Congress Abstracts

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SPE1

RECENT ADVANCES IN BLOOD-BASED BIOMARKERS OF DEMENTIA

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Neurological disorders, including Alzheimer's disease (AD), frontotemporal dementia (FTD), dementia with Lewy bodies (DLB) and vascular dementia (VaD), represent a significant global health challenge characterized by progressive cognitive decline and impaired daily functioning. In recent years, blood biomarkers have emerged as promising tools in clinical settings and clinical trials, offering potential for early detection, diagnosis, and monitoring of dementia-related disorders.

Amyloid-beta (Aβ) and tau proteins, central to AD pathology, have been extensively studied. Blood levels of phosphorylated tau and the Aβ1-42/Aβ1-40 (ratio) are linked to increased risk and progression of AD, making them tools valuable for early screening. Diagnostic biomarkers for non-AD disorders are also advancing.

Neurofilament light chain (NfL), released during neurodegeneration, has emerged as a key biomarker across dementia types, including AD, VaD, DLB, and FTD. While NfL may be less useful for diagnostic purposes, it can serve as a marker of disease progression, prognosis, and treatment response.

Neuroinflammation plays a critical role in dementia pathology. Glial fibrillary acidic protein (GFAP), reflecting astroglial activation, and YKL-40, sTREM1, and sTREM2 have shown associations with cognitive decline. However, just like NfL these biomarkers may not be suitable in the context of diagnosis due to their unspecific nature.

Despite the promise, challenges remain in validating and implementing blood biomarkers in clinical practice. The heterogeneity of dementia requires understanding of the specific biomarkers for each condition. Factors such as comorbidities, age, and genetics influence biomarker levels, necessitating clear guidelines.

In conclusion, blood biomarkers offer transformative potential for diagnosing and managing dementia. As personalized medicine advances, integrating biomarker analysis into clinical practice could improve early detection, intervention, and patient outcomes.

SPE2

PRE-ANALYTICAL PITFALLS IN BIOMARKERS ALZHEIMER'S DISEASE

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Bodily fluid biomarkers detected in the cerebrospinal fluid or the blood plasma aid in dementia risk assessment, diagnosis, prognosis and monitoring. Several fluid biomarkers for Alzheimer's disease are integrated into clinical care. Efforts are ongoing to discover and validate novel biomarkers for Alzheimer's disease and other forms of dementia. However, sample handling factors in the pre-analytical phase, from sample collection to biobanking, can affect proteins measurable in bodily fluids, potentially impacting biomarker discovery, validation and interpretation. In this presentation I will discuss challenges and potential consequences of pre-analytical factors during biomarker discovery, validation and implementation for Alzheimer's disease and other forms of dementia.

SPE3

SUCCESSFUL TREATMENT OF BRAIN ABCESS CAUSED BY NOCARDIA FARCINICA WITH CEFTRIAXONE DESPITE IN VITRO RESISTANCE: A CASE REPORT AND REVIEW OF DIAGNOSTICS AND THERAPEUTICS CHALLENGES

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Objectives
*Nocardia spp.*is an environmental Gram-positive bacterium that may cause opportunistic infections in humans. Nocardial brain abscesses are rare and the result of dissemination from another primary lesion, essentially observed in immunocompromised hosts. The diagnosis relies on direct examination and bacterial culture, but antibiotic susceptibility testing (AST) remains controversial due to technical challenges, limited standardisation, and a paucity of studies correlating in vitro sensitivity with clinical efficacy. Management is challenging and usually based on expert opinion as robust evidence is limited. The objective is to highlight the microbiological and clinical challenges in diagnosing and managing *Nocardia* infections, with a focus on brain abscesses caused by *Nocardia farcinica*, through the example of a successfully treated clinical case.

Material and Methods
We present the case of a 30-year-old immunocompromised female diagnosed with a large frontal brain abscess caused by *Nocardia farcinica*. Two antimicrobial susceptibility tests (AST) were performed: the first at the beginning of treatment using the Etest method, and a second at the French Nocardiosis Reference Center, employing the broth microdilution method.

Results
Antimicrobial susceptibility testing initially conducted using the Etest method showed sensitivity to ceftriaxone, but subsequent testing with the broth microdilution method revealed resistance. Despite the in vitro resistance, the patient was successfully treated with high-dose ceftriaxone for 12 months, achieving full clinical and radiological recovery, and remains well at 18 months of follow-up.

Conclusion
There is variability in antimicrobial susceptibility tests for nocardiosis and limited evidence to guide clinical decisions making. The interpretation of susceptibility testing of *Nocardia spp.* should be taken with precaution, as it has not been rigorously correlated with clinical outcomes.

SPE4

BIOCHEMICAL BIOMARKERS FOR MTBI

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Mild traumatic brain injury (mTBI) is commonly defined as “a brain trauma secondary to the transmission of a kinetic energy to the head responsible for a transient cerebral dysfunction”. Many different mechanisms of injury can be responsible for the occurrence of mTBI explaining why mTBI remains a common cause of emergency department admissions. Despite its high prevalence, diagnosis of mTBI remains challenging relying primarily on clinical assessment and imaging techniques such as CT-scans. The wide variety of symptoms and the pressure from public authorities to reduce imaging techniques has led to the development of biochemical biomarkers to easier this diagnosis.

S100B as well as the "GFAP/UCH-L1" mTBI test are now on the market to reduce the burden of computed tomography (CT) scans by ruling out the presence of mTBI. These biomarkers have several pros and cons as well as different preanalytical constrains. In this talk, we will review international and Belgian data on these biomarkers and discuss about the challenges and opportunities of introducing these biomarkers into routine practice. Perspectives other biochemical biomarkers will be given.

SPE5

THE RAPIDLY EVOLVING LANDSCAPE OF THERAPEUTIC TRIALS IN ALZHEIMER DISEASE: HOW PARTICIPANTS SCREENING HAS BECOME KEY TO SUCCESS

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Until 2011, a definite diagnosis of Alzheimer's disease (AD) could only be made after autopsy and confirmation of amyloid and tau pathology in the brain. Neurologists could only give the diagnosis of probable AD to patients with dementia. The absence of biomarkers to confirm the biological diagnosis made it impossible to diagnose AD early, prior to dementia. The development of neuroimaging and fluid biomarkers (first in the cerebrospinal fluid, then in plasma) has conducted to (1) revising the definition of Alzheimer's disease and (2) accelerating the conduct of therapeutic trials targeting either amyloid or tau pathology.

The Louvain Aging Brain Lab has been among the first in Europe to describe the spatio-temporal progression of Alzheimer's pathology in living humans, using specific radiotracers and positron emission tomography to detect amyloid and tau deposits in the brain. We have "brought to life" neuropathological classifications, obtained at post-mortem, by transposing them into brain imaging classifications, applicable to detect Alzheimer's pathology before the onset of symptoms. More recently, the development of blood-based biomarkers has allowed investigating the preclinical stage of the disease, screening for Alzheimer's pathology in older adults before cognition starts declining.

This work is of particular importance in the context of ongoing therapeutic trials aiming at preventing the onset of AD in non-demented individuals with evidence of Alzheimer's pathology. The first anti-amyloid therapies have been recently approved in the USA, China, Japan, England, and could soon be approved in Europe too.

SPE6

A COMPARISON BETWEEN PROXIMAL AND DISTAL CSF SAMPLING SITES IN PATIENTS WITH EXTERNAL VENTRICULAR DRAINS

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Introduction

Routine cerebospinal fluid (CSF) sampling in patients with external ventricular drains (EVDs) is a standard neurosurgical practice to screen for infections and steer CSF diversion management. Although proximal CSF sampling (through CSF aspiration from the tubing) permits analysis of fresh intraventricular CSF, it carries a risk of iatrogenic infection, hemorrhage and catheter blockage, contrary to distal CSF sampling (collected passively from the fluid chamber). This study assesses the agreement in CSF characteristics obtained through proximal and distal sampling in EVD patients.

Methods
An open, prospective, monocentric study was conducted between January 2022 and December 2023. All patients undergoing EVD placement were eligible, irrespective of age and etiology. CSF was sampled twice weekly until EVD removal as per routine institutional practice. Samples were obtained synchronically proximally and distally. The primary endpoint was the agreement between sampling methods of the white cell count as quantified with the intra-class correlation (ICC), the within standard deviation and mean absolute difference, and visualized using a Bland-Altman plot. Secondary endpoints were the inter-method agreement of lactate, glucose, total protein and microbial culture and the evaluation of the agreement over time.

Results
61 patients (2x197 samples) were analyzed. An ICC of 0.731 (95%CI: 0.650;0.796) was observed for white blood cell counts between proximal and distal samples. Microbial culture results showed perfect agreement. Strong ICC's were found for lactate (0.966), glucose (0.822), and total protein (0.910). These relations were maintained over time (>4 weeks). Although there was a relatively small number of infectious samples (n=10), study strengths were the real-world setting, inclusion of all ages and etiologies and the longitudinal sampling over time.

Conclusion
To minimize iatrogenic complications of proximal EVD sampling, routine infectious screening on distal CSF samples from the fluid chamber is a reliable alternative.

SPE7

FLUID BIOMARKERS IN MULTIPLE SCLEROSIS: CURRENT & FUTURE APPLICATIONS

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Fluid biomarkers hold diagnostic and prognostic implications in Multiple Sclerosis. They potentially contribute to therapeutic decision making. In this presentation the implications of blood and CSF biomarkers in diagnosis, prognistification and treatment of people with MS will be discussed.

C1

THE VALUE OF TDM FOR BETA-LACTAM ANTIBIOTICS (FOCUSING ON CEFTAZIDIM-AVIBACTAM)

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Objectives
The limited number of antibiotics in development, the increase in resistance, and the high mortality rate related to infections emphasize the importance of correct antibiotic use to preserve their effectiveness as much as possible. Beta-lactam antibiotics are the simplest and most commonly used antibiotics due to their broad therapeutic-toxic spectrum. However, changes in pharmacodynamics (PD) and pharmacokinetics (PK) in patients, for example in intensive care units, complicate the correct use of these antibiotics. Therefore, various guidelines recommend individualized dosing of β-lactam antibiotics using TDM (therapeutic drug monitoring) in these patient groups. Ceftazidim-avibactam is a highly effective combination that is active against MDR aerobic gram-negative microorganisms. However, there are currently no official dosing recommendations for this antibiotic in patients undergoing CVVH in the ICU (intensive care unit). This study will investigate whether TDM of ceftazidime-avibactam addresses this issue and will map the evidence for monitoring ceftazidim-avibactam.

Material and Methods
Based on a literature study via PubMed, international guidelines, and evidence-based clinical resources, we examined recent and relevant guidelines, recommendations, systematic reviews, meta-analyses, randomized controlled trials, and current practices in Belgian hospitals.

Conclusion
A limited number of large prospective studies shows that routine monitoring of β-lactam antibiotics positively impacts achieving PK/PD targets. However, more knowledge is needed for proper implementation, including optimal PK/PD targets, toxicity thresholds, and rules for interpreting TDM results. Furthermore, large RCTs evaluating the impact on achieving favorable clinical outcomes are lacking. For ceftazidim-avibactam, TDM may be beneficial in guiding antibiotic dosing for patients undergoing continuous renal replacement therapy. However, the evidence is currently limited due to a lack of knowledge about the PK of avibactam in patients on CVVH and insufficient data on toxicity. Finally, the low reimbursement by the Belgian National Institute for Health and Disability Insurance (RIZIV) and the new IVDR regarding in-house developed methods pose challenges for monitoring ceftazidim-avibactam.

Competing interests: The authors have no relevant financial or non-financial interests to disclose.

C2

NON-INVASIVE BILIRUBIN MEASUREMENT FOR NEONATES: VALIDATION OF TRANSCUTANEOUS BILIRUBINOMETER JM-105 AND METHOD COMPARISON TO INVASIVE BILIRUBIN MEASUREMENT METHOD

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Objectives
Visual assessment is the most used non-invasive screening for neonatal hyperbilirubinemia. Transcutaneous bilirubin (TcB) is a more objective way to estimate plasma total bilirubin (TB) in newborns with a gestational age of more than 35 weeks according to the AAP and NICE guidelines. The aim of this study was to validate the non-invasive transcutaneous bilirubinometer JM-105 and compare it with the formerly used invasive bilirubin measurement using Cobas Pro integrated solutions (Roche).

Material and Methods
Forty-seven neonates, aged 24–96 hours with a gestational age of 37–41 weeks, were included. Each neonate underwent a triple TcB measurement with the JM-105. Blood was taken at the same time and TB was measured using the fully validated BILT3, Bilirubin Total Gen.3 (Roche) on Cobas Pro integrated solutions (Roche). Analytical and clinical performance of TcB were evaluated and TcB was correlated with TB. Significant hyperbilirubinemia was defined as TB values ≥ 95th percentile of the Bhutani nomogram.

