure. However, the PRESTO report also shows that the Covid-10 pandemic provided opportunities to bring in reforms outlined in Sláintecare ahead of schedule. These included free healthcare for Covid testing and diagnostics, as well as new pathways of care in the community and online.

The PRESTO report is the result of a collaboration between researchers from the Centre's RESTORE and the global Partnership for Health System Sustainability and Resilience (PHSSR). Other stakeholders from the Department of Health, Department of Finance, Health Service Executive (HSE), Irish College of General Practitioners (ICGP), Economic Social and Research Institute (ERSI), Tampere University (Finland), and Personal and Public Involvement (PPI) representatives are involved in an advisory capacity. This provided great collective learning for policy makers and managers throughout different institutions.

This research is funded through the HRB-funded RESTORE project, which is led by Prof Steve Thomas, Edward Kennedy Chair of Health Policy and Management, Director of Health Policy and Engagement for the School of Medicine.

HEALTH POLICY IMPACT

Well-informed health technology assessment safeguards value for money for tax payer

The National Centre for Pharmaco-economics (NCPE), Trinity College Dublin, undertake health technology assessments (HTAs) of novel drugs from the perspective of the state health-payer.

The centre evaluate HTA submissions from pharmaceutical companies. Often these submissions use evidence synthesis to compare the relative efficacy of novel drugs versus drugs on the market, which have not been compared head-to-head in the same clinical trial.

The standard anchored indirect treatment comparison (ITC) is the most established evidence synthesis method. Matching-Adjusted Indirect Comparisons (MAIC) is a novel method which is gaining prevalence in the global literature. Several simulation studies have been performed to assess its suitability as a method. However, simulation studies alone cannot assess bias for MAIC given the subjective nature of how or when MAIC is performed. In a recent study, the team at NCPE analysed published MAICs to ascertain if they tend to favour the treatment for which individual patient data (IPD) is available, relative to the results of respective standard anchored ITCs.

80 comparisons were identified from 17 peer-reviewed publications through a systematic rapid review. A standardised metric that used reported relative treatment efficacy estimates and their associated uncertainty was used to compare the methods across different treatment indications and outcome measures.

On aggregate, the MAICs presented tended to report a more favourable relative efficacy estimate for the treatment for which IPD were available, relative to the reported ITC estimate.

This work provides an insight into how relative efficacy estimates compare when MAIC results are reported or not reported. This can be useful for HTA assessors and healthcare decision makers globally when interpreting the relative-efficacy outputs of MAICs.

A comparison of relative-efficacy estimate(s) derived from both Matching-Adjusted Indirect Comparisons and Standard Anchored Indirect Treatment Comparisons

Authors: Owen Cassidy MSc, Marie Harte MSc, Lea Trela-Larsen PhD, Cathal Walsh PhD Arthur White PhD Laura McCullagh PhD and Joy Leahy PhD.

HEALTH POLICY IMPACT

Best European paper award at the 2023 European Health Management Association Annual Conference on Public Policy

Dr Padraic Fleming, Discipline of Public Health & Primary Care, has been awarded the best European paper award at the 2023 European Health Management Association annual conference held in Rome, Italy.

The paper "A realist review of the international literature demonstrating how governance and decision-making during the 2008 financial crisis impacted health workforce resilience for COVID-19 and future health system shocks" is based on an article published in the International Journal of Health Policy and Management. The paper was also presented at the 6th Annual Conference on Public Policy, which took place in Toronto Metropolitan University on June 28th. The paper was also presented at the 6th Annual Conference on Public Policy, which took place in Toronto Metropolitan University on June 28th.

The research shows the importance of transparency, effective communication and shared decision-making between health managers and their workforce in a crisis.

Dr Fleming presented the paper during the methodological panel: "Using realist evaluation, synthesis and research in public policy practice" where he outlined the real-world application of realist synthesis to inform policy and practice in relation to health system resilience. The paper has also been presented to the Department of Health and the HSE in Ireland.

The paper is available here: https://www.ijhpm.com/article_4354.html This research was funded by Professor Steve Thomas' HRB Leaders Award [grant number RLA-2020-001]

HEALTH POLICY IMPACT

Shaping Future Research Directions for Pancreatitis

Dr Sinead Duggan, Senior Research fellow in the Department of Surgery (TUH) was an invited faculty member at the NIDDK workshop at this year's PancreasFest meeting in the University of Pittsburgh/UPMC.

PancreasFest is an annual meeting of pancreas physicians and translational researchers who convene during the last week of July to find new ways of working together to improve care for patients with pancreatic disease.

This year's workshop focused on interventions for knowledge gaps and research gaps for pancreatitis: Sinead was invited to speak to describe her research over the past 10 years, and to specifically discuss nutrition-based research priorities for chronic pancreatitis, as well as rationale and approach to future study design. Sinead was one of only two non-USA based speakers at the workshop.

