

Clinical Biochemistry News



November 2024

Newsletter of the Association of Clinical Biochemists in Ireland
and the Association for Laboratory Medicine (Republic of Ireland Region)



The ACBI visits Athlone this year for its Annual Conference. Pictured are St. Peter and Paul's Church and the walls of Athlone Castle, both in the town centre. The venue for the conference is the Hodson Bay Hotel, a 10 minute drive from the town.

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A Selection of Members' Recent Publications

Mineralocorticoid receptor antagonist monotherapy in pediatric non-classical 11 β -hydroxylase deficiency.

Kennedy EC, Stack M, Carolan E, Durkan M, **Joyce CM**, Hawkes CP. *J Pediatr Endocrinol Metab.* 2024 Sep 20. doi: 10.1515/jpem-2024-0194.

Proof-of-concept study: Remote capillary blood collection for hCG analysis in early pregnancy.

Joyce CM, **O'Shea PM**, Lynch R, **Costelloe SJ**, McCarthy TV, Coulter J, Hayes-Ryan D, O'Donoghue K. *Eur J Obstet Gynecol Reprod Biol.* 2024 Sep;300:309-314. doi: 10.1016/j.ejogrb.2024.07.040.

Programmed intermittent epidural bolus regimen vs continuous epidural infusion: a retrospective study of motor block and obstetric outcomes using the Robson's Ten Group Classification System.

Joyce C, Free R, Calpin P, Browne I, Robson M, Ffrench-O'Carroll R. *Int J Obstet Anesth.* 2024 Aug;59:104215. doi: 10.1016/j.ijoa.2024.104215.

Postnatal Cardiometabolic Health After Metformin Use in Gestational Diabetes: A Secondary Analysis of the EMERGE Trial.

Dunne F, Newman C, Alvarez-Iglesias A, **O'Shea P**, Devane D, Gillespie P, Egan A, Donnell MO, Smyth A.J. *Clin Endocrinol Metab.* 2024 Jul 26:dgae522. doi: 10.1210/clinem/dgae522.

Direct-to-consumer testing as consumer initiated testing: compromises to the testing process and opportunities for quality improvement.

Shih P, Sandberg S, Balla J, Basok BI, **Brady JJ**, Croal B, De Vos N, Karlsson M, Kedars P, Ozben T, Pijanovic M, Plebani M, Orth M. *Clin Chem Lab Med.* 2024 Aug 14. doi: 10.1515/cclm-2024-0876.

Some issues to consider with the use of serum indices.

Reeve JLV, Housley D, Twomey PJ. *J Clin Pathol.* 2024 Jul 11:jcp-2024-209422. doi: 10.1136/jcp-2024-209422.

Symptom burden, coagulopathy and heart disease after acute SARS-CoV-2 infection in primary practice.

Colleran R, Fitzgerald S, Rai H, McGovern L, Byrne RJ, Mansur A, Cradock A, Lavery R, Bisset J, McKeogh S, Cantwell G, O'Ciardha D, Wilson H, Begossi N, Blake N, **Fitzgibbon M** et al. *Sci Rep.* 2024 Sep 11;14(1):21229. doi: 10.1038/s41598-024-71535-8.

Trends in polysubstance use among patients in methadone maintenance treatment in Ireland: Evidence from urine drug testing 2010-2020.

Durand L, O'Kane A, **Stokes S**, Bennett KE, Keenan E, Cousins G.J. *Subst Use Addict Treat.* 2024 Sep 5;167:209507. doi: 10.1016/j.josat.2024.209507.

Reviews / Articles of Interest

MicroRNAs control protein synthesis throughout living organisms. They are also associated with pathophysiological processes, such as cancer. The review below examines their diagnostic validity in detecting hepatocellular carcinoma.

Circulating microRNAs as promising diagnostic biomarkers for hepatocellular carcinoma: a systematic review and meta-analysis.

Alemayehu E, Fasil A, Ebrahim H, Mulatie Z, Bambo GM, Gedefie A, Teshome M, Worede A, Belete MA. *Front Mol Biosci.* 2024 May 14;11:1353547. doi: 10.3389/fmolb.2024.1353547.