Results
In 47 triplo TcB measurements, six (13%) high standard deviation errors (HSDE) occurred according to the manufacturer's prescriptions (> ± 1,5 mg/dL). Examining the HSDE TcB measurements, there was no statistically significant relationship between occurrence of HSDE and significant hyperbilirubinemia (χ^2-test with p=0,17). TcB measurements with a HSDE should not be interpreted and were therefore excluded from further analysis. The JM-105 inter-assay CV ranged from 0,00% to 14,56% (mean 6,17%), meeting the minimum EFLM CVa criteria (15,1%). TcB and TB method comparison using Pearson correlation showed a very high correlation (0,90), and Passing-Bablok regression indicated no significant constant or proportional bias. The mean difference between the two methods, as shown by the Bland-Altman plot, was 0,44 mg/dL 95%CI [0,04–0,84]. The JM-105 achieved an AUC of 0,85 95%CI[0,65–1,00] for detecting significant hyperbilirubinemia. If used as a screening tool with 100% sensitivity for significant hyperbilirubinemia, TcB values ≥ 11,7 mg/dL should be confirmed with a TB measurement. TcB values ≥ 15,6 mg/dL are diagnostic for significant hyperbilirubinemia.

Conclusion
The transcutaneous bilirubinometer JM-105 demonstrated good analytical and clinical validation parameters, indicating that it can be used as a safe and accurate screening tool for bilirubinemia management in neonates.

Competing interests: The authors have no relevant financial or non-financial interests to disclose.

C3

DRUGS OF ABUSE IMMUNOASSAY SCREENING: QUICK AND DIRTY OR DIAGNOSTICALLY VALUABLE?

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Objective
Our aim was to evaluate the performance of a semiquantitative immunoassay on the Roche Cobas Pro as a potential tool for early detection of drug abuse.

Material and methods
A retrospective data analysis from 1 January to 31 December 2023 was performed. A total of 3182 urine samples, initially screened for Drugs of Abuse (DAT II immunoassay) on the Roche Cobas Pro c503, were included. Cutoff values according to the Substance Abuse and Mental Health Services (SAMHSA) guidelines were used for the respective drugs, except for tetrahydrocannabinol (THC), which was lowered to 20 ng/mL (1). Among these samples, 1179 were further analysed using LC-MS. We calculated the diagnostic performance of the immunoassays, including sensitivity and specificity. Additionally, for each sample the urinary creatinine (Ucr) concentration was measured with the CREP2 reagent on the Roche Cobas Pro c503 to detect possible sample manipulation. Ucr levels < 40 mg/dL were considered “suspect” for manipulation, while Ucr levels < 20 mg/dL were considered “evident” for manipulation (2).

Results
The sensitivity and specificity for each drug were calculated to be respectively 96.1% and 59.4% for amphetamines, 99.5% and 100% for cocaine, 100% and 35.1% for methadone, 100% and 97.0% for opiates, and 100% and 76.9% for THC. For amphetamines and methadone, 34.5% (29/84) and 28.6% (18/63) false positive samples respectively, could not be explained by known cross-reactivities. Also, all false positive samples for opiates (5) and THC (15) remained unexplained. Furthermore, 1.2% (6/497) negative screened samples with the immunoassay were confirmed positive by LC-MS (5 positive for amphetamines and 1 for cocaine). Other negative screened samples without confirmation on LC-MS were assumed negative. Approximately 9.6% (306/3182) samples were considered “suspect” for manipulation, of which 5.2% (166/3182) samples were considered to be “evident” for manipulation. The median Ucr was calculated to be 127 mg/dL.

Conclusion
The semiquantitative immunoassay on the Roche Cobas Pro demonstrated strong correlation with the LC-MS results, confirming its reliability and effectiveness as an early screening tool for drug abuse.

References
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(2) Love, S. A., Seegmiller, J. C., Kloss, J., & Apple, F. S. (2016). Urine Creatinine Concentrations in Drug Monitoring Participants and Hospitalized Patients. J Anal Toxicol. 2016;40:659–662. doi:10.1093/jat/bkw092.

C4

USE OF LABILE HBA1C AS A SCREENING TOOL TO MINIMIZE CLINICAL MISINTERPRATION OF HBA1C

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Objectives
Hemoglobin A1c (HbA1c) is an established tool in the diagnosis and follow-up of patients with diabetes. However, in some patients the interpretation of HbA1c results faces challenges due to additional biological variation or non-steady-state conditions. This study aimed to demonstrate the value of the L-HbA1c/HbA1c-ratio as a tool to flag HbA1c results, which do not reflect average glycemia “as expected” in routine clinical practice.

Methods
450 samples of unique patients were selected based on the L-HbA1c/HbA1c-ratio determined on a Tosoh G8 analyzer resulting in a group with a high ratio (≥0.50), a group with a low ratio (≤0.27) and a group with a normal ratio (0.27–0.50). The relationship between HbA1c and glycemic markers (fructosamine and random glucose) was established for all ratio groups.

Results
The correlation between HbA1c and glycemia (random glucose and fructosamine) differs significantly between the ratio groups. For the same HbA1c level random glucose levels and protein-corrected fructosamine are higher in the high ratio group compared to the normal and low ratio groups, pointing to an underestimation of the glycemic status by HbA1c in patients with high L-HbA1c/HbA1c-ratios. The sensitivity of a high ratio to predict a glycation gap lower than –1.5 NGSP units is 82% and the specificity is 65%.

Conclusion
The results of this study reveal the usefulness of the L-HbA1c/HbA1c-ratio as an additional check in the interpretation of HbA1c results in order to detect HbA1c results not reflecting glycemia as expected.

C5

IMPROVEMENT IN THE TURNAROUND TIME OF PTH(1-84) AS PART OF THE INTRAOPERATIVE PTH MONITORING FOR PARATHYROIDECTOMY

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Objective(s)
At present, parathyroidectomy is the only effective curative treatment for primary hyperparathyroidism. Intraoperative PTH (IOPTH) monitoring ensures complete removal of hyperfunctioning parathyroid tissue.[i] In order to avoid spurious PTH results [ii] and the risks this entails during surgery, our laboratory has decided to switch from rapid PTH STAT (2nd generation) assay to PTH (1-84) assay (3rd generation). As this change has taken us from a 9-minute automated analysis to an 18-minute analysis, we have investigated ways of improving the pre-analytical conditions to provide a result with the shortest possible turnaround time (TAT).

Materiel and Methods
Blood samples (n=30) were collected in Vacuette® K2-EDTA separator tubes (Greiner Bio-one International, Kremsmünster, Austria). Each sample collected was divided into 2 to allow comparison of two centrifugation methods: conventional centrifugation (2904 G for 8 minutes) and ultracentrifugation (centrifugation at 10,000 G for 1min30s).

Analysis of PTH(1-84) was carried out on the cobas® 8000 analyzer series cobas® e 602 module (Roche Diagnostics International ®, Basel, Switzerland). Method comparison was carried out in compliance with the EFLM's acceptability criteria.

Results
Ultracentrifugation has an overall bias of −0,34% [−6,90% – 6,22%] when compared with conventional centrifugation. This bias is lower than the EFLM's definition of acceptable bias (Optimal < 3,7%, Desirable <7,3%, Minimal <11%). Centrifugation method does not affect the quality of the results for PTH(1-84) analysis.

Passing-Bablok linear regression equation:

(Conventional centrifugation) = −0,7489 + 1,022*(Ultracentrifugation).

Alongside this, pre-coding (before the intervention) has also been introduced to save even more time.

Current TAT in lab: 3 minutes (encoding) + 8 minutes (pre-analytical phase) + 9 minutes (assay) = 20 minutes

TAT post modification: 3 minutes (encoding) + 1,5 minutes (pre-analytical phase) + 18 minutes (assay) = 19,5 minutes

Conclusion(s)
Implementation of enhancements at various stages of the pre-analytical and analytical procedures has resulted in a slight reduction in TAT while providing optimal analysis for IOPTH.

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C6

VERIFICATION OF A MODIFIED DATA-BASED LIPID PHENOTYPING ALGORITHM

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Objective
To validate a data-based dyslipidaemia phenotyping algorithm aiming to replace the current in-house agarose gel-lipoprotein electrophoresis method if the concordance is favourable.

Material and methods
A retrospective data validation study involving a sample size of 217 adult outpatients who underwent standard-of-care lipid testing. The input data for the algorithm incorporate elements from the algorithm developed by Sampson et al.[1], including triglycerides, total cholesterol, HDL-cholesterol (HDL-C) and Non-HDL-C which will generate the corresponding lipid phenotype according to the Frederickson classification. We additionally included apoB and apoB/non-HDL-C ratio to refine the classification. The results were compared to those obtained using agarose gel-electrophoresis (Sebia Hydrasys Lipogel®). Agreement between the two classification methods was evaluated using Cohen's Kappa statistics in Medcalc.

Results

Lipid Phenotype:	Algorithm vs. Lipogel®
Hypobetalipoproteinemia	4/5 (80%)
Type I chylomicronemia	1/1 (100%)
Type IIa hypercholesterolemia	3/11 (27%)
Type IIb combined hyperlipidemia	14/13 (108%)
Type III dysbetalipoproteinemia	4/4 (100%)
Type IV hypertriglyceridemia	127/122 (104%)
Type V mixed hyperlipidemia	24/26 (92%)
Normolipidemia	40/35 (114%)
	Total: 2x 217

A kappa value of 0.822 (95%CI 0.757–0.888) was obtained which corresponds to 'nearly perfect' agreement (defined as kappa 0.81–0.99).

Conclusion

Agreement between the two methods is very good (kappa: 0.822), which justifies transition to the less labour-intensive and cost-effective lipid test-based algorithm with more favourable TAT for dyslipidemia phenotyping. The modified algorithm is enhanced by the inclusion of ApoB to better distinguish between type I and type V dyslipidaemia, and apoB/non-HDL-C ratio to identify type III dysbetalipoproteinemia. Additionally, it can detect hypobetalipoproteinaemia.

References

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C7

THE VANCOMYCIN MIRAGE: LOW LEVEL IGM PARAPROTEIN INTERFERENCE CREATES A DIAGNOSTIC ILLUSION IN SIEMENS AG, ATELLICA CH® VANC ASSAY

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Objective

A 63-year-old patient underwent surgical intervention for bladder clot evacuation and right nephrostomy repositioning. Perioperatively, a vancomycin loading dose of 1500 mg was administered, followed by a continuous infusion of 500 mg/24h (eGFR (CKD-EPI) 41 mL/min/1.73m^2). Therapeutic drug monitoring revealed 24h post-loading dose toxic serum vancomycin concentrations (35 mg/L, ref. 20–25 mg/L), necessitating discontinuation of therapy. However, serum vancomycin levels sustained elevated for multiple days after therapy cessation, which raised the suspicion of analytical interference from an endogenous substance with the assay used (Siemens AG, Atellica CH® Vanc (PETINIA), REF. 11097511).

Methods & Materials

Fourteen days after discontinuing vancomycin, toxic vancomycin levels (40 mg/L) were still measurable. To determine the interference cause, the patient's medical history including medication use was reviewed.To confirm the absence of vancomycin, the latter sample underwent serial dilution (1:10), polyethylene glycol (PEG) precipitation and was assessed using different analytical methods in external laboratories, including evaluation of the free vancomycin fraction.

Results and conclusion
The serial dilution, PEG precipitation, and evaluation at different platforms confirmed that no vancomycin was detectable in the sample (<LOQ). The patient's medical history revealed a low-level IgM kappa paraprotein (serum total IgM 3.96 g/L, ref. 0.5–3.0 g/L) and negative rheumatoid factor. Therefore, selective IgM precipitation was performed using anti-IgM antiserum (Sebia). Vancomycin levels became undetectable confirming IgM paraprotein as the root cause of the interference. During the patient's hospitalization vancomycin was re-administered and TDM was successfully performed using an alternative assay in an external laboratory. Laboratories must remain vigilant regarding this interference, even with low levels of paraprotein, as it may delay appropriate treatment and compromise patient safety.

C8

DEVELOPMENT OF A NEW CLINICAL DIAGNOSTIC TOOL FOR CARDIOVASCULAR RISK ASSESSMENT BY LC-MS/MS

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Objective
Cardiovascular diseases (CVD) are the leading cause of mortality in Belgium, accounting for approximately one-third of annual deaths, or 31,000 deaths per year. Ceramides, which are bioactive lipids, are strongly associated with cardiometabolic conditions and play a crucial role in cellular processes such as apoptosis, inflammation, and atherosclerosis. Due to their involvement in these processes, ceramides could serve as diagnostic biomarkers for assessing cardiovascular risk.