For the past 10 years, Sinead has managed Professor Kevin Conlon's Research Group (based in the Trinity Centre at Tallaght University Hospital), focusing on the clinical management of chronic pancreatitis, including bone metabolism, nutrient deficiency, type 3c diabetes, sarcopenia, dietary intake, physical activity, integrated care, and digital tools for management.

Guide international funding: Discussions arising at the workshop will shape research priorities and guide international funding authorities regarding pancreatitis-related studies over the years ahead. A summary of the workshop findings is currently under peer review for publication. Read more

Sinead pictured with Professor David Whicomb, University of Pittsburgh, Founder of PancreasFest

SIGNIFICANT COLLABORATIONS AND PARTNERSHIPS

Oesophageal Cancer-An All-island initiative launched.

Oesophageal adenocarcinoma (OAC) is one of the biggest cancer challenges with a 5-year survival rate of just 24% in the Republic of Ireland (NCRI) – only 1 out of every 4 people diagnosed will survive 5 years.

UK and Ireland report some of the highest incidence rates of OAC. Breakthrough Cancer Research is investing €1 million into the Oesophageal AllCaN Programme grant (2023-2027) with additional collaborative funding and support coming from CROSS and the Oesophageal Cancer Fund.

It was awarded to an all-Ireland network of the best minds in Ireland working in this area, led by Prof. Jacintha O'Sullivan (Trinity St. James's Cancer Institute, TSJCI), and co-led by Prof. Helen Coleman (Queen's University Belfast) and Prof. Juliette Hussey (TSJCI). The collaboration links six major academic institutions across the island of Ireland – Trinity College Dublin, Queen's University Belfast, University College Cork, Royal College of Surgeons in Ireland, University College Dublin, and University of Galway – along with their associated hospitals, the National Cancer Control Programme and the Belfast Health and Social Care Trust.

They share decades of collective experience in Oesophageal Cancer and Barrett's oesophagus (a significant risk factor for oesophageal cancer). Therefore, identification of, and improved treatments for people with Oesophageal Cancer and Barrett's oesophagus, could significantly control the progression of the disease. This unique cross-border collaboration of researchers across two health jurisdictions will enable for the first time the sharing of data from the Northern Ireland and Republic of Ireland Barrett's oesophagus registries (over 34,000 patients) to answer important epidemiological studies using one of the largest platforms available worldwide for studying this disease.

Prof. Jacintha O'Sullivan, Professor in Translational Oncology at Trinity St James's Cancer Institute, who is leading AllCaN said, *'The new all-island collaborative structure will provide research-led innovation addressing key gaps in knowledge across the oesophageal cancer patient's journey from cancer prevention, diagnosis, treatment to survivorship. This will lead to new cancer prevention strategies, lifestyle interventions and identify those at risk of disease progression and identify new treatment approaches for these patients.'*

SIGNIFICANT COLLABORATIONS AND PARTNERSHIPS

TCD hosts Global network for Ageing Studies

In August 2023, the Irish Longitudinal Study on Ageing (TILDA) hosted the meeting of the Health and Retirement Study (HRS) global network of ageing studies in Trinity College.

Principal Investigators and key researchers from the National Institutes of Health (U.S.) and ageing studies in Chile, China, England, India, Ireland, Northern Ireland, Japan, Malaysia, Mexico, South Africa, Scotland, Thailand, Colombia, Egypt, and Lebanon attended to provide updates on key studies, collaborate on joint research projects, and facilitate introductions between new and existing network members. The meeting was held in Dublin as a memorial to Dr. James P. Smith, the chair of TILDA's Scientific Advisory Board for over 12 years, a member of the MISA advisory board and an honorary fellow of Trinity College (2017).

To culminate this memorial to Dr. Smith, Trinity College, TILDA, and Mercers Institute for Successful Ageing (MISA) welcomed Angus Deaton (Nobel Laureate) and Anne Case, authors of the New York Times bestseller 'Deaths of Despair and the Future of Capitalism' for a fascinating discussion of how the flaws in capitalism are fatal for America's working class. Filling Stanley Quek Hall, over 300 people attended this far-reaching lecture, coming from all backgrounds including government organisations, the healthcare field, academic institutions, and the current student body of various universities, among others. They presented data showing that, as the college educated have become healthier and wealthier, adults without a degree are suffering from deaths of despair including suicide, drug overdose, and alcoholism.

Link here to the Health and Retirement Study (HRS)

CLINICAL RESEARCH & NEW STUDIES

Wellcome HRB Clinical Research Facility at St. James's Hospital Funding Award

Since opening in May 2013, the CRF has been re-awarded operational funding in 2018 (four years) and again in 2022 (five years) to the value of €5.3 million.

The CRF's impacts are wide ranging and exemplify how academic medical centres make a direct impact on the communities they serve.

New medical devices
To date two TCD Spinout companies have developed devices that have or are undergoing clinical trials supported by the CRF. The CRF was used for the TENT A3 trial of a device used for the treatment of Tinnitus and more recently the CRF is the only European trial site for a trial of a medical device developed by Proverum, a TCD spinout company, for the treatment of benign prostate hyperplasia.