Bone marker assays have been available for many years but are not widely integrated into monitoring therapy and compliance in osteoporosis. This review examines current evidence of their utility.

Insight into the potential of bone turnover biomarkers: integration in the management of osteoporosis and chronic kidney disease-associated osteoporosis.

Brouwers P, Bouquegneau A, Cavalier E. *Curr Opin Endocrinol Diabetes Obes.* 2024 Aug 1;31(4):149-156. doi: 10.1097/MED.0000000000000869.



Educational

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Core concepts for value-based clinical laboratories

A vision to the future: value-based laboratory medicine.

Plebani M, Cadamuro J, Vermeersch P, Jovičić S, Ozben T, Trenti T, McMillan B, Lowe CR, Lennerz J, Macintyre E, Gabelli C, Sandberg S, Padoan A, Wienczek JR, Banfi G, Lubin IM, Orth M, Carobene A, Zima T, Cobbaert CM, van Schaik RHN, Lippi G. Clin Chem Lab Med. 2024 Sep 13;62(12):2373-2387. doi: 10.1515/cclm-2024-1022

Some basic advice for those embarking on a career in diagnostic laboratories

CLSI President Dr. James Nichols on the Importance of Preparing Students for Laboratory Medicine Careers.

The clinical laboratory metaverse is coming. Read on.

A new door to a different world: opportunities from the metaverse and the raise of meta-medical laboratories.

Gruson D, Greaves R, Dabla P, Bernardini S, Gouget B, Öz TK. Clin Chem Lab Med. 2023 Mar 2;61(9):1567-1571. doi: 10.1515/cclm-2023-0108

Information from Federation / Societies

HSE Strategic Plan: The current draft of the HSE Outline Strategic Plan for Laboratory Services (2025 – 2034) has been circulated to ACBI members via email. Check your in-box. It is as yet unpublished. Some specific points are still being clarified. The document is for information only, not consultation.

EuroLabNews: The current edition of the EFLM Newsletter, EuroLabNews (September/October 2024), is available [here](#).

CCLM: A new issue of Clinical Chemistry and Laboratory Medicine (CCLM Volume 62 number 12 November 2024) is available [here](#). Free for ACBI and EFLM Academy Members.

International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) eNews: The October 2024 edition is available [here](#).

eJIFCC: The current issue of the IFCC's journal, eJIFCC (April 2024), can be found [here](#).

Link from the IFCC eAcademy:

[Advancing Healthcare Webinar Series - Siemens Healthineers USA](#)

All ACBI members' can sign up for EFLM Academy access. The following journals are available subscription free. Click the journal name to take you to the home page.

[Clinical Chemistry and Laboratory Medicine](#)

[Clinical Chemistry](#)

[Journal of Applied Laboratory Medicine](#)

[Critical Reviews in Clinical Laboratory Sciences](#)

[Clinical Biochemistry Journal](#)

[Scandinavian Journal of Clinical and Laboratory Investigation](#)

The joint IFCC / EFLMEuroMedLab meeting is taking place in Brussels May 18-22, 2025. The venue is the Brussels Expo. More information can be found [here](#). The provisional programme is [here](#).



2024 Nobel Prizes

Physiology or Medicine: Awarded to Victor Ambros and Gary Ruvkun “for the discovery of microRNA and its role in post-transcriptional gene regulation”. MicroRNAs (miRNA) are critical in controlling the translation of protein coding genes in humans and mammals. Current estimates suggest that about 30% of human genes are regulated by miRNA. They play a vital role in biological processes which include cell growth and differentiation and apoptosis, cell to cell interactions and homeostasis. Dysregulation of miRNA production can result in numerous pathologies, especially cancer initiation and progression, by compromising regulation of cell growth. Active research is ongoing to develop therapies using miRNA strands to prevent tumorigenesis. Some of these are in trial phase but none have been licensed to date.