First, we aim to develop a method for quantifying ceramides using LC-MS/MS to measure Cer (18:1/16:0), Cer (18:1/18:0), Cer (18:1/24:0), and Cer (18:1/24:1). Next, we plan to apply this method to well-defined clinical populations to demonstrate the feasibility of using these markers in a Belgian population. Our goal is to provide clinicians with new emerging markers to support existing parameters and scores, enhancing diagnosis and improving prevention.

Materials and Method
Quantification was achieved on a Nexera X2 UPLC (Shimadzu Corporation, Kyoto, Japan) coupled to a QT6500 mass spectrometer (Sciex, CA, USA). Chromatographic separation was performed on a Acquity UPLC BEH C18 130Å column (100 × 2,1 mm, 1.7 µm) (Waters, Massachusetts, USA). The mobile phases composition was H_2O and ACN:IPA (4:3) both containing 0,1% formic acid (FA) and 10 mM ammonium acetate. The samples were extracted by protein precipitation and then concentrated.

Results
Transitions were optimized for each ceramide, as well as the LC-MS parameters. After sample preparation in plasma, each ceramide showed good separation and resolution.

Different concentrations were tested for the calibration curves due to the biological concentration differences between Cer (18:1/16:0) and Cer (18:1/18:0) on one hand and Cer (18:1/24:0) and Cer (18:1/24:1) on the other.

Conclusion
The method optimization is nearly complete and will soon be analytically validated according to the guidelines provided by the Clinical and Laboratory Standards Institute (CLSI) (C62A) for use in the quantification of various ceramides.

C9

THERAPEUTIC MONITORING OF PATIENTS WITH HEREDITARY TYROSINEMIA TYPE I – A BELGIAN MONOCENTRIC EXPERIENCE

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Background
Despite published recommendations, therapeutic drug monitoring (TDM) of patients with hereditary tyrosinemia type 1 (HT-1) treated with nitisinone (NTBC) still faces some questions. According to the latter, the TDM of NTBC is based on the achievement of target values for NTBC and/or succinylacetone (SA). However, there is currently no available evidence supporting one monitoring approach over another. The chosen approach is often guided by local guidelines and the ability of laboratories to perform those analyses. In addition, current recommendations for dietary monitoring are based exclusively on the achievement of tyrosine (Tyr) and phenylalanine (Phe) concentrations in plasma. Few data are available on dried blood spots (DBS), which severely limits its use in home dietary monitoring of patients with HT-1.

Objective
This study aimed to evaluate the clinical utility of monitoring NTBC and key biochemical markers using DBS.

Material and Methods
This study presents a retrospective analysis of 12 patients diagnosed with HT-1 and treated with NTBC at the University Children's Hospital Queen Fabiola (HUDERF) in Brussels, Belgium, from January 2019 to June 2024. During that time, DBS, plasma, whole blood and urine samples from the 12 HT-1 patients were collected at the same time from each patient, during their follow-up visits. The following parameters were retrospectively collected: SA in DBS and urine, NTBC in DBS, alpha-fetoprotein (AFP) in serum, delta-aminolevulinic acid (d-ALA) in urine, Tyr/Phe in DBS and plasma.

Results
The study found that lower NTBC concentrations (<40 µmol/L) were often sufficient to control SA levels in blood and urine, suggesting that current guidelines might require adjustment. However, no significant correlation was found between NTBC levels and AFP or δ-ALA, indicating the need for further research. The study also highlights the challenges of dietary compliance among these patients, as well as discrepancies in Tyr and Phe measurements between DBS and plasma. The study's limitations include the small sample size and variability in sample collection timing.

Conclusion
The results emphasize the importance of individualized treatments and the potential benefits of DBS monitoring for patients diagnosed with HT-1, although the latter should be supplemented by plasma measurements for Tyr and Phe in critical cases.

C10

INTEGRATING BLOOD-BASED BIOMARKER ASSAYS INTO THE DIAGNOSTIC PATHWAY OF ALZHEIMER'S DISEASE: A BELGIAN SITUATION ANALYSIS

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Upcoming disease-modifying therapies (DMT) for Alzheimer's disease (AD) will require timely diagnosis. Blood-based biomarkers (BBBM) could facilitate and accelerate the diagnostic journey. However, the feasibility of implementing BBBM assays in Belgium is unknown.

Objectives
The aim of this project is to define the current Belgian AD diagnostic pathway, and to identify the needs, challenges and opportunities of integrating BBBM into it.

Material and methods
Stakeholders with a high interest in the BBBM integration and potential impact on its uptake in Belgium were selected and interviewed during the first half of 2024. Semi-structured questionnaires, tailored to each stakeholder group and including quantitative questions, were used during face-to-face or online interviews. Collected statements were thematically analyzed using the Braun and Clarke method.

Results
Stakeholder mapping led to 21 interviews with neurologists, geriatricians, psychiatrists, general practitioners (GPs), patient associations, lab and genetic-experts. The interviews revealed the heterogeneity of the Belgian diagnostic journey, including different referral and testing approaches. Consequently, the need for standardization and awareness was emphasized to facilitate AD timely diagnosis. Physicians agree that BBBM will likely be implemented in the AD diagnostic pathway, which will be facilitated by CE-IVDR claim and DMT availability. All stakeholders underline the importance of restricting the initial access to BBBM to AD specialists and to later extend it to GPs. The willingness-to-pay is expected to be at least equal to the cost of CSF testing.

Conclusion
The current AD diagnostic journey is heterogeneous. Although there is no drastic change required yet, there is a high demand for its standardization. BBBM might have a key role in the future diagnosis of Belgian AD patients. Implementation challenges include providing appropriate caregiver training, managing patients' expectations and raising awareness of BBBM in the AD community.

Acknowledgements: We acknowledge the interviewed participants for their time and their valuable insights.

Disclosure: This project has been initiated by Roche Diagnostics Belgium. YP was completing an internship in the medical affairs department of Roche Diagnostics. XK, JDK, FC are Roche Diagnostics employees.

C11

VALIDATION OF THE MAGLUMI FOR GASTRIN (GST) AND REVERSE T3 (RT3) DETERMINATION

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Objectives
Gastrin is a hormone that stimulates gastric acid secretion, and its measurement is crucial for diagnosing conditions like Zollinger-Ellison syndrome and chronic atrophic gastritis. Reverse T3 is an inactive form of triiodothyronine, and its levels are useful in evaluating thyroid function in conditions such as non-thyroidal illness syndrome and distinguishing types of hypothyroidism. The study aims to validate the analytical performance of the Maglumi (Snibe) for determining gastrin (GST) and reverse T3 (RT3) levels, and to compare these results with those obtained using standard laboratory methods.

Material and methods
The Maglumi, a chemiluminescent immunoassay analyzer, was evaluated for quantifying GST and RT3 in human whole blood/serum/plasma. An analytical evaluation was conducted at five concentration levels to validate intra- and inter-assay variation, trueness, and measurement uncertainty. The comparison was performed using 80 residual samples for GST and RT3. The laboratory methods for GST and RT3 were a radioimmunoassay (RIA) from DiaSource. Passing-Bablok regression and Bland-Altman tests were used for comparisons (MedCalc), and analytical validation was performed using Enoval (Arlenda).

Results
On the Maglumi, the maximum intra- and inter-assay CVs were 3.26% and 5.30% for GST, 1.87% and 2.53% for RT3, respectively. The maximum relative bias was 6.00% for GST and 4.20% for RT3. The maximum relative expanded uncertainty was 11.3 % for GST and 5.41% for RT3. The regression equation for GST was: GST Maglumi = −2.017 + 0.2233 GST RIA (95% CI of the intercept: −3.465 to −0.8477, 95% CI of the slope: 0.1902 to 0.2572). For RT3, the regression equation was: RT3 Maglumi = 0.02124+ 0.5187 RT3 RIA (95% CI of the intercept: 0.008949 à 0.03136, 95% CI of the slope: 0.4773 to 0.5630). A systematic and proportional difference was found between the two methods for both compounds, likely due to different antibodies used in the kits.

Conclusion
Maglumi device is accurate and correlates well with RIA lab method used before. Despite some variation in results, the diagnostic outcome remains consistent for both compounds. This device can aid emergency physicians in quickly identifying conditions related to abnormal gastrin and reverse T3 levels with confidence in the accuracy of the results.

C12

THE MEDCAPTAIN: A POINT-OF-CARE DEVICE FOR MAJOR CARDIAC BIOMARKER DETERMINATION

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Objectives
Concerns exist regarding the accuracy of point-of-care (POC) tests in emergency department (ED) settings compared to laboratory testing. This study aims to validate the Medcaptain Troponin I (hs-TnI), Heart Fatty Acid Binding Protein (HFABP), Suppression of Tumorigenicity 2 (ST2), and N-terminal Prohormone of Brain Natriuretic Peptide (NT-proBNP) assays, and to compare these results with routine laboratory methods.

Material and methods
We evaluated a new chemiluminescent immunoassay analyzer, the Medcaptain (Analis), for quantifying HFABP, hs-TnI, ST2, and NT-proBNP in human whole blood/serum/plasma. An analytical evaluation at three concentration levels was conducted to validate intra- and inter-assay variation, trueness, and measurement uncertainty. A comparison was performed using 23 residual samples for hs-TnI and NT-proBNP. The laboratory methods for NT-proBNP and hs-TnI were microparticle chemiluminescence immunoassays (CMIA) on the Alinity i analyzer. Passing-Bablok regression and Bland-Altman tests were used for comparisons (Medcalc), and analytical validation was performed with Enoval (Arlenda).

Results
On the Medcaptain device, the maximum intra- and inter-assay CVs were 7% and 8.7% for hs-TnI, 11% and 15.74% for NT-proBNP, 5.5% and 6.7% for ST2, and 3.2% and 6.4% for HFABP. The maximum relative bias was 12.8%, 20.4%, 5.8%, and 9.8%, and the maximum relative expanded uncertainty was 18.9%, 34.8%, 14.7%, and 14.3% for hs-TnI, NT-proBNP, ST2, and HFABP, respectively. The regression equation for NT-proBNP was: NT-proBNP Medcaptain = 104.02 + 1.01NT-proBNP Alinity (95% CI intercept: 50.27–280.90; 95% CI slope: 0.90–1.06). A small systematic difference of 2.3% on average was observed between the two methods. For hs-TnI, the regression equation was: hs-TnI Medcaptain = −685.26 + 1.83 hs-TnI Alinity (95% CI intercept: −1363.78–215.96; 95% CI slope: 1.66–2.07). A proportional difference of 42.2% was found between the two methods, likely due to different antibodies used in the kits.

Conclusion
POC testing using the Medcaptain device is accurate and correlates well with routine laboratory testing methods. However, troponin results exhibit significant variation due to a lack of standardization. Importantly, the diagnostic outcome remains consistent. This device can assist emergency physicians in quickly identifying cardiac injury with confidence in the accuracy of the results.