Access to Clinical Trials for Irish Patients
The CRF and the infrastructure it provides has attracted clinical trials to Ireland that would normally be conducted in other countries. This has allowed Irish patients to participate in clinical trials without having to travel overseas. Notable examples include:

- The first gene therapy treatment in Ireland for patients with Haemophilia, Read more
- Eleven Irish children with SMA Type 1 treated with a gene therapy – four of which were treated at no cost to the state Read more
- First CAR-T trial in Ireland for patients with Multiple Myeloma. Read more
- Phase I/II trials of treatments for genetically rare forms of Motor Neuron Disease/ Amyotrophic lateral sclerosis (ALS) Read more
- Large scales medical device trials/studies for a device treating tinnitus. Read more
- Only EU site for a trial of an implanted device (stent) for the treatment of Benign Prostate Hyperplasia. Read More
- National Covid vaccine trial (BOOSTVAC) The CRF is currently supporting a national Covid vaccine trial (BOSTVAC) and to date has collected samples and clinical information from over 1,000 patients and healthcare workers with COVID and contributes to the National COVID Biobank. This resource has underpinned world class COVID research undertaken across the university.

CLINICAL RESEARCH & NEW STUDIES

Increasing capacity and capability for dementia trials in Ireland

Some 150,000 people will be living with dementia in Ireland by 2045*. Starkly, less than 0.5% of people with dementia participate in research in Ireland.

Established in 2021 Dementia Trials Ireland (DTI), a HRB Clinical Trials Network led by Prof. Iracema Leroi and Prof. Seán Kennelly, TCD, aims over 5 years to triple dementia trial activity in Ireland and to enable research opportunities for people with dementia and carers.

DTI's all-Ireland multidisciplinary team comprises professional and lay stakeholders at its core working alongside some 25 research and third-sector partners endowing DTI with the expertise range to develop and deliver investigator-led and industry sponsored trials spanning the full life course of dementia and dementia subtypes. Recent highlights reflecting the success of the Network are:

- A developing portfolio of industry-led RCT (4) and investigator-led studies (15) for dementia with its first global RCT delivered on time & to target.
- Network of 44 core members.
- National clinical workforce development and trial delivery training events.
- 2 early career research 'seed funding' awards.
- Trial methodology studies, i.e., core outcome set (COS) development, research priority setting partnership for post-COVID dementia.
- National public survey to scope acceptability and implementation of new disease modifying treatments for Alzheimer disease.
- National trial site feasibility review to establish an evidence base in support of future network and policy development.
- PPI Featured Research Session, AAIC 2023, world's largest Alzheimer Disease conference.

Further information at: dementiatrials.ie

Photo Caption: (left to right) JP Connelly (Dementia Research Group (DRG); Prof. Iracema Leroi (DTI Lead); Rachel Fitzpatrick (kneeling) (DRG); Anne-Marie Miller (kneeling) (DTI, Senior Network Manager); Adam Roche (DRG); Lara Gibney (DTI, National Trial Coordinator).

CLINICAL RESEARCH & NEW STUDIES

State-of-the-art next generation sequencing/genomics facility

Prof John O'Leary, Head of Discipline Histopathology, School of Medicine, in collaboration with Eurofins Ireland, has led the establishment of a new State-of-the-art next generation sequencing/genomics facility at St. James Hospital.

Located at one of Trinity's key research centres -Trinity Translational Medicine Institute the investment will support research in the critical areas of cancer genomics, viral genomics, non-invasive testing, cancer metastasis, cancer neutrigenomics and neutrigenetics, cancer metabalomics and spatial transcriptomic and proteomic (multi-omic) profiling. Read more

CLINICAL RESEARCH & NEW STUDIES

Important Study explores the needs of Childhood Cancer Survivors

Information on the experiences and needs of childhood cancer survivors and their parents in Ireland is limited. The CHILDHOOD CANCER SURVIVORSHIP PROJECT was designed to address this need.

The study is expected inform the future development of childhood cancer services nationally.

Participants were recruited by a mixed methods approach including letters of invitation to randomly selected parents (n=152), and adult survivors (n=53), a social media campaign, and voluntary organisations/healthcare professionals support. Separate on-line focus groups, utilising the Webex platform, were held for adult survivors (n=12) and parents (n=24) in brain, leukaemia and solid tumours, respectively. Teenage survivor (14-17 years), perspective was captured through a "pooled" focus group.

Strengths and priority areas for improvement in childhood cancer care nationally were identified from survivors and parents/guardians/carers perspectives. The results will inform childhood cancer survivorship service development in Ireland. Phase 2 of the project seeking survivorship service provider's perspectives through semi-structured interviews with 42 staff has been completed and pending publication.

The resultant data will help generate a Treatment Summary/ Survivorship Passport which can be given to cancer survivors to facilitate their transition on the difficult graduation from paediatric to adult care. The aim is that the survivorship passport will be electronically available to survivors and health care professionals – possibly through the proposed National Clinical Information System (NCIS) of the National Cancer Control Programme (NCCP) or an alternative platform. The database will provide infrastructure to facilitate research on Irish childhood cancer survivorship to ultimately deliver quality patient-centred care, improve survival, and increase quality of life.