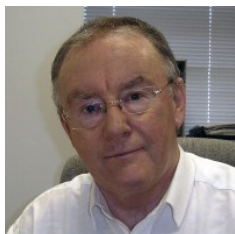
Chemistry: Awarded to David Baker “for computational protein design”, and Demis Hassabis and John Jumper “for protein structure prediction”. Prof. Baker is a US biochemist based in the Howard Hughes Medical Institute and the University of Washington. Profs. Hassabis and Jumper work at Google Deep Mind in London. Hassabis is a co-founder of the company. Both Hassabis and Jumper developed an artificial intelligence program they named AlphaFold2 which can predict a protein’s 3-D conformation based on its sequence of amino acids. Linking this information with function has the potential for development of major advances in therapeutics. The AlphaFold algorithm is open-source and has been utilized by hundreds of labs internationally.

Professor Baker developed a computerised method to create proteins not previously known, many of which have newly discovered functions. Construction of new proteins has great potential for development of novel pharmaceuticals. Prof. Baker’s research has resulted in developing proteins that neutralize viruses and target cancer cells. In addition, his work resulted in a COVID-19 vaccine based on a computer-designed protein. His work is also open-source.

Physics: Awarded to John J Hopfield and Geoffrey E Hinton "for foundational discoveries and inventions that enable machine learning with artificial neural networks". Prof. Hopfield, an Emeritus Professor in Princeton University, developed computational neural networks which had the ability to associate different inputs, combine them and arrive at connections which provide enhanced information, a novel approach when compared to the limited practice of examining large amounts of data statistically. The process mimics, to an extent, the human brain's function of integrating separate inputs to form a connection. e.g. a date and a historical event.

Geoffrey Hinton, Emeritus Professor at the University of Toronto, was instrumental in developing artificial neural networks, the technology behind the huge advances in machine learning leading to the development of programs such as ChatGPT. He built on the work of Hopfield by developing an algorithm that lets neural networks learn and formulate responses based on the input of vast amounts of data. He has earned the name ‘Godfather of AI’. He has also been called an ‘AI Doomer’. Having worked with Google to develop their AI platform, he resigned in 2023 alarmed at the rate AI was developing. His fear is that the exponential rate of AI integration into society is an existential threat to humanity. At a basic level, use of AI in generating and disseminating fake news, for example, is an early indication of its pernicious effects. Opinions are divided, however, on AI’s possible malign influence. Time will tell. [An interview with the first computer scientists to transmit a message between remote computers on October 29th 1969 can be found [here](#). This ultimately led to the birth of the internet we know today].

All three of these prizes have AI as a common denominator. Without any borders, use of AI, machine learning and analysis of big data encourages cross-disciplinary scientific research and development. Sharing the data benefits everyone.



Dr. Joe McPartlin B.Sc. (NUI), M.Sc.
Ph.D. (NUI), FRCPath, Dip. Cancer
Research Techniques (U.I.C.C.) (GENEVA)

Joe McPartlin died on the 3rd of October, 2024 aged 72. Many will remember Joe, both within the ACBI and beyond, for the multilayer character he was. He was born in Phibsboro Dublin, one of five siblings. Joe took on his parents' advice "do your best" with relish. His brother, Peter, remembers that Joe excelled in school, in sport, at work, and he especially did his best for family, friends and neighbours. He became a first class hurler, an accomplished guitar player and a highly respected and recognised scientist. His love of music came to the fore when, as a patient in St. James's Hospital Dublin, he met and became friends with Donal Lunny, a fellow patient. Together they recorded about 20 songs on mobile phones from Joe's bedside. The recordings became known as the St. James's Infirmary Sessions and can be listened to on YouTube.

Joe became the first of the McPartlin generation to go to college. He qualified from UCD (Earlsfort Terrace) in 1973 with a BSc in Biochemistry. After qualifying he successfully completed a PhD in 1980 at the Mater Hospital (*The effect of PTH on bone enzyme activity: a quantitative cytochemical study*) under the guidance of Professor David Powell, Consultant Endocrinologist. The degree was conferred by the NUI in 1980.