C13

PLASMA PHOSPHORYLATED TAU 217 (P-TAU217) PREDICTS AMYLOID-SS & TAU PATHOLOGY IN PATIENTS WITH (PRECLINICAL) ALZHEIMER'S DISEASE (AD)

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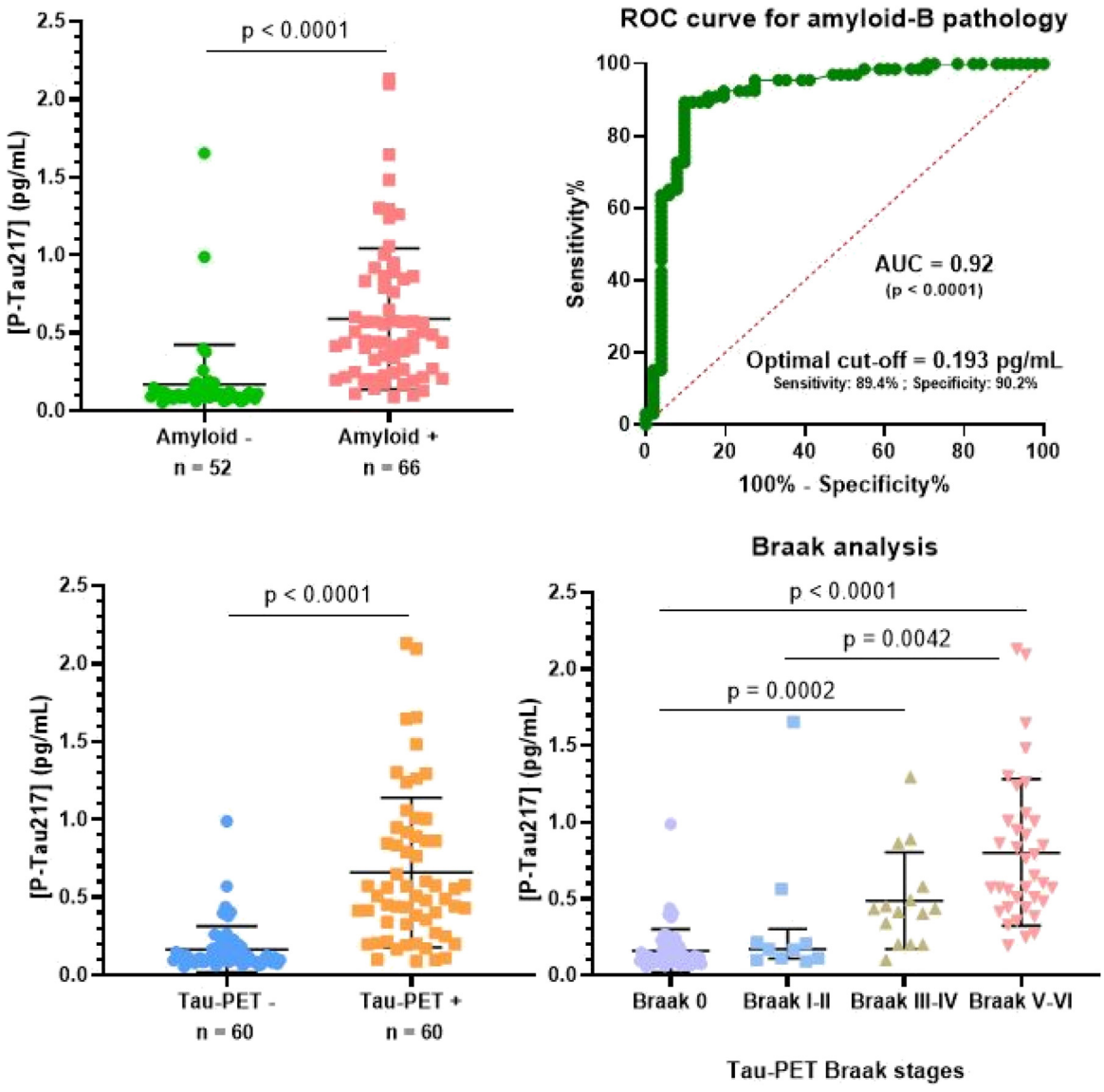
Objectives
Blood-based biomarkers hold great promise for simplifying diagnosis of Alzheimer's disease. The aim of this study is to assess the analytical and clinical validity of plasma p-tau217 as a marker of AD pathophysiology (brain amyloid-ß pathology and tau load).

Material and methods
We included 122 patients (M/F ratio : 0.46), of which 73 cognitively normal (CN) individuals (mean age : 68.7 years), 16 demented people (DEM) (mean age : 68.6 y) and 33 patients presenting mild cognitive impairment (MCI) (mean age : 72.2 years). Each patients underwent a Mini-Mental State Examination (MMSE) and tau load assessment with positron emission tomography (Tau-PET). Amyloid-ß status was assessed with Aß-42 CSF measurement (n = 40) or with PET (Amyloid-PET (n = 82)).

Results
Regardless of the cognitive status, plasma p-tau217 mean concentration was significantly higher in patients presenting amyloid pathology (0.590 $\pm$ 0.451 pg/mL) versus patients without amyloid pathology (0.171 $\pm$ 0.253 pg/mL) ($p < 0.0001$). Similarly, p-tau217 mean concentrations was higher in Tau-PET positive patients (0.659 + 0.481 pg/mL) versus Tau-PET negative patients (0.165 + 0.149 pg/mL). The areas under the receiver-operating characteristic curve to predict amyloid pathology and Tau-PET status curve were 0.92 ($p < 0.0001$) and 0.90 ($p < 0.0001$), respectively. P-tau217 concentrations were significantly associated with tau pathologic burden, according to Tau-PET Braak stages ($p < 0.0001$). Optimal cut-point to predict brain amyloid pathology was 0.193 pg/mL, with a sensitivity of 89.4% and a specificity of 90.2%. The use of the same cut-off predicts Tau-PET status with 89.8% sensitivity and 80.0% specificity. CN individuals presenting already amyloid pathology, as assessed with amyloid-PET, showed higher p-tau217 concentrations compared to CN individuals without amyloid deposition ($p = 0.0005$).

Conclusion
Plasma p-tau217 effectively identify brain amyloid pathology in patients with and without existing cognitive complaints. P-tau217 concentrations correlate with Tau-PET Braak stages. Therefore, this marker offers promises as a tool to identify and staging patients suffering from AD as well as patients which may evolve to AD.



C14

CURRENT URINALYSIS PRACTICES IN BELGIAN LABORATORIES TOWARDS THE 2023 EFLM EUROPEAN URINALYSIS GUIDELINE

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Objectives
We aimed to investigate routine urinalysis practices in Belgian laboratories and verify these findings against the 2023 European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) European Urinalysis Guideline.[1]

Material and methods
A survey was developed to collect information on pre- and postanalytical aspects of urine test strip and particle analysis. The survey was distributed by Sciensano to all Belgian laboratories, licensed to perform urine particle analysis.

Results
Sixty-six percent of the Belgian laboratories (75/113) participated. The responding laboratories serve physicians in private (25%), hospital (60%) and university hospital (15%) settings. All laboratories perform test strip and particle analysis, predominantly performed automatically (97% and 96%, respectively). In addition, most laboratories (87%) use intelligent verification criteria to optimize diagnostic accuracy. Almost all laboratories (≥90%) screen and report a minimal biochemistry panel (glucose, protein, pH, ketones) and particle count (red and white blood cells). Independent of the technology, a notable variability is observed regarding medical cut-off values and advanced particle differentiation and reporting. Internal quality control (QC) is extensively performed for urine test strip (91%) and particle analysis (96%), while external QC is significantly less common (32% and 36%, respectively). Consequently, only few laboratories are ISO15189 accredited for urine test strip (15%) and particle analysis (17%).

Conclusion
There is considerable variability in current urinalysis in Belgian laboratories. The 2023 EFLM urinalysis guideline has the potential to guide clinical laboratories towards improving their urinalysis practices. Additional efforts are required to implement these recommendations into clinical practice.

References
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C15

EVALUATION OF AUTION EYE AI-4510 FLOW CELL MORPHOLOGY ANALYZER FOR COUNTING PARTICLES IN URINE

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Objectives
We evaluated the performance of the urine particle analyzer AUTION EYE AI-4510 (Arkray Inc., Kyoto, Japan) using digital flow cell morphology against phase-contrast visual microscopy.

Material and methods
Imprecision, linearity, limit of quantity (LoQ) and carry-over were evaluated according to established guidelines. 1012 midstream urine specimens were compared in accuracy of RBC, WBC and SEC counts against visual microscopy, using Passing-Bablok regressions with non-parametric Spearman's correlations. Bland-Altman plots were assessed against clinically acceptable analytical performance specifications for urinary particles. Significance of the ordinal scale agreements was assessed by weighted Cohen's kappa coefficient. The results were evaluated using the analytical performance specifications suggested in the EFLM European urinalysis guideline 2023.

Results
By applying Dahlberg's procedure, a desirable relative coefficient of variation, *R(CV)* ≤2 was obtained for fixed WBC and RBC. Linearity was achieved up to 7 RBC x 10^6/L and about 20–30 WBC x 10^6/L; the estimated LoQ were 6.5 x 10^6/L for RBC and 6.8 x 10^6/L for WBC; carry-over was negligible. Spearman's correlation coefficient against visual microscopy was 0.89, 0.93 and

0.90 for RBC, WBC and SEC, respectively. Agreement with visual microscopy (Cohen's weighted kappa) was 0.93 for RBC, 0.95 for WBC, 0.90 for SEC, 0.79 for non-squamous epithelial cells (NSEC), 0.67 for combined casts and 0.90 for crystals. Accuracy of bacteria counting by AUTION EYE AI-4510 was not included in the study.

Conclusion
The Arkray AUTION EYE AI-4510 provides a desirable imprecision for RBC and WBC, and meets the criteria for linearity, LoQ and carry-over, and shows an optimum comparison to visual microscopy for RBC, WBC, SEC and crystals. The identification of casts and crystals can be improved, e.g. by the implementation of review rules when clinically significant.

C16

PERFORMANCE EVALUATION OF STATSTRIP® GLU/KET HOSPITAL METERS ACCORDING TO CLSI-EP STANDARDS

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Objectives
This study evaluated the performance of 169 StatStrip®Glu/Ket Hospital Meters before use across seventy rooms in seven hospital sites, where 216 000 blood glucose tests are performed annually.

Material and methods
We evaluated 169 StatStrip®Glu/Ket Hospital Meters (Gen 2.0) (Nova Biomedical Corporation®), using an enzymatic electrochemical assay for whole blood glucose, following CLSI-EP standards with a total allowable error of 11% (RiliBÄK guidelines). Precision was assessed using three control levels (59, 115, and 300 mg/dL), tested twice daily for 5 days. Bias was calculated against the method's mean for each control level. For method comparisons, we first compared StatStrip®(Gen 1.0) (A.Menarini Diagnostics) and StatStrip®(Gen 2.0) in 20 patients' whole blood. Then, we compared StatStrip®(Gen 2.0) using heparinized whole blood and the Alinity (Abbott) with the centrifuged plasma hexokinase method in 40 patients. Results were analyzed using Bland-Altman plots and Passing-Bablok regression. Sciensano's external quality control was evaluated in duplicate over 5 days. Two biases were calculated: one using Sciensano's hexokinase target value and a second using the mean of the peer group with StatStrip®(Gen 1.0).

Results
Mean inter- and total imprecision was 2.4% and 2.9%, respectively. Eight devices exceeded the desirable bias (2.33%) for level-1, two for level-2, and five for level-3. Comparison between the Alinity and StatStrip®(Gen 2.0) showed a non-significant bias of 2.5%, with a slope of 1.04 (95%CI: 0.981–1.08) and an intercept of −0.367 (95%CI: −3.82–3.20). StatStrip®(Gen 1.0) and (Gen 2.0) indicated good agreement, with a slope of 1.03 (95%CI: 0.960–1.09), an intercept of −1.24 (95%CI: −6.67–3.92), and a non-significant bias of 0.6%. Bias using Sciensano's target value was −7.4% and bias using peer's target value was 1.36%.

Conclusion
StatStrip®(Gen 2.0) results were comparable to peer group. However, they showed lower results than Sciensano's target value when using artificial matrix, while non-significant bias was observed in patient samples. This might be due to non-human sample commutability issues. CV and bias were within minimal biological ranges (2.3–3.45% and 2.33–3.49%, respectively), the total error remained within the 11% limit, validating the method according to CLSI-EP standards.

C17

PERFORMANCE EVALUATION OF AFINION®2 POINT-OF-CARE DEVICES FOR MEASURING GLYCATED HEMOGLOBIN

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Objectives

Glycated hemoglobin (HbA1c) is a key marker for the monitoring of diabetic patients and the effectiveness of their treatment, as its level reflects blood glucose over the lifespan of red blood cells. The aim of this study was to validate Afinion®2 point-of-care testing (POCT) devices for measuring HbA1c in under 3 minutes before use in pediatric department.

Material and methods

We evaluated the performance of two Afinion®2 POCT devices (Abbott Laboratories) for measuring HbA1c levels using a colorimetric assay, following CLSI-EP standards with a total allowable error of 3.14% (EFLM guidelines). Precision was evaluated over 5 days using two control levels (42 and 67 mmol/mol), analyzed in duplicate. A bias was calculated against the method's mean for each control level. The manufacturer's announced reference range for HbA1c (20–42 mmol/mol) was verified by testing 20 healthy subjects. Two method comparisons were carried out. The Afinion®2 device was first compared to the laboratory's reference method of capillary electrophoresis on the Capillarys 3 Octa®(Sebia), using 20 patient samples. A second comparison was performed between the two Afinion devices on the same set of 20 samples. Among these 20 patients included in both comparisons, three had heterozygous AS hemoglobin.