The Irish Childhood Cancer Survivorship Project is led by Dr Michael Capra, Paediatric Oncologist at Children's Health Ireland (CHI) at Crumlin and Trinity's Senior Clinical Lecturer in Paediatrics at the School of Medicine along with Dr Katherine Gavin and Ms Frieda Clinton, Department of Haematology Oncology, National Children's Cancer Service, Children's Health Ireland at Crumlin Hospital, Dublin.

NEW SCIENTIFIC DISCOVERIES

Harnessing the power of the T cell to treat cancer

The augmentation of a cancer patient's immune system with, for example, antibodies or cells (immunotherapy) has the potential to prolong life and/or cure disease.

The selection and in vitro expansion of functional patient T cells that can infiltrate and kill the tumour (TILs) is an approach gaining much attention.

The core study objective of a new study entitled: HEALED (**tHe pErsonalised Active ceLl thErapy paraDigm**) Consortium, led by Trinity Principal Investigators, Professor Aideen Long, Professor Jacintha O'Sullivan and Professor Maeve Lowery is to harness the power of the T cell to treat cancer. Funded by Enterprise Ireland (€10.5m), through the Disruptive Technologies Innovation Fund (DTIF). HEALED has four key partners: TTMI and St. James's Hospital (SJH), Remedy Biologics Ltd, aCGT Vector and University of Galway (UoG). HEALED combines the use of Remedy Biologics' novel nanoreactor technology, aCGT Vector's experience creating Good Cell Manufacturing Hubs, the patient-focused translational cancer research in TTMI/SJH and UoG's experience in bioinformatics, to create a pre-clinical package on TIL (tumour infiltrating lymphocyte) therapies.

The overall objective is to enable a novel, revolutionary immunotherapy to treat currently incurable cancers. HEALED is working on solid tumours of the ovary, breast, lung, colon, rectum, stomach, and oesophagus. The research will explore the effects of energy metabolism, hypoxia and inflammation on the number and phenotype of TILs in these tumours, profiling the inflammatory proteins released by tumours and matching this information with that of the TIL cell phenotype in these tumours. This will help us answer important questions on the role of these biological processes in the tumour microenvironment and how this influences the TIL cell biology. The study will also advance understanding about the genetic changes in tumour tissues by conducting whole exome sequencing and RNA sequencing.

This will be used by UoG to predict appropriate neoantigens in the tumours and will help us find the most effective TILs that can be used as a cancer therapeutic for future oncology patients. In collaboration with The National Centre for Pharmacoeconomics (NCPE), the next step will be to investigate the expected cost effectiveness of TIL therapies from health-payers' perspective globally. This will be informed by clinical data, SLRs and collaborations.

NEW SCIENTIFIC DISCOVERIES

Too much of a good thing?

A new collaborative study between Trinity's School of Medicine and the Trinity College Institute of Neuroscience (TCIN) recently published in the journal Cellular Immunology aimed to assess the actions of IFN alpha on the immune response to tuberculosis.

Dr Gina Leisching, Senior Research Fellow who led the study, and her PhD student, Ms. Anjali Yennemadi have shown new evidence that chronic exposure type I interferons, specifically, IFN alpha, blunt the macrophage immune response to M. tuberculosis and explain why patients with diseases that are driven by IFN alpha are prone to infections. We now have new targets to test to see if we can reverse this poor response by either boosting immune cell function or limiting the effects of type I interferons. We are now working with immune cells from SLE patients to gain more insight into whether these effects are observed in all immune cells or only a select few. These findings now identify type 1 interferons as a potential target for the development of host-directed therapies in patients who suffer from excess production of this cytokine.

Study link: https://www.sciencedirect.com/science/article/pii/S0008874923000801

NEW SCIENTIFIC DISCOVERIES

Improving insights into inflammatory responses following neonatal brain injury

The main aim of the project is to evaluate inflammation in children who experienced Neonatal Brain Injury at birth, correlate inflammation to neurodevelopmental outcomes and assess potential immunomodulation treatments.

Thirty-four patients and twenty controls were recruited for the project and had clinical evaluation. Their samples were processed for innate immunity activation, inflammasome activation and cytokine production. The results of the project will be compared to previous data from a neonatal Brain injury study called NIMBUS. So far, the results have been presented at two international conferences and one national..