He subsequently moved to St. James's Hospital where he joined Professor John Scott and Professor Donald Weir and their team to work on the biochemistry of homocysteine, folic acid and vitamin B₁₂. Here he contributed to the seminal work on the influence of folic acid on the pathophysiology of neural tube defects (NTD), including spina bifida, and featured on many publications related to this work. The findings have been adapted globally and have contributed significantly to lowering the risk of NTDs developing during early pregnancy. The current standard advice for all women entering pregnancy is to supplement with folic acid. The group also published important work on food fortification with folate and currently over 70 countries have adopted this practice. The impact of this research on reducing infant morbidity and mortality associated with NTDs has been profound. His research publications have been cited over 3,000 times.

Joe was never afraid to buck the trend when he felt it needed to be. One issue that troubled him was the dominant role cholesterol played in cardiovascular health. He felt the association was over-simplified and other factors were being shoved aside. He spoke passionately about this and gave several presentations outlining his arguments.

Another issue that exercised him was the pending decision to locate the new National Children's Hospital on the St. James's Hospital site. He (and others) felt this was wrong and outlined his reasons by sending an open email to the heads of all departments in the Faculty of Health Sciences related to St. James's Hospital. Despite these efforts, though, permission was subsequently granted in 2016. The email can be viewed on the Jack and Jill Children's Foundation website.

The Trinity Biobank was established in 2004 in the Trinity Translational Medicine Institute, located in St. James's Hospital, and Joe subsequently became its Director. The Biobank's remit is to ensure proper processing, storage and distribution of biosamples relevant to epidemiological and clinical research across the TCD and St. James's Hospital sites. Joe established standardised procedures for these processes and ensured they adhered to internationally accepted harmonisation guidelines. He remained in this post until he retired.

Apart from his scientific endeavors, Joe had a lifetime interest in theatre and performed in many plays. He also turned his hand to directing several productions. He was a member of the Sandyford Little Theatre Company and later played a pivotal role in co-founding the Mill Theatre in Dundrum. The theatre opened in 2005 and Joe was appointed to its board of directors.

Joe will be remembered by all who knew him for his many great qualities, including his contagious laugh and infectious sense of humour. In particular he was a loving father to Myra and Caitríona. He will be endlessly missed by them, by his granddaughter Robyn, his brothers Jim, Peter, Fran and Gerard, and by his extended family, friends, and colleagues.

Scíth a ligean go sámh.



IEQAS Annual Conference 3rd Oct 2024, Ashling Hotel, Dublin

Report by Micheál Ryan, Senior Clinical Biochemist, University of Limerick

First Plenary Session

Dr. Peadar McGing opened the conference with a call out for all Irish clinical Laboratories to consider enrolling with IEQAS, their national external quality assessment scheme provider. He highlighted the value of the scheme and the quick response time to queries provided by the dedicated IEQAS office staff. Dr. McGing gave a special mention to Patricia Howley on her retirement. Patricia has spent 25 years as Operations and Quality manager at IEQAS and she was wished a very happy and healthy retirement.



Prof. Martin Cormican, Clinical Lead for the Laboratory Services Reform Programme, was warmly welcomed to the conference, where he presented a detailed overview of the Draft Strategic Plan for Laboratory Service Reform.

He outlined the plan's core principles and objectives, stressing the importance of collaboration and compromise among all stakeholders. He described the strategic plan as a "starting point" that would serve as a roadmap for the future of laboratory medicine in Ireland. Notably, the scoping process revealed public perspectives on laboratory professionals, especially regarding cases where a laboratory might decline a test request from a patient's GP. This feedback underscored the need to enhance public awareness of the expertise offered by laboratory professionals and the crucial role of laboratory medicine in the patient care journey. Addressing this issue, Prof. Cormican highlighted the importance of establishing clear national guidelines on test refusals and ensuring sufficient capacity regulation.



A key recommendation from the review group is the development of service networks, rather than isolated laboratories, to enhance resilience. Regarding the repatriation of tests currently sent abroad, Prof. Cormican stated that the aim is to centralise these tests within a single National lab, rather than across multiple facilities.



It was stressed that for the Health Service Executive (HSE) to adopt these recommendations, senior HSE management must view the plan as a credible roadmap for the future. He also noted that providing patients with direct access to their test results—a practice already common in several countries—will soon become a priority in Ireland.

Following this forward-looking vision for laboratory medicine, attendees engaged in a lively Q&A session before breaking for coffee with plenty of insights to discuss.