Results

The repeatability and total imprecision of the Afinion®2 devices demonstrated mean coefficients of variation (CV) of 0.75% and 1.0%, respectively. No device had a bias exceeding the desirable bias (1.82%). The recommended reference range was confirmed, with all patients' values included within a narrower range (30–37 mmol/mol). Comparison between the Afinion and Capillarys method showed a non-significant bias of –1.1%, with a slope of 0.984 (95%CI: 0.939–1.02) and an intercept of 0.512 (95%CI: –1.98–2.65). The two Afinion devices showed good agreement, with a slope of 1.01 (95%CI: 1.00–1.05), an intercept of –0.428 (95%CI: –2.10–0.500), and a non-significant bias of 0.6% mmol/mol.

Conclusion

Total imprecision CV was within the minimal biological CV (<1.2%), and bias was within the desirable biological bias (<1.82%). The total error remained within the 3.14% limit, validating the method according to CLSI-EP standards.

C18

ASSESSMENT OF MALE ANDROGEN STATUS: A SURVEY ON MEASUREMENT AND REPORTING OF TOTAL TESTOSTERONE, SEX HORMONE-BINDING GLOBULIN AND FREE TESTOSTERONE IN CLINICAL LABORATORIES ACROSS EUROPE

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Objectives

Standardization for biochemical assessment of suspected hypogonadism is lacking, leading to methodological inconsistencies between clinical laboratories and varying reference ranges, warranting careful interpretation by clinicians.

This survey investigated methodological differences regarding biochemical assessment of androgens in men, focusing on total testosterone (T), sex hormone-binding globulin (SHBG) and free T, in clinical laboratories throughout Europe.

Methods

An internet-based survey was distributed from December 2022 till December 2023 by the Royal Belgian Society for Laboratory Medicine (RBSLM), the Dutch Association for Clinical Chemistry and Laboratory Medicine (NVKC), the European Academy for Andrology (EAA), the European Federation for Laboratory Medicine (EFLM), the European Society for Sexual Medicine (ESSM) and Andronet. Additionally, all Belgian clinical laboratories were directly contacted by e-mail. Survey topics included sampling, methodology, reference ranges and reporting.

Results

A total of 124 unique records were analyzed, representing clinical laboratories from 27 different European countries. For total T, only 43.0% (52/122) recommended a sampling time, even fewer recommended sampling in a fasting state (25.4%, 31/122). Total T was quantified by enzyme-linked immunoassay (IA) (72.7%, 88/121), mass spectrometry (MS) (8.3%, 10/121), radioimmunoassay (RIA) (1.7%, 2/121), or a combination (17.3%, 21/121). Age-stratified total T reference ranges were used by most laboratories (IA: 79.0% [74/94] vs MS: 70.8% [17/24]) with IA reference ranges often supplied by the assay manufacturer (70.8%, 63/89), while MS reference ranges were often in-house developed (42.9%, 9/21). SHBG quantification was uniformly performed by IA, with age-stratified reference ranges (65.0%, 52/80), mainly provided by the assay manufacturer (83.1%, 64/78). Free T was used by 69.0% (66/95) of laboratories, either through calculation (cFT, 79.3%, 46/58) or measurement (mFT, 10.3%, 6/58) or a combination (10.3%, 6/58). cFT was predominantly calculated with the Vermeulen formula (84.2%, 48/57). mFT was assessed by direct IA/RIA (60.0%, 6/10 and 20.0%, 2/10) or MS after equilibrium dialysis or liquid-liquid extraction (20.0%, 2/10).

Conclusion

This survey highlights methodologic variability in assessing androgen status, suggesting inconsistent adherence to clinical guidelines. It emphasizes the need for harmonization, the adoption of age-specific reference ranges and, specifically for free T, standardized methods.

C19

EVALUATION OF A NEW FULLY AUTOMATED IMMUNOESSAY FOR METHOTREXATE THERAPEUTIC DRUG MONITORING

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Objective

Methotrexate (MTX) is a widely used chemotherapeutic and immunosuppressive agent. Due to its narrow therapeutic index and significant inter-patient variability, Therapeutic Drug Monitoring (TDM) is essential. Our aim was to investigate the analytical performance of ONLINE TDM Methotrexate assay (Roche Diagnostics GmbH).

Material and Method

Repeatability and intermediate precision were evaluated at two concentration levels (0.08 and 0.8 µmol/L) using internal quality control (IQC) samples, following the EP15-A2 CLSI protocol. A comparative analysis was performed with the ARK™ Methotrexate Assay (ARK Diagnostics) (range of 0.04 to 1.20 µmol/L; n=60). Additionally, 12 external quality assessment (EQA) samples (Randox Laboratories Limited) were analyzed to evaluate the trueness of both assays.

Results

For low and high IQC levels, repeatability was 4.8% and 1.0%, while intermediate precision was 4.4% and 0.8%, respectively. The Bland-Altman analysis revealed a mean bias of 3.0%, characterized by a significant dispersion of data points, particularly at lower concentrations. Below the threshold of 0.20 µmol/L, a larger bias of −20.9% was noted with higher results for the ARK

than for the Roche assay. With the EQA samples, a bias of −3.3% for the ARK assay and −14.3% for the Roche assay was observed.

Conclusion
The repeatability and intermediate precision of the Roche immunoassay for methotrexate were within acceptable limits. The comparison of methods showed an acceptable bias, but the dispersion of results was significant, particularly at lower concentrations where the ARK assay tended to produce higher values. This observation aligns with findings from Descoeur et al., who suggested that the lower specificity of the ARK method for the 17 OH-MTX metabolite could be responsible for an overestimation. Additionally, while trueness was within acceptable limits, the ARK assay showed a better agreement with target values, possibly due to the lack of the 17 OH-MTX metabolite. A comparison with mass spectrometry would be of interest.

References
Descoeur et al. 2022 Jan; doi: 10.1177/1078155220983407.

C20

METHOD COMPARISON OF FOUR SERUM ALBUMIN ASSAYS

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Objectives
Discrepancies among serum albumin assays are well-known[1,2] and the JCTLM recommends immunological methods as reference methods[3]. This work aimed at comparing the accuracy of four serum albumin assays.

Material and methods
Serum samples (n=81) of patients with EKFC-GFR ranging from 2 to 90 mL/min/1.73m^2 were collected. Albumin was measured by four assays: BromoCresol Green (BCG) (Alinity®, Abbott®), BromoCresol Purple (BCP) (Alinity®, Abbott®), Immuno-Nephelometry (IN) (Atellica®, Siemens®) and ImmunoTubidimetry (IT) (Optilite®, Binding Site®). The chosen BCG, BCP and IT assays are standardised by ERM-DA470k, whereas the chosen IN assay does not specify standardisation. Passing-Bablok regressions, Bland-Altman plots and correlation analysis were performed to compare each method to IT.

Results
When compared to IT, BCG (mean 6.16 g/L, 95% CI [2.92; 9.40] g/L) and IN (mean 3.18 g/L, 95% CI [1.38; 4.97] g/L) showed a significant systematic bias, while no significant bias was revealed with BCP (mean 1.26 g/L, 95% CI [−1.17; 3.69] g/L). Our data showed no significant proportional bias and no significant difference between biases from healthy (GFR>60), chronic kidney disease (CKD) (30<GFR≤60) and dialysis (GFR≤10) patients.

Conclusion
As described in the literature, our data showed an important bias of BCG and a lower bias of BCP, confirming that BCP should be preferred when using colorimetric assays[1,2]. Unexpectedly, our data showed a bias between IT and IN although they are considered interchangeably as reference methods. Bachmann *et al.* also described a bias between an IT assay and BN II® (Siemens®) IN assay, while there was no bias with another IN assay, suggesting an incorrect calibration of Siemens® IN assay[4], which is a conclusion that our data support. There is a need for standardisation in serum albumin assays as serum albumin levels are clinically relevant for CKD and dialysis patients[1]. This work suggests BCP or IT should be preferred.

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C21

EVALUATION OF A COLORIMETRIC ASSAY FOR SERUM COPPER

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Objectives
We evaluated the Randox colorimetric assay for serum copper as a simple and regulatory sound alternative to the cumbersome, rather expensive, and often lab-developed ‘gold standard’ methods AAS or ICP-MS

Material and methods
Precision and bias of the assay (Randox, Parramatta, Australia) on Abbott Alinity c (Abbott Park, IL,USA) were evaluated with Seronorm Trace Elements Serum (Seronorm, Billingstad, Norway), a serum-based quality-control, using a CLSI EP15-based protocol. We compared the colorimetric method to an atomic absorption spectrometry (AAS) assay by testing 30 serum samples with both assays.

Results
Precision was 2,3% at 95,1 µg/dL and 1,4% at 183 µg/dL, acceptable values when compared to themanufacturer’s claims and the desirable biological performance specification (3,8%). Average biaswas –13,2% and –8,4% on respectively level 1 and 2, compared to the Seronorm ICP-AES target values. The observed biases exceeded the minimum biological performance specifications (5,7%). Method comparison with AAS showed no fixed or systemic bias in the Passing-Bablok fit and aPearson coefficient of 0,96. Bland-Altman analysis showed a significant negative bias of –10,75%. Clinical interpretation was concordant for all but 2 samples with concentrations around the cutoff.

Conclusion
In our experiments, the Randox colorimetric assay for serum copper proved precise and showed excellent linear correlation with AAS. A significant negative bias was observed as compared to AASand third party iQC target values. However, the bias did not give rise to important different clinical conclusions for the samples in our experiment. Moreover, the clinical value of serum copper is often supportive rather than conclusive. A (not tested) specific serum calibrator might further improve the observed bias.

C22

VERIFICATION OF A COLORIMETRIC ASSAY FOR SERUM ZINC

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Objectives
We evaluated the Randox colorimetric assay for zinc in serum as a as a simple and regulatory sound alternative to the cumbersome, rather expensive, and often lab-developed ‘gold standard’ methods AAS or ICP-MS.

Material and methods
Precision and bias of the assay (Randox, Parramatta, Australia) on Abbott Alinity c (Abbott Park, IL, USA) was verified with Seronorm Trace Elements Serum (Seronorm, Billingstad, Norway), a serum-based quality-control, using a CLSI EP15-based protocol. We compared the method to an atomic absorption spectrometry (AAS) assay by testing 25 serum samples with both assays.

Results
Precision was 4,0% at 121,2 µg/dL and 4,3% at 167,6 µg/dL; both acceptable compared to the manufacturer's claims and the desirable biological performance specification (4,3%). Average bias was –16,4% and –14,5 % on the two levels, compared to the Seronorm ICP-AES target values. The observed bias exceeded the minimum biological performance specifications (4,6%). Method comparison with AAS showed a Pearson coefficient of 0,79. Passing-Bablok and the Bland-Altman analysis showed no significant bias, but with very large confidence intervals, potentially due to the small concentration range of the serum samples tested.

Conclusion
In our experiments, the Randox colorimetric assay for zinc in serum was precise, but a large significant negative bias was observed compared to third party iQC target values as well as a large spread with AAS results. A (not tested) serum calibrator could improve bias, but the relative large spread as compared to AAS casts doubt on the potential to replace AAS in clinical routine.

C23

INVESTIGATION OF THE VITAMIN D METABOLITE RATIO (VMR) AS A MARKER OF FUNCTIONAL VITAMIN D DEFICIENCY: FINDINGS FROM THE SARCOPHAGE COHORT

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Background
The vitamin D metabolite ratio (VMR) has recently been identified as a potential better indicator of vitamin D deficiency than 25-hydroxyvitamin D (25(OH)D) alone. This study aims to validate these findings by demonstrating that VMR is more strongly correlated with parathyroid hormone (PTH) levels than 25(OH)D and 24,25-dihydroxyvitamin D (24,25$(OH)_2$D). In addition, the study investigates VMR as a more effective predictor of mortality than 25(OH)D and 24,25$(OH)_2$D.

Methods
The SarcoPhAge cohort is a Belgian cohort of community-dwelling older adults. Levels of 25(OH)D and 24,25$(OH)_2$D were measured in 204 serum samples collected at the second year of follow-up using liquid chromatography-tandem mass spectrometry (LC-MS/MS). VMR was calculated using the formula: VMR = (24,25(OH)D / 25(OH)D) * 100. Vitamin D deficiency cut-offs were defined at 25(OH)D < 20 ng/mL or 24,25$(OH)_2$D < 1.2 ng/mL or VMR < 4% according to previously proposed cut-offs. Participants were followed for up to 9 years.

Results
A total of 35 individuals (17.2%) had 25(OH)D < 20 ng/mL, 40 individuals (19.6%) had 24,25$(OH)_2$D < 1.2 ng/mL, and 14 individuals (7.0%) had VMR < 4%. All three markers, 25(OH)D, 24,25$(OH)_2$D and VMR, were independently associated with PTH levels, with VMR showing the strongest correlation (rho: –0.292; $p < 0.0001$). When categorized into quartiles, only 24,25$(OH)_2$D and VMR showed significant increases in PTH levels across quartiles ($p = 0.002$ and $p < 0.0001$, respectively). When cut-offs for low vitamin D status were applied, patients with low VMR had the highest rate of all-cause mortality.