This research will enhance our knowledge of the aetiology, the prognosis and adjunctive treatments in addition to Therapeutic Hypothermia to improve the high morbidity and mortality associated with NE. It will also allow the development of interventions to end persistent inflammation in neonatal brain injury may improve clinical outcomes and have the potential for patents, commercialization and a platform for future clinical trials. The study has resulted in 5 publications and potentially 5 more, including a Guideline for parents and healthcare workers, including:

- Multi-organ dysfunction scoring in neonatal encephalopathy (MODE Score) and neurodevelopmental outcomes doi 10.1111/apa.16111.
- Dysregulated Monocyte and Neutrophil Functional Phenotype in Infants With Neonatal Encephalopathy Requiring Therapeutic Hypothermia. doi: 10.3389/fped.2020.598724.
- Newborn Brain Society Guidelines and Publications Committee. Haematological issues in neonates with neonatal encephalopathy treated with hypothermia. doi: 10.1016/j.siny.2021.101270.
- Altered inflammasome activation in neonatal encephalopathy persists in childhood. doi: 10.1111/cei.13598.
- Altered Cytokine Endotoxin Responses in Neonatal Encephalopathy Predict MRI Outcomes. doi: 10.3389/fped.2021.734540.

NEW SCIENTIFIC DISCOVERIES

Investigating Cardiovascular and Neurovascular Function Using Signal Entropy

SFI-funded FRAILMatics research group led by Prof. Roman Romero-Ortuno, has led ground-breaking research using signal entropy to quantify neuro-cardiovascular instability (NCVI) via peripheral blood pressure (BP) data analysis. Key findings include:

- **Associations:** Higher BP signal entropy correlates with worse frailty status, cognitive decline, older biological brain-age, and increased risks of all-cause mortality, falls, syncope, and fear of falling.
- **Health Index:** Integrating cardiovascular sample entropy with gait speed and cognitive performance yields a superior 3-item health index for predicting 12-year cardiovascular/respiratory mortality compared to traditional frailty measures.

This work holds substantial promise:

- **Clinical Utility:** Provides a clinically relevant method for tracking cardiovascular and neurovascular dysregulation, helping identify individuals at higher risk of adverse health outcomes.
- **Healthcare Policy:** Insights may inform policies advocating early intervention for individuals with elevated BP signal entropy.
- **Research Advancement:** Paves the way for further investigations into the intricate relationships between neurovascular function, frailty, and mortality, offering potential intervention strategies.

Publication Links:

- Cardiovascular Sample Entropy and 3-item Health Index (2023)
- Signal Entropy versus Frailty in a Clinical Cohort (2023)
- Signal Entropy versus Future Falls, Syncope, and Fear of Falling (2022)
- Signal Entropy versus All-cause Mortality (2022)
- Signal Entropy versus Physiological Brain Age (2021)
- Signal Entropy versus Cognitive Performance (2021)
- Signal Entropy versus Frailty in TILDA (2020)

This work has been presented at prestigious conferences, including the IGS ASM, EUSIPCO 2022, and Entropy 2021.

This research, based on population-level data from The Irish Longitudinal Study on Ageing (TILDA) and validated in a clinical cohort, has the potential to reshape our understanding of cardiovascular and neurovascular health. It also offers the prospect of advancing clinical care, influencing health policy, and shaping future research endeavours.

NEW SCIENTIFIC DISCOVERIES

A new avenue for the therapeutic use of cannabinoids

Dr. Eric Downer leads the Translation Neuroimmunology Research laboratory at the Trinity Biomedical Sciences Institute (TBSI), conducting research in MS and related neuroinflammatory disorders.

In projects funded by the Irish Research Council and the Provosts PhD Project Awards at TCD, the laboratory is investigating cellular targets with relevance to the pathogenesis of MS. The targets are toll-like receptors (TLRs), a family of receptors expressed on immune cells in the human body that act to detect and combat infection by microbes, most notably viruses and bacteria. These receptors control intricate inflammatory signalling responses within cells and tissues. For quite some time, a body of peer-reviewed published research has identified that these receptors are associated with the pathogenesis of MS. Indeed, data published from Dr. Downer's laboratory has shown that in immune cells isolated from people with MS, compared with immune cells from non-MS subjects, the TLR receptor signalling mechanisms are "switched on" in terms of their inflammatory status [1].

Dr. Downer's team was recently awarded an Irish Research Council Enterprise Partnership Scheme grant in partnership with Dr. Jack Prenderville, Director, Transpharmation Limited. This research will build on the expertise of Dr. Downer's team and Transpharmation's expanding inflammation service portfolio. Under this award, PhD candidate Almudena Otálora Alcaraz, is establishing assays to investigate novel therapeutics in human immune cells, initially focusing on the nucleotide-binding oligomerization domain-like receptor family, pyrin domain-containing 3 (NLRP3) inflammasome. The NLRP3 inflammasome has a well-established function in innate immunity. Importantly, the NLRP3 inflammasome is closely associated with the pathogenesis of neuroinflammatory conditions, and evidence suggests that the inflammasome may be a therapeutic target in disorders such as MS. This project is establishing inflammasome assays in cells associated with MS pathogenesis, and this suite of in vitro assays will provide a platform for assessing novel compounds (including cannabinoids) for anti-inflammatory efficacy. The overarching goal of this project is to define the role of the inflammasome in MS and to identify novel inflammasome inhibitors that have efficacy in cells from people with MS.