The second plenary session was opened by Dr. Ann Leonard & Ms Caroline Murray from the Laboratory Medicine Innovation Hub (LMIH) at Tallaght University Hospital.

They provided an insight into a pilot programme to review Pathology practice in Ireland which was initiated by the LMIH in conjunction with Pre/Post Analytics & Laboratory Medicine Society (PALMS). An audit tool was kindly provided by the NHS Getting It Right First Time (GIRFT) team, which was adjusted for an Irish context.

Six large teaching hospitals were invited to participate in the pilot and the audit tool was sent to participants in July 2024. The returned completed audit tool data was reviewed for completeness and checked for accuracy. Variation in the requisition of common analytes from primary care formed part of the initial analysis of the data. Dr. Leonard and Ms Murray provided evidence of the variation across sites in HbA1c, Vitamin D, BNP and TSH test requisition, using Sodium as the denominator. (e.g. HbA1c requests per 1000 GP Sodium requests). The requisition patterns in Ireland were then compared to those generated by the NHS GIRFT team.

According to Dr. Leonard, the data reviewed to date has been interesting with important trends and variations in practice identified. Follow up interviews with participating hospital sites are planned in Autumn 2024 with a further data 'deep dive'. It is then planned to extend the audit to additional hospitals across the country and widen its remit beyond Clinical Chemistry to other laboratory disciplines. Scientists who wish to participate or help with this audit are encouraged to contact the team through PALMSoc@tcd.ie.

Following this clinical chemistry-focused presentation, Dr. Alana Lawlor provided an enlightening talk regarding the clinician-patient interaction in the Granby Clinic, which provides a primary care service for the homeless and those suffering from addiction. Dr. Lawlor explained the needs of this patient cohort and although a younger population by age they are, in general, physiologically much older. The importance of providing as comprehensive a consultation as possible with patients, on their first visit to the clinic (getting it right first time!), was emphasized as these patients can prove very difficult to follow-up.



From a laboratory perspective, the requirement to provide more extensive testing for this patient cohort in comparison to standard primary care providers is wholly justified.

Dr. Lawlor described the potential for development of an Infectious Disease Surveillance Unit which will rely on the use of quality assured Point of Care Devices. She was grateful to learn

that the expertise was available within clinical laboratories to support the validation of these devices when required.



Following a delicious lunch, it was time for the Clinical Chemistry workshop. The first talk of this session was given by Dr. Lucille Kavanagh, Mater UH, on Renal Stone Analysis. Dr. Kavanagh provided a comprehensive overview of renal stone epidemiology, causes, types (composition), management/treatment options and stone analysis with associated reporting procedures (great learning material for any students in the audience!).

Dr. Kavanagh referred to the European Association of Urology Guidelines on Urolithiasis (2024) which recommend that

renal stone analysis be performed on all first-time stone formers. Further reference was made to the NICE guideline [NG118] which advises that stone analysis be considered for adults with ureteric or renal stones.

Ms Lorraine McGovern, Letterkenny UH (LUH), provided the next talk on their evaluation and implementation of the new Roche Elecsys sFlt1/PLGF ratio in the diagnosis and management of pre-eclampsia in Letterkenny UH.

Ms McGovern opened her comprehensive presentation by giving an overview of pre-eclampsia and its pathophysiology (with special reference to HELLP syndrome) and referred to its classification as provided in the Clinical Practice Guideline for the Diagnosis and Management of Severe Pre-eclampsia and eclampsia.

NICE DG49 supports the use of the sFlt-1/PLGF ratio to allow stratification of patients into low-risk and increased risk of developing pre-eclampsia.

The study itself was performed in two phases. Phase 1 involved verification of the two assays on the Roche Cobas 801 in accordance with ISO 15189 standards and CLSI guidelines for assay verification. This phase also included an assessment of the clinical agreement of the calculated ratios. In the second phase of the study, the ratio was made available to the obstetrics team on a pilot basis and included in the primary pre-eclampsia toxemia (PET) panel of tests which are performed on query pre-eclampsia patients > 20 weeks gestation.