However, in a cox proportional-hazard regression model, both low VMR profile and low 25(OH)D profile were risk factors for all-cause mortality.

Conclusions
This study confirms that VMR is an efficient biomarker for assessing functional vitamin D deficiency.

C24

STUDY OF THE COST-EFFECTIVENESS OF THE MTBI TEST, THE CANADIAN CT HEAD RULE AND THE CT SCAN IN AN ADULT POPULATION

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Objective
New biomarkers to diagnose mild traumatic brain injury (mTBI) have emerged and multiple studies demonstrated their efficacy in ruling-out mTBI. Still, studying the cost-effectiveness of mTBI biomarkers was required before including the biomarkers in clinical practice.

Material and Methods
Decision tree models of 10 000 individuals were created to assess the cost-effectiveness of the mTBI test (GFAP+UCH-L1) compared to the cost-effectiveness of sending every patient to the CT scan or using the Canadian CT Head Rule (CCTHR) to rule patients out of the CT scan. This study is based on the population of the CHU of Liège (2022) using costs of the INAMI (2023).

Results
When the mTBI test was used to rule patients out of the CT scan compared to performing a CT scan to all patients, 4 065 CT scans and 9 hospitalisations were spared for extra costs of 349 909€ per 10 000 patients. The mTBI test scenario spared 688 CT scans and 2 hospitalisations compared to the CCTHR scenario for an added cost of 1 251 221€ per 10 000 patients.

In younger adults, the mTBI test scenario spared 6 480 CT scans while saving 291 075€ per 10 000 patients compared to the CT scan scenario. The CCTHR scenario spend additional 2871 CT scans while sparing 9 hospitalisations and 447 003€ compared with the mTBI test scenario.

In older adults, when the mTBI test was used to rule-out patients for the CT scan, 1500 CT scans and 3 hospitalisations were spared for extra costs of 1 037 011€ per 10 000 patients compared to the CT scan scenario. Finally, with the CCTHR scenario, 2063 CT scans and 1775 hospitalizations are spared while being 2 412 717€ cheaper compared to the mTBI test scenario.

Conclusion
In the entire population, the mTBI test scenario spares CT scans while inducing extra-costs whereas in younger adults the mTBI test scenario is cost-effective, saving both scans and money. Increasing the mTBI test specificity in older adults might increase the cost-effectiveness of the mTBI scenario.

C25

OPTIMIZING THE ELECSYS® HCV ASSAY THRESHOLD TO IMPROVE HEPATITIS C DIAGNOSIS ALGORITHM AND REDUCE HEALTHCARE COSTS BY MINIMIZING SUPPLEMENTARY TESTS

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Objectives
Viral hepatitis remains a leading cause of infectious mortality worldwide. To address this major public health concern, our objective was to improve the serological screening process by reducing unnecessary testing and healthcare costs through the establishment of a precise cut-off for our assay method.

Material and methods
Three screening methods (Elecsys® Anti-HCV II, Alinity s Anti-HCV and Ortho® HCV 3.0) were compared between themselves using a composite gold standard. The method showing the best sensibility and specificity was subsequently used to establish a more optimal screening S/CO cut-off for our screening method (Elecsys® Anti-HCV II), predictive of true-positivity. A confirmatory serological method (Vidas® anti-HCV) was employed at this stage to differentiate between true positives and false positives. A simulation of the use of this cut-off was conducted on a retrospective cohort to ascertain whether this would optimize the HCV diagnosis algorithm and to assess its economic impact on healthcare costs.

Results
260 samples were analyzed for the comparison of the screening methods. The test with the highest sensitivity (100%) and specificity (98.2%) was the Alinity s Anti-HCV II assay.

The Alinity s Anti-HCV II assay was therefore used to establish the S/CO cut-off threshold for our screening method (Elecsys® Anti-HCV II). The best Youden's index was obtained for a cut-off value of 17.8 (sensitivity (95.6%), specificity (96.4%)).

In a retrospective cohort of 667 patients with a positive initial HCV screening (Elecsys® Anti-HCV II, S/CO ≥ 1), 124 had an S/CO ratio of ≤17.8. The second serological method (Vidas® anti-HCV) yielded a confirmation of 105 negative results (15.74% of the cohort) out of the 124 samples initially tested. Therefore, PCR/VL testing was deemed unnecessary for these 105 patients. In Belgium, healthcare insurance covers 85% of the cost of PCR/VL, which represents €68.44 per test. The estimated theoretical saving for a 7-month assessment period is 68.44 x 105 = €7934.21 ($7934,21).

Conclusion
In this study, a positivity S/CO cut-off of 17.8 was established for the Elecsys® Anti-HCV II screening method, accurately predicting true positives in 97% of cases and reducing the need for unnecessary PCR/VL confirmatory testing. Implementation of this modified diagnostic algorithm based on this cut-off should theoretically result in savings to the healthcare insurance over a 7-month assessment period in our cohort.

C26

MSUD: A SWEET SMELL THAT LEAVES A BAD TASTE

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Introduction
Maple Syrup Urine Disease (MSUD) is a rare autosomal recessive metabolic disorder, which can result in severe neurological distress with neonatal-onset. Accumulation of branched-chain ketoacids can result in a typical burned sugar smell of sweat and urine. Although neonatal screening is straightforward, confirmation and follow-up pose analytical challenges.

Case description
A ten days old, lethargic male was transferred to the Antwerp University Hospital after neonatal screening showed extreme accumulation of leucine/isoleucine and valine on a dry blood spot. Upon arrival, the patient showed severe encephalopathy with excessive lethargy and no response to manipulation or pain stimuli. The diagnosis of MSUD was confirmed after the finding of extreme elevation of urinary ketoacids by GC-MS, elevation of leucine in plasma by LC-MS/MS and the concomitant presence of alloisoleucine accumulation in plasma, pathognomonic for MSUD. Next to the administration of IV glucose, dietary restrictions were set to avoid aggravation by protein catabolism. During hospitalization, monitoring of blood leucine is important, as this amino acid is considered the main neurotoxicant in MSUD and its concentration can be used as a guidance to estimate the need for hemodialysis. Although FIA-MS/MS is a fast method that has proven to be very useful in

neonatal screening, this technique is not able to separate close isobars or isomers such as leucine and isoleucine. Due to the structural similarities and the identical *m/z*-value of these latter two compounds, laboratories of inborn errors of metabolism should invest in a fast-track LC separation method to enable urgent diagnosis and follow-up of MSUD.

Conclusion
Increased awareness of MSUD is important, as early recognition of this rare condition improves the long-term outcome and treatment is relatively straightforward. Differentiation of leucine from its isomers is necessary for accurate follow-up and highlights the importance of chromatography in diagnostic laboratories.

C27

EARLY HEPATOCELLULAR CARCINOMA DETECTION WITH GAAD AND PIVKA-II

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Objectives
Early diagnostic tools are crucial for detecting hepatocellular carcinoma (HCC) and improving survival rates. PIVKA-II stands for Protein Induced by Vitamin K Absence II, which appears during hepatic pathology causing post-transductional carboxylation defect. The aim of this study is to assess the clinical utility of the GAAD score (based on Gender, Age, Alpha-Fetoprotein, Des-gamma-carboxyprothrombin or PIVKA-II) developed by Roche, as well as the analytical performance of the PIVKA-II biomarker.

Methods
Plasma samples from 17 patients were collected, and PIVKA-II and AFP levels were measured. The GAAD score was calculated by manually entering data into the Navify® Portal (Roche Diagnostics, Mannheim, Germany). Analytical performance of PIVKA-II, measured by electrochemiluminescence on the Cobas 8000 module e801, was evaluated over 10 days using Roche's Elecsys® kit, following the CLSI EP05-A2 protocol, with two levels of internal controls performed in duplicate.

Results
Fourteen cases had a positive GAAD score (> 2.57), indicating a risk of HCC, while three had a negative score. Seventy-six percent of patients (N=13/17) presented with a clinical risk factor, consisting of alcohol abuse, smoking, arterial hypertension, obesity, Hepatitis B virus, Hepatitis C virus or type 2 diabetes.

The analytical performance study showed compliance with predefined goals for bias, reproducibility, and total error (< 17.6%). Repeatability complied with one of the two control levels.

Conclusion
This study shows that GAAD scores are consistent with patient profiles. Elevated levels reflect deteriorating hepatic pathology, evolving from fibrosis and cirrhosis to early HCC. At the basis, the analytical performance of PIVKA-II adhered to the predefined acceptability goals set by EFLM.

C28

THE ADDED VALUE OF FREE VALPROIC ACID CONCENTRATRIONS IN A CASE OF MEROPENEM – VALPROIC ACID INTERACTION: FOCUS ON THE POST CO-ADMINISTRATION PERIOD

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Objectives
In hospital setting, valproic acid and meropenem are widely used drugs to treat seizures and severe infections, respectively. However, co-administration of meropenem induces fast and significant decline of total (VPA) and free valproic acid serum (VPA_{free}) concentrations. There exists quite some awareness for this serious drug-drug interaction. Nevertheless, there is less knowledge of the VPA and VPA_{free} concentrations after discontinuation of meropenem.

Methods
In a male patient of 42 years under VPA maintenance therapy, meropenem was co-administered for 20 days to treat infection, while VPA dosing was kept unchanged. VPA and VPA_{free} concentrations were monitored until 4 weeks after discontinuation of meropenem therapy with Chemiluminescent Microparticle ImmunoAssay (Abbott Architect i2000SR). Measured VPA_{free} concentrations (using ultrafiltration) were compared with calculated concentrations.

Results
At day 2 of co-administration, VPA concentrations dropped to 17,2 mg/L. After meropenem discontinuation, a gradual increase in VPA was seen up to 64.2 mg/L at day 21 after stopping meropenem. Increasing deviations between measured and calculated VPA_{free} were found, with a maximal difference of 36–68% between supratherapeutic measured and therapeutic calculated VPA_{free} concentration at d21.

Conclusion
We describe a case of VPA-meropenem co-medication, resulting in a steep decline in VPA($_{free}$) concentration. Here, we focus on the less known normalization phase of the VPA concentration after meropenem stop, a period that can take several weeks. While correction formulas have shown to reliably estimate VPA_{free} in cases of hypoalbumenia, toxicity might be missed in cases with drug-drug interactions. Therefore, VPA_{free} measurement is indicated in the first weeks after stopping meropenem therapy. Based on this case, we implemented a fast method to measure VPA_{free} in clinical routine at the Ghent University Hospital using Vivacon® Filter Devices (Sartorius).

C29

METHOD VERIFICATION OF FERRITIN ON COBAS 8000 C702 AND COMPARISON WITH ROCHE 8000 E801

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Objective
To perform a method verification of the immunoturbidimetric assay of Roche Cobas 8000 c702 for the determination of ferritin in plasma. This is followed by a comparison between this assay and the electrochemiluminescence assay of Roche Cobas 8000 e801.

Material and Methods
Retrospective data of 118 subjects was collected between November 2023 and January 2024 at UZ Brussel. Method verification of the Roche Cobas 8000 c702 was conducted by evaluating the imprecision (CLSI EP15-A3), the autodilution 1:50 (EP34) and the high-dose hook effect. The comparison with Roche Cobas 8000 e801 was conducted by performing a correlation using Passing-Bablok regression and by calculating the clinical performance.

Results
The precision of the medium (mean: 122 µg/L) and the high control (mean: 249 µg/L) was within the optimal CV (3.2%), predetermined by EFLM.

The prozone-cut-off of 80000 µg/L mentioned in the instructions for use was verified for a sample with an original ferritin concentration of 77612 µg/L determined on Roche Cobas 8000 e801. No false result without a “prozone flag” was observed.

The recovery of diluted samples with a ferritin concentration approaching the upper limit of quantification (1000 µg/L) was 101.9%, which is between the acceptable range of 92.8%–107.2%.

The overall Passing-Bablok regression analysis showed a good correlation between the two methods (y=1.09–1.11, r=1, range: 8–997 µg/L). Bland-Altman analysis showed that 95% of the samples are within the d% criterion of Sciensano (16%).

For the determination of the clinical performance, each sample was classified according to sex and whether the value was low (n=26), normal (n=59) or high (n=30) using the Roche Cobas 8000 e801 as the reference method. The sensitivity and specificity were between 95% and 100%.