NEW SCIENTIFIC DISCOVERIES

Advancing treatment breakthroughs for Stroke patients

Stroke is the leading cause of acquired physical disability in adults, is a major risk factor for dementia, and is the 2nd commonest cause of death in Europe and worldwide.

Professor Dominick McCabe runs an innovative translational research programme in Vascular Neurology/Stroke Medicine and Platelet Science/Haemostasis, which is led from the Meath Foundation Research Laboratory, TUH-TCD. Prof McCabe's research in this field will hopefully lead to optimised, 'precision-based antiplatelet treatment' in patients following a non-cardioembolic TIA or ischaemic stroke, with immense benefits to patients, carers and society, and significant healthcare savings in Europe and worldwide. The group has contributed to key international clinical practice guidelines which are already impacting on the care of CVD patients nationally and internationally and has published several recent peer-reviewed manuscripts in this field, over the last 12 months and contributed to key international clinical practice guidelines including:

- Lim ST,…., McCabe DJH. Profile of reticulated platelets in the early, subacute and late phases after transient ischaemic attack or ischaemic stroke. Platelets 2022; 33: 89-97.
- Subramanian A, …, McCabe DJH. Platelet biomarkers in patients with atherosclerotic extracranial carotid artery stenosis: A systematic review. Eur J Vasc Endovasc Surg 2022; 63: 379-389.
- Lim ST, ….., McCabe DJH. Assessment of on-treatment platelet reactivity at high and low shear stress and platelet activation status after the addition of dipyridamole to aspirin in the early and late phases after TIA and ischaemic stroke. J Neurol Sci 2022; 441: 120334.
- Naylor AR, ….., McCabe DJH, et al. European Society for Vascular Surgery (ESVS) 2023 clinical practice guidelines on the management of atherosclerotic carotid and vertebral artery disease. Eur J Vasc Endovasc Surg 2023; 65: 7-111.

Prof. McCabe is also PI of the ongoing multicentre 'Optimal Antiplatelet Therapy in TIA and Ischaemic Stroke-International (OATS-I) observational study which is assessing 'high on-treatment platelet reactivity (HTPR)' status and performing individualised pharmacogenetics testing in participants following TIA/ischaemic stroke. The Vascular Neurology Research Foundation supports the work (VNRF.ie secure website link: https://www.vnrf.ie/).

CELEBRATING EXCELLENCE IN DOCTORAL TRAINING

Celebration of upcoming graduates of Doctor in Medicine (M.D.) with previous publication

The inaugural Public presentation of medals by the School of Medicine to Trinity College Dublin's first upcoming graduates of Doctor in Medicine (M.D.) with previous publication was held on October 11th 2023 in Tercentenary Hall, Trinity Biomedical Sciences Institute (TBSI), Dublin.

At the special ceremony, which was launched by Prof. Colin Doherty, Head of the School of Medicine, Trinity College Dublin, Medical Doctors, Dr Helena Ferris and Dr Declan Byrne were presented with a medal each in recognition of being the first graduates with a Doctor in Medicine (M.D.) with previous publication.

Presenting the Medals, Professor Roman Romero-Ortuno, Associate Director for M.D. Studies, School of Medicine, said "Thanks to the efforts of the entire PGT Office in the School of Medicine, a new M.D. route was approved by Trinity's Graduate Studies Committee in May 2021. This route allows permanent Consultants or General Practitioners who work in our network and are Trinity graduates to obtain the M.D. based on previously published work."

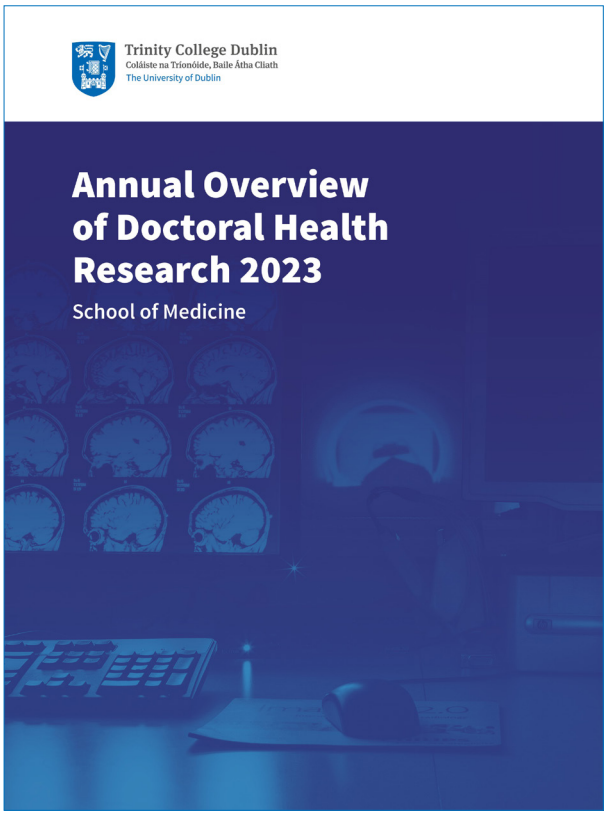
Accepting her medal, Dr Ferris, a specialist in Public Health Medicine in the HSE South said: "I am honoured to be awarded an M.D. from Trinity College Dublin. An M.D. with prior publication is a wonderful opportunity for Consultants with a track record of high quality research to gain formal recognition for their contribution to medical knowledge. I look forward to implementing the findings of my research, which focuses on optimising health outcomes for hip fracture patients and improving cost effectiveness within the health service."