The data generated during the study period showed that the median sFlt-1/PLGF ratio was significantly higher in pre-eclampsia patients compared to non-pre-eclampsia patients with an AUC of 0.9 for diagnostic accuracy. The study data was consistent with the findings from both the PROGNOSIS study by Zeissler et al. (2019) and the INSPIRE study by Cerdeira et al. (2019).

Ms McGovern concluded that the introduction of the sFlt-1/PLGF ratio would be a beneficial adjunct to the pre-eclampsia diagnostic algorithm at LUH with more accurate differentiation of patients at high risk of developing pre-eclampsia. Despite the high cost per reportable of this

ratio, it was asserted that this cost of testing would be offset (for the hospital) by the savings from unnecessary hospital admissions of patients with a low risk of developing pre-eclampsia.

Ms. Noreen Montgomery, Chief Medical Scientist, Clinical Biochemistry in Sligo UH provided a thought-provoking presentation on a Near Patient Testing (NPT) Quality Improvement (QI) Project relating to the introduction, verification, implementation and on-going audit of additional Blood Gas analysers across different clinical areas of the Hospital.

Ms. Montgomery emphasised how the 2021 Guidelines for Safe and Effective NPT were hugely important to guide the implementation of this QI project. She highlighted the challenges when undertaking a project that goes outside the laboratory and one which requires a multidisciplinary approach to ensure a successful and sustained quality improvement.

As part of the post implementation verification and training audits, poor compliance was indicated, where the patient identifiers (PCNs) were being omitted by operators in the ED. Ms Montgomery highlighted the different attempts, in partnership with the clinical facilitator in the ED, made to improve compliance. This was central to changing the “culture” around the use of the POC Blood Gas analysers. As indicated by Ms. Montgomery real and sustained change takes time and engagement with all stakeholders.

Dr. Peadar McGing, IEQAS chair and retired Principal Biochemist Mater UH, provided the penultimate talk of this session and it was a real treat. Peadar described his personal journey when becoming a patient and the biochemical deviations that he endured.

His initial and self-determined presentation was that if he closed his left eye, vision through the right eye was partly blurred. Further investigations included visual field testing, neurological examinations, blood tests and CT scans, which underlined the multi-disciplinary approach required. As Peadar reminded us, ‘ruling out’ is just as important as ‘ruling in’ a diagnosis. ESR and CRP blood tests ruled out Giant cell arteritis as a cause of his symptoms. Pituitary function blood tests helped to rule out a secretory pituitary adenoma.

An MRI of brain revealed a mass near the pituitary which was pressing against the optic chiasm. This was subsequently surgically removed and identified as a benign craniopharyngioma.

He described his post-op period in ICU, with an initial rising urine output, which was transient, and did not result in development of Diabetes Insipidus. Magnesium and Potassium supplementation was also necessary, even though Peadar, with his Biochemist hat on, stated that these were within their reference intervals pre-supplementation; ICU protocols trumped his opinion on this occasion.

A common late presentation of transsphenoidal surgery is SIADH, which Peadar unfortunately developed. He explained how his regime of fluid restriction was particularly difficult with the polypharmacy required post-op and also his general tea drinking ‘addiction’! Thankfully, his sodium level bounced back to normal and Peadar quickly turned his attention back to his master’s athletics career, with great success.

The final presentation of this workshop was given by Ms. Bernadette Jackson, Naas General Hospital (IEQAS specialist advisor).

Ms. Jackson commenced her presentation by outlining the benefits of being enrolled on the IEQAS schemes, with particular reference to the use of residual patient pooled samples which



ensures commutability.



She proceeded to give an overview of the reports provided by IEQAS, including the generation of the z-score and the flagging system used for ‘out of consensus’ analytes.

She included report examples that highlighted pre-analytical, analytical and post-analytical errors in the processing of EQA samples.

Ms. Jackson concluded by underlining the need for participants to make contact with IEQAS when changing platforms or assay methods, to ensure that analytes were registered correctly for performance monitoring purposes.

The IEQAS conference organising committee must be commended for the excellent programme that was offered, with attendees provided with plenty of food for thought, as they returned to their respective laboratories.



Patricia Howley (retiring) with new office staff member Yvonne Burke