Conclusion
Roche Cobas 8000 c702 meets the requirements of verification for the determination of ferritin and is comparable to Roche Cobas 8000 e801.

C30

WHAT IS THE ADDED VALUE OF A CORRECTION FORMULA OF BLOOD POTASSIUM CONCENTRATION BASED ON THE HEMOLYTIC INDEX

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Background
Errors occuring during the blood collection and transportation process might cause ex vivo hemolysis, falsely increasing the measured serum/plasma potassium levels. In addition to pseudohyperkalemia, hemolysis can also cause masked hypokalemia. As there exists a linear relationship between the increase in hemolysis index (H-Index) and potassium, several correction formulas have been published as an alternative approach for managing potassium results in hemolyzed samples. In our study we established our correction formula and set up a phone alerting and monitoring workflow for potentially critical potassium retesting.

Methods
Blood Li-heparin tubes (n=2) were drawn from healthy volunteers (n=1). Hemolysis was induced by push-pulling the blood of one tube multiple times (n=100) through a blood collection needle (20G) into a syringe, hereby creating substantial shear stress. After centrifugation, the non-hemolysed and hemolysed plasma were used to prepare a mixing series. On the sample series H-index and K levels were determined using the Architect c16000 (Abbott Diagnostics). The correction formula was validated with a set of increased potassium levels from hemolytic patient samples of which we also received a control sample (n=2278).

Results
The change in potassium was calculated and plotted against the H-index (range 1-4052). From these results we derived a correction factor to adjust the measured potassium levels: K (adjusted) = K (measured) – 0,0036 * H-index. The validation of the dataset had a p-value of <0.0001 (95% CI: 0.85–0.89).

Conclusions
A correction formula for increased serum/plasma potassium levels in hemolytic samples could be used to alarm the laboratory technicians to call for an urgent recollection sample and to follow up the receival of this sample. This could lead to a shorter time to diagnosis and treatment, and thus could possibly be life-saving.

C31

COMPARISON OF FRIEDEWALD-, SAMPSON- AND (EXTENDED) MARTIN-HOPKINS EQUATIONS FOR THE ESTIMATION OF LDL-CHOLESTEROL WITH MEASURED LDL-CHOLESTEROL IN PATIENTS WITH HYPERTRIGLYCERIDEMIA

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Objective
To compare the clinical performance and concordance of the Friedewald, Sampson, Martin-Hopkins and extended Martin-Hopkins equations with the direct LDL-cholesterol (LDL-C) in patients with hypertriglyceridemia.

Material and Methods
Retrospective data of 8388 subjects was collected between July 2020 and February 2023 at UZ Brussel. Triglycerides (TG), total cholesterol, HDL- and LDL-C concentrations were determined by enzymatic colorimetry on Cobas® 8000 c702 (Roche Diagnostics). The clinical performance (clinical cut-off=100 mg/dL LDL-C) and concordance between the direct LDL-C and the equations were compared in samples with hypertriglyceridemia (200–4414 mg/dL).

Results
The correlation of direct LDL-C and LDL-C calculated by the different formulas was similar for TG between 200 and 799 mg/dL (r=0.87–0.96; n=8230). Best correlation was found for LDL-S (r=0.9; n=879) for samples with TG between 400 and 799 mg/dL. The correlation coefficient was lower than 0,5 for all formulas for TG higher than 799 mg/dL (n=159).

LDL-MH showed the lowest average bias (14%) for samples with TG between 200 and 799 mg/dL. Half of the samples in the group of TG between 400–799 mg/dL (n=879) had a bias higher than the desirable total error of EFLM (11.8%). However, in this latter group the clinical specificity was the highest for the LDL-F formula (98%), whereas the clinical sensitivity was the highest for the LDL-MH formula (94%).

Finally, the LDL-MH formula places the largest number of results in the same category as the direct LDL-C (76.3%). However, even in the group of TG between 200 and 399 mg/dL, LDL-MH resulted in a misclassification towards lower values in 21% of direct LDL-C results between 55 and 100 mg/dL.

Conclusion
The Martin-Hopkins formula is more concordant with direct LDL-cholesterol than the other formulas. To avoid underestimation in patients under cholesterol-lowering therapy direct LDL-C measurement is still an added value.

C32

VALIDATION OF ADAPTED CUT-OFFS FOR S100B, GFAP AND UCH-L1, IN A MTBI BELGIAN REAL-LIFE SETTING PROSPECTIVE STUDY: THE MITICBRAIN COHORT

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Objective
Studies on biomarkers of mild traumatic brain injury (mTBI) have been carried out in different countries with comparable results but data in the Belgian population were still expected. This study evaluates the accuracy of the mTBI biomarkers in a mTBI Belgian Multicentric cohort, the MiTicBraIn cohort.

Material and Methods
The MiTicBraIn cohort is a prospective study composed of 78 mTBI patients recruited in several Walloon hospitals (CHU de Liège, Godinne, Clinique Saint-Pierre Ottignies and Tivoli). Inclusion criteria were fulfilled if the mTBI patient was aged from 18 years old, got a CT scan and signed an informed consent. S100B, GFAP and UCH-L1 were measured in each patient.

Results
In the MiTicBraIn cohort, the mean time-interval between the head trauma and the blood sample is of 9.9 hours. In this cohort, GFAP, S100B and UCH-L1 possessed areas under the curve of 0.813 ($p<0.001$), 0.747 ($p=0.001$) and 0.732 ($p=0.008$), respectively.

In the entire MiTicBraIn cohort, the "GFAP+UCH-L1" mTBI test had a sensitivity and NPV of 100% and a specificity of 42% and S100B had a sensitivity of 89%, a NPV of 100% and a specificity of 54%.

In adults from 65 years (42 individuals), all biomarkers revealed significantly reduced specificities. Indeed, the "GFAP+UCH-L1" mTBI test had a sensitivity of 100% and a specificity of 11.76% with 4 patients correctly ruled-out and S100B had a sensitivity of 87.5%, a NPV of 99.9% and a specificity of 26.47%.

Conclusions
The measurement of S100B within the manufacturers' time recommendations seems unfeasible in Walloon hospitals in a real-life setting. The "GFAP+UCH-L1" mTBI test has a high sensitivity for mTBI in the Walloon population with still a significantly decreased specificity in the older population.

C33

EVALUATION OF MAGLUMI X3 FOR THE DETERMINATION OF GASTRIN, EPO, 17-OH PROGESTERONE AND IAA

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Objective
The Clinical Chemistry and Radio-Immunology lab at UZ Brussels currently uses manual radiobinding assays to measure 17α-hydroxyprogesteron (17OHP) and insulin autoantibodies (IAA), and chemiluminescence for erythropoietin (EPO) and gastrin on Immulite 2000 XPi (Siemens Healthineers). The aim was to evaluate whether the automated Maglumi® X3 (Snibe) based on chemiluminescent technology can consolidate these parameters and replace the separate (radioactive) methods.

Material and methods
Imprecision and accuracy were evaluated using internal quality controls (CLSI EP15-A3). EPO carry-over was determined by measuring 3 high and 3 low. The comparison between the current methods with the Maglumi® X3 was conducted by performing a Passing-Bablok regression analysis on at least 40 serum samples. To determine clinical performance, each result was interpreted according to the Maglumi® X3 reference values in comparison with the interpretation achieved with the current reference methods. Interference of 17-OH-pregnenolonesulphate in the 17OHP assay was tested in samples from children under one year, pre- and post-diethyl ether extraction.

Results
Maglumi® X3 met the expert-based criteria for imprecision and bias. EPO carry-over was negligible (<0,1%). Passing-Bablok analysis showed correlation coefficients varying from 0,91 to 0,98. The clinical sensitivity and specificity were resp. 100% and >80% (mainly explained by borderline false positives) for 17OHP, EPO and gastrin, and resp. 63% and 87% for IAA. Without extraction, 4/10 children's samples showed elevated 17OHP, compared to only 2/10 after extraction.

Conclusion
The Maglumi® X3 appears acceptable as an alternative to the current methods for 17OHP, EPO and gastrin. However, determination of reference values for the Caucasian population is still needed. For children under one year extraction seems to be necessary to achieve reliable 17OHP results. For IAA, the clinical performance needs to be further evaluated.

PA1

CALCULATED GLOBULIN AS SCREENING TOOL FOR HYPO-AND HYPERGAMMAGLOBULINEMIA AND ASSOCIATED PARAPROTEINEMIA

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Objectives

To investigate calculated globulin (CG; total protein – albumin) as screening tool for hypo- and hypergammaglobulinemia (hypo-/hyperG) and paraproteinemia.

Material and methods

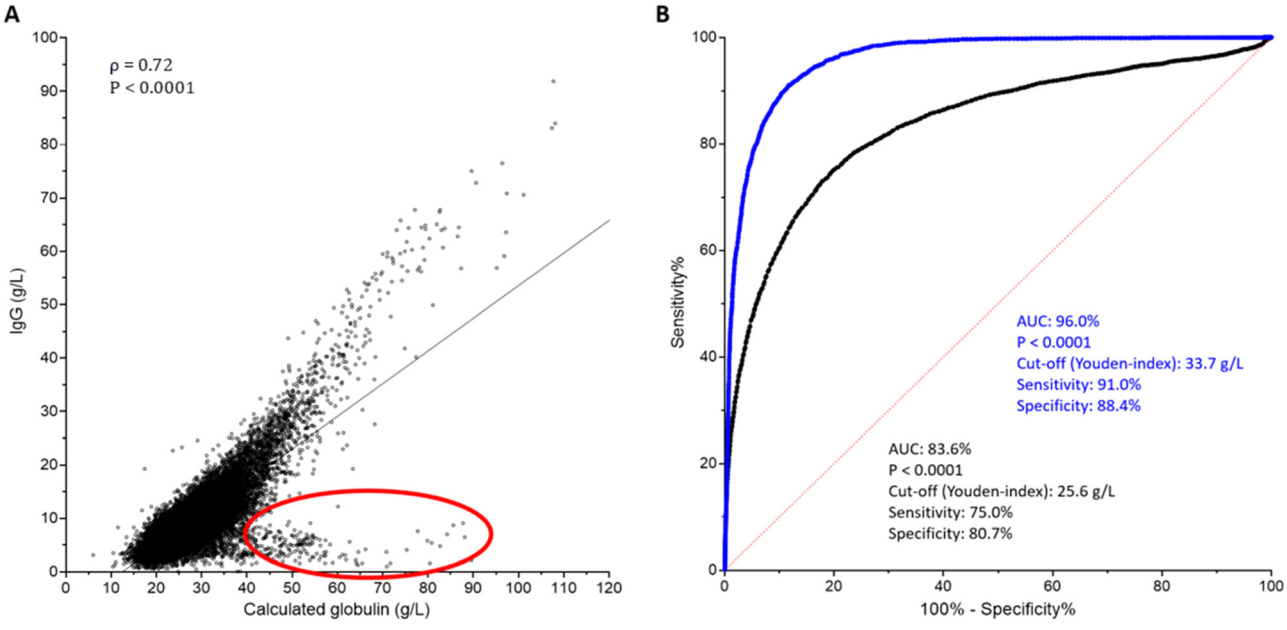
In a retrospective cohort of 25667 samples, CG levels were correlated with IgG levels after which ROC-curve analysis was utilized to determine CG cut-offs for detection of hypo- and hyperG. Cut-offs were then prospectively applied to samples encountered in routine practice for whom IgG or serum protein electrophoresis (SPEP) was not requested by consulting physicians. Next, in samples exceeding the CG cut-offs (N=188), IgG was measured quantitatively to assess the performance of CG in predicting hypo- and hyperG. Lastly, samples of prospectively included patients who demonstrated increased IgG levels were, if sufficient volume was available, further evaluated for paraproteins via SPEP and immunotyping analysis.

Results

In the retrospective cohort, CG displayed good correlation with IgG (Figure 1A) and was significantly different between patients demonstrating hypo- or hyperG and those who did not ($P < 0.001$). For detection of hypo- and hyperG, ROC-curve analyses yielded AUCs of 83.6% and 96% with Youden-index based CG cut-offs of 25.6 g/L and 33.7 g/L, respectively (Figure 1B). In the prospective cohort, 114 patients (60.6%) displayed CG levels < 25.6g/L with 65/114 (57%) showing decreased IgG levels while of 74 patients (39.4%) with CG values >33.7 g/L, 36 (48.6%) showed elevated IgG. Lastly, 30/36 patients displaying increased IgG-levels were further evaluated via SPEP and immunotyping, with 13 (43.3%) shown to harbour paraproteins.