Dr Helena Ferris and Dr Declan Byrne with their inaugural medals in recognition of being the first graduates with a Doctor in Medicine (M.D.) with previous publication.

Commenting on his medal, the other recipient, Dr Declan Byrne, a Consultant Physician and Executive Medical Director in St James's Hospital, said: "I am absolutely delighted to have been one of the first candidates to complete the M.D. by previous publications. The process was clear and well managed by the University. There was a lot of learning in preparing the thesis. I had to revisit and update my literature review and critically re-review my methodology. This has benefitted the planning cycle for future work. The rigour and accountability of the examination process provided an excellent focal point for my CPD activities. I think this option will be very useful for working doctors across the community and hospital domains who are research active, or are interested in joining research groups. I highly recommend it."

Speaking about the important ceremony, Professor Catherine Darker, Director of Postgraduate Teaching & Learning, School of Medicine, commented "the M.D. with previous publications showcases a way for our School to keep connected with our diaspora. Both of these recipients are a testament to the real and tangible benefits that can arise when working doctors apply research to their areas of interest."

Information on this procedure is available on the School of Medicine website: https://www.tcd.ie/medicine/education/courses/postgraduate/research/md.php



CELEBRATING EXCELLENCE IN DOCTORAL TRAINING

Annual Overview of Doctoral Health Research 2023

The School of Medicine is delighted to announce the publication of its Annual Overview of Doctoral Health Research 2023.

The report is a celebration of the School of Medicine's research Excellence, one of the factors that make Trinity the leading university in Ireland. The School's commitment to being a research-led school with strong clinical-scientific academic partnerships, is fundamentally supported by the hard work of our postgraduate students undertaking PhD and MD programmes. In any higher level institution it is the hard work of students undertaking PhD and MD degrees that lays the foundation for excellence in medical and health research.

The inspiration and motivation of the school's 160 PhD and MD Doctoral students reflects a formidable and powerful body of health research, embedded in clinical translation, which will ultimately enhance our understanding of science and technology to the ultimate benefit of patients, health professionals, and society as a whole.

The report is also a testament to the immense contributions made by our academic Doctoral Research supervisors across the school who are shaping and mentoring PhD students who will become the health research leaders of tomorrow.

In addition to a comprehensive directory of doctoral research project titles, the document offers a selection of one page articles penned by our students, that reflect the vibrancy and variety of the school's research strengths as well as showcasing the talents of its mentors.

We hope you enjoy reading about our Doctoral research stories. The Annual Overview of Doctoral Health Research 2023 is available to enjoy here.

Multidisciplinary Innovation and Research Advancing Neurological care in a Digital Age

The MIRANDA PhD programme, a Collaborative Doctoral Award (CDA) in patient-focused research funded by the Health Research Board, commenced in the Academic Unit of Neurology in 2022.

This comprehensive research programme was co-created with international experts in clinical practice and research. The principal investigator of the MIRANDA programme is Dr Miriam Galvin. Five PhD research scholars, with backgrounds in healthcare provision/health research, are undertaking research to improve care and outcomes for people living with motor neurone disease (MND).

- Project 1
  Construction of an evidence-based digital platform to deliver rehabilitation to people living with MND that can be utilized by occupational therapists and physiotherapists. PhD scholar: Avril Mc Tague.
- Project 2
  Examination of information use and knowledge transfer in multidisciplinary MND clinics to support better patient care. PhD scholar: Ruairí Weiner
- Project 3
  Exploration of experiences and challenges for healthcare professionals working with MND to support them to deliver optimal care to people with MND. PhD scholar: Megan Walls
- Project 4
  Development of digital technologies to accurately track speech and swallow function for home monitoring and as precise outcome measures in clinical trials. PhD scholar: Lesley Doyle
- Project 5
  Optimisation of the 'TiM (Telemedicine in MND) on MyPathway' app, to remotely collect accurate, meaningful patient and caregiver measurements to facilitate improved communication with healthcare professionals and MND service planning. PhD Scholar: David Murphy

Research undertaken as part of the MIRANDA programme will directly benefit people living with MND and their families, translating research findings to a clinical setting providing improved patient care. Future translational research in other settings, particularly neurological and long-term conditions, can build upon the methodologies developed within MIRANDA.

CELEBRATING EXCELLENCE IN DOCTORAL TRAINING

Neonatal Encephalopathy PhD Training Network goes from strength to strength

The HRB Neonatal Encephalopathy PhD Training Network (NEPTuNE) boasts a number of significant research highlights over the last 12 months.