Conclusion

CG enabled us to detect hypo- and hyperG in patients for whom IgG levels or SPEP was not requested by the consulting physician. Hence, it might allow earlier detection of abnormal Ig-levels and hence, immunodeficiency or plasma cell dyscrasias. In this regard, it could also allow earlier discovery of paraproteins present in the patient.



PA2

SAMPLE TRANSPORT: A POTENTIAL PITFALL IN PLATELET FUNCTION TESTING

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Objective
The platelet function analyzer (PFA) is a useful screening tool in the diagnosis of platelet function disorders and monitoring of antiplatelet therapy. The aim of this study was to compare the accuracy and reliability of closure time (CT) measurements between an in-house (intramuros) and an outsourced (extramuros) PFA-200.

Material and Methods
A method comparison was conducted between intra- and extramuros PFA-200 testing using leftover samples and samples of (male) volunteers. Additionally, in order to estimate the impact of sample transport, an intramuros PFA-100 was added to the comparison

Results
Initially, nine samples were analyzed using the Col/Epi cartridge and six using the Col/ADP cartridge on the PFA-200 (intra-muros as well as extra-muros). Discrepancies in interpretation were observed in two Col/ADP results. One sample had normal Col/Epi values, making the difference irrelevant. The other sample had an aspirin-like effect (intramuros) versus a possible thrombocytopathy result (extramuros). However, these external results were not confirmed in the follow-up tests.

The average percentual differences were 22% for Col/Epi and 12% for Col/ADP results, primarily due to prolonged CT in the external method. A possible explanation for these discrepant results are sample transport effects causing ADP-release or bubble formation.

Therefore, the method comparison was repeated and cross-validated with an additional intramural PFA-100. Only one Col/ADP sample showed a significant percentual and interpretational difference between intra- and extramuros results, which appeared clinically irrelevant due to normal Col/Epi values. However, the intramuros method demonstrated higher consistency, with fewer discrepancies and lower average percentual deviations compared to extramuros. This supports the hypothesis of significant impact of transport on CT measurements.

Conclusion
Transporting samples to external laboratories might impact the reliability of CT measurements with the PFA-200. In-house testing is recommended for accurate diagnosis and monitoring of platelet function disorders.

Acknowledgments
We would like to acknowledge Siemens Healthineers for providing access to a PFA-100 device, which was essential for this study.

PA3

FALSELY ELEVATED CALCINEURIN-INHIBITOR TROUGH LEVELS: A CASE SERIES OF CATHETER ADSORPTION

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Objectives
Treatment with (and monitoring of) calcineurin inhibitors is essential in the management of transplant patients. Oral administration is generally preferred, however intravenous (IV) administration is considered in patients with impaired gastrointestinal absorption. Two transplant patients, treated intravenously, were included in this study.

Material and methods
Tacrolimus (TAC) and cyclosporin A (CSA) concentrations are measured using Chemiluminescent Microparticle ImmunoAssay (Abbott) and Electrochemiluminescence ImmunoAssay (Roche), respectively. For the first patient, at ICU, IV TAC therapy had been guided by trough concentrations, ranging from 1.3 to 8.2 ng/mL, after which he was transferred to the haematology department and was switched back to oral TAC administration. Irregular TAC levels were found post-switch (21.2 to 34.0 ng/mL). The second patient initially received IV TAC but was switched to oral CSA treatment because of irregular TAC levels and subsequently to IV CSA. In the next 2 months, unexpectedly elevated CSA levels were found (606 to 730 ng/mL).

Results
For both patients, analytical interferences were excluded using an in-house developed LC-MS/MS method. As blood collections were performed from the central venous catheters (CVC), all different CVC lumina, in parallel with peripheral blood collection, were sampled. Lab analyses showed that at least one lumen was contaminated due to previous IV TAC administration (first patient). Samplings from the two lumina of the CVC, confirmed CSA contamination: 572 and 308 ng/mL, versus 134 ng/mL from peripheral blood sampling (second patient).

Conclusion
Although blood collection using central venous access is more patient friendly, these case series indicate that the use of multi-lumen CVC (previously) used for drug administration is a serious risk for (cross-)contamination and inappropriate dose adjustments. Hence, peripheral sampling should always be favoured for TDM-samplings.

PA4

RECURRENT, UNEXPECTED HIGH ESTRADIOL QUALITY CONTROL CONCENTRATIONS: A PRE-ANALYTICAL CAUSE

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Objective
To emphasize a potential pre-analytical cause of recurrent, unexpected high oestradiol quality control (QC) concentrations in a clinical laboratory setting.

Material and methods
In the clinical laboratory of AZ Delta General Hospital, oestradiol serum levels are measured using the Elecsys Estradiol III kit (Roche Diagnostics) on the Cobas Pro platform. PreciControl Universal (Roche Diagnostics) is used for quality control. QC results are monitored using Levey-Jennings charts based on Westgard rules, with a fixed coefficient of variation of 6.7% and an allowable total error (aTE) of 16%.

Results
During routine QC assessments, the oestradiol concentration in the low level control material showed a bias of 29%, exceeding the aTE, despite previous results being close to the target value. Although a fresh aliquot tested within range, the following QC runs showed biases ranging from 49% to as high as 235%. The second time, the problem was solved using freshly reconstituted control material. During the third problematic QC run, the issue persisted, even after reconstituting

new control and calibrator materials. Eventually, it was discovered that one of the lab technicians responsible for QC management had recently started using a transdermal oestrogel, applied daily to her forearms. This raised the likelihood of inadvertent contamination during manual QC sample handling, for example, by touching pipette tips before pipetting. Once new calibrators and control materials were prepared with uncontaminated pipette tips, the QC values returned to normal. To prevent future contamination, lab technicians using oestrogel are now required to wear gloves when handling QC material and pipette tips. These preventive measures successfully eliminated further QC errors.

Conclusion
Recurrent, unexpected high oestradiol QC levels, particularly at low QC concentrations, can be attributed to operator contamination from dermal oestrogel use. Implementing protective measures, such as wearing gloves and careful handling of materials, can effectively prevent contamination, avoiding unnecessary QC reruns or calibrations.

PA5

CREATION OF A DYNAMIC VISUALIZATION TOOL OF POPULATION STATISTICS OF MEDICAL LABORATORY DATA

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Objective
To create a web-based user-friendly application to make selections in datasets of laboratory results and visualize them. Selections can be based on test, age, gender and time period. The application should be intuitive and a clear graphic view needs to be generated with only a few clicks.

Material and Methods
With a data-extract of the year 2022 for 22 analytes a first concept of the application was made. Using a MySQL database to store the data, the graphics were created using Plotly (Java). The interface itself was built using HTML and CSS with PHP-forms.

Results
We built a working interface where the user can select the dataset and view the data in a year-overview showing the data per month, in an age-overview per age-class of ten years (as shown for Potassium in Figure 1), in a week-overview per weekday, or as a box-plot to show sample size, median, average, Q1-Q3 range and outliers. One can also choose one datapoint and show how that point relates to the dataset. Below each graph the descriptive statistics are shown in tabular form. The tool offers a simple way of visualizing how a single result relates to the patient population of the laboratory, and can also be used for result-based real-time quality control where no control material is available.

Conclusion
Since this tool is self-built new functionalities can be added where needed and new tests can conveniently be added to the database. It allows the users to visualise datasets and effortlessly draw conclusions. The user doesn’t need to have knowledge of programming or even Excel to calculate the statistics. Physicians, clinical pathologists and researchers can use this tool to discover trends in analytes and perform statistics on their own patient population data.

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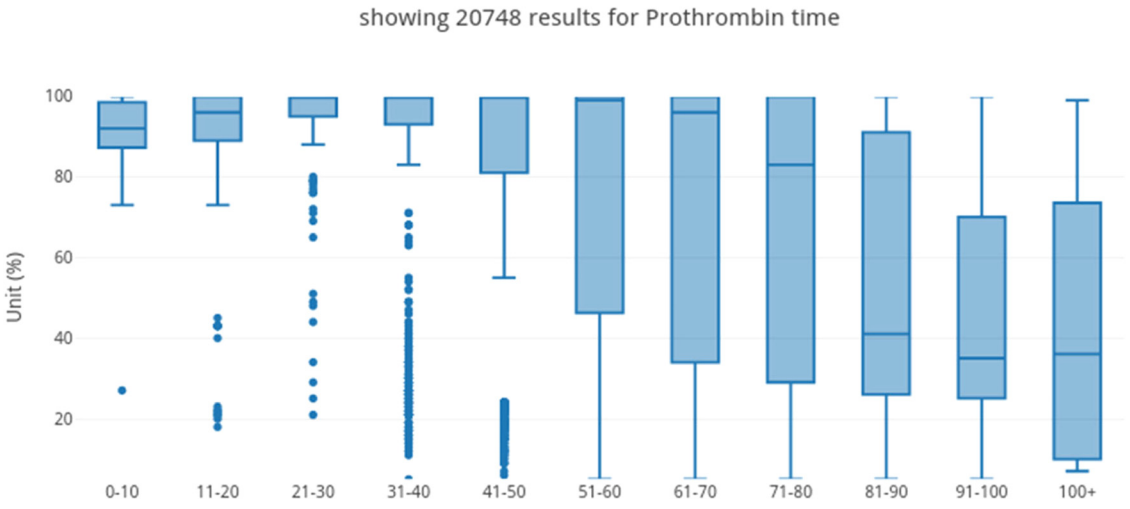
Here you can see the boxplot for your selection:
For the test: Prothrombin time
For the period between 2022-01-01 and 2022-12-31.
For all genders



boxplots											
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	91-100	100+
min	73,000	73,000	88,000	83,000	55,000	5,000	5,000	5,000	5,000	5,000	7,000
q1	88,000	89,000	95,000	93,000	81,000	47,000	34,000	29,000	26,000	25,000	10,000
median	93,000	96,000	100,000	100,000	100,000	99,000	96,000	83,000	41,000	35,000	42,000
q3	100,000	100,000	100,000	100,000	100,000	100,000	100,000	100,000	91,000	70,000	98,000
max	100,000	100,000	100,000	100,000	100,000	100,000	100,000	100,000	100,000	100,000	99,000
mean	88,294	91,072	96,085	88,032	81,223	78,725	73,939	65,938	55,201	45,947	43,125
n=	17	305	631	1080	1632	3355	4440	4714	3512	1054	8

PA6

SEASONAL VARIATION OF SERUM POTASSIUM CONCENTRATIONS IN AMBULATORY PATIENTS

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[1]CRI, Division of Cerba Healthcare Belgium, Zwijnaarde, Belgium

Objective(s)

As potassium (K^+) concentrations are 25 times higher in erythrocytes than in serum, this analyte is very sensitive to pre-analytical variables, in particular environmental temperature. When a sample is exposed to low temperatures, K^+ leaks out of the cells because of low activity of the Na^+/K^+ pump.

Material and Methods

Samples are collected by general practitioners or by nurses, stored locally before being collected by drivers and transported in thermostated boxes at 17–18°C to the laboratory. Potassium is measured by indirect potentiometry and the haemolytic index (HI) by photometry on a cobas® c702 analyser (Roche Diagnostics). Anonymised potassium concentrations and HI were extracted from the laboratory information system from January 2021 to September 2024. Statistical analysis was performed by Medcalc.

Results

277937 K^+ results were analysed. ANOVA analysis yielded a significant difference between potassium levels in the different months: F-ratio 2291.829, $P < 0.001$, with higher values in the colder months. For the haemolytic index, the difference was also significant (F-ratio 39.767, $P < 0.001$), with highest values and largest percentage above 70 in the colder months. In the coldest months, 18% more K^+ results were above normal compared to the warmest months.

Table 1: Monthly variation in potassium and haemolytic index.

Month	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Median K^+ concentration (mmol/L)	4.80	4.70	4.70	4.65	4.55	4.40	4.39	4.30	4.40	4.60	4.70	4.71
K^+ % above reference range	25%	22%	20%	18%	14%	8%	8%	7%	10%	15%	22%	23%
Median HI	8	7	7	7	6	6	6	6	6	7	8	8
HI % above 70	3.1%	2.5%	2.2%	2.3%	1.7%	1.9%	1.7%	1.9%	2.1%	2.0%	2.8%	3.2%

Conclusion

Our data show that there are indeed seasonal differences in potassium concentrations, with a 0.5 mmol/L higher concentration in January compared to August, 18% more higher K+ concentrations, versus only 1.5% more high HI. More efforts are needed to improve the pre-analytical phase in the winter months.

H1

EVALUATION OF HEMOLYSIS INTERFERENCE BY 2 DIFFERENT HEMOSTASIS AUTOMATES USING AUTOMATED HIL-INDEX

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Objective