In April 2023, NEPTuNE scholars and PIs attended the PAS conference in Washington, USA where Aoife Branagan's poster describing Anakinra (Il1 Receptor Antagonist) and *Immune Dysfunction in Infants with Neonatal Encephalopathy* was displayed. Members of the NEPTuNE team will also attend the JENS conference in Rome in September 2023.

NEPTuNE's March 2023 annual report to the HRB reported 42 publications (including Management of Acute Kidney Injury in Extremely Low Birth Weight Infants, Branagan A. et al and Neonatal encephalopathy and hypoxic–ischemic encephalopathy: moving from controversy to consensus definitions and subclassification, Molloy E.. et al.) and 48 conference presentations. There are a further 11 publications in progress.

Having coordinated training and build sessions for a database that will store Neonatal Clinical Data, the NEPTuNE programme was able to launch its CASTOR database earlier this year. This database will exist beyond the lifespan of the programme and will be a great resource to current and future researchers.

PPI continues to be a key element of the NEPTuNE programme. There is regular communication between scholars, PIs and PPI representatives from its PPI partner, the INHA. NEPTuNE PIs, Professor Eleanor Molloy, Dr Jean Quigley and programme manager Beth Corcoran (PPI representative for Down Syndrome Research Group) participated in the Down Syndrome Conversation Cafe as part of TCD's PPI Ignite Festival in October 2022. Seventy parents/advocates and other clinicians, therapists and professionals working in the field of Down Syndrome attended the event and parents mentioned that it was inspiring and hopeful.

STRATEGIC COMMUNICATIONS

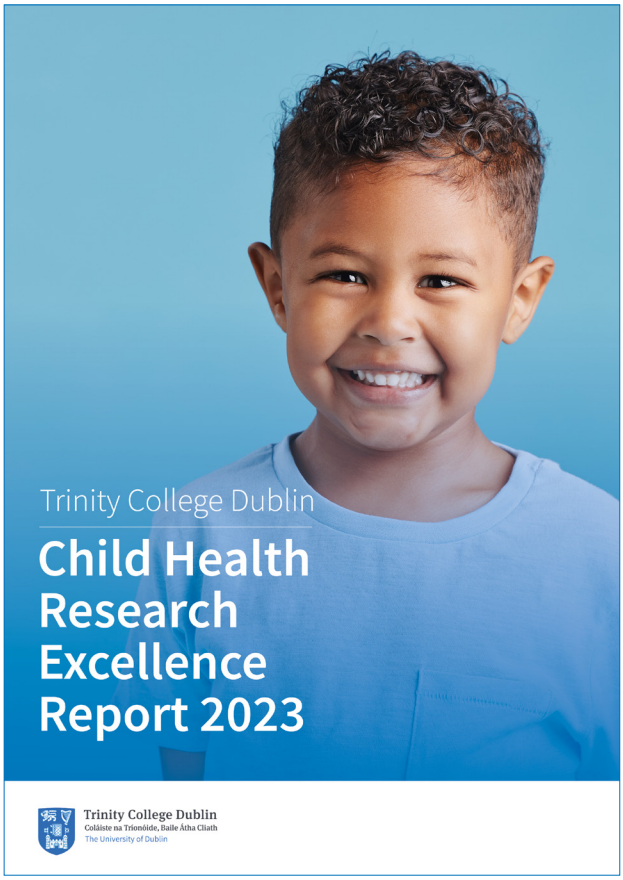
Child Health mapping paves way for Child Health Strategy to 2040

The launch of the Child Health Research Excellence Report 2023 took place in Tercentenary Hall in May 2023.

Coordinated by Professor Eleanor Molloy and Bridget Gavin, the report provides an overview of Trinity's research expertise in all areas of child health including cancer, genomics, immunology, infectious disease, neurology, neonatology, dermatology, mental health, and child health policy. A further objective of the report is to highlight active child health research projects in Trinity and its institutions (TRICC) and to promote interdisciplinary collaboration both within the university and internationally. The research outlined in the report emphasises the importance of PPI and family input in the research paradigm such as the Public Patient Involvement in Professor Molloy's HRB funded NEPTuNE programme.

The launch event featured keynote presentations from Professor Eleanor Molloy, Professor of Paediatrics & Child Health, Professor Rhodri Cusack, Director, Trinity Institute of Neurosciences (TCIN), Professor Padraic Fallon, Professor Of Translational Immunology, Associate Dean of Research, Professor Trevor Spratt, AIB Professor In Childhood Research, Professor Owen Smith, Professor of Child, Adolescent and Young Adult (CAYA) Oncology, Professor Anne O'Connell, Head of Paediatric Dentistry, School of Dental Science and Professor Martina Hennessy, Wellcome-HRB Clinical Research Facility, St James's Hospital. The presentations are available as podcasts to enjoy.

The presentations were followed by an animated panel discussion on the theme *Building Trinity's Vision for Child Health Research in 2040*.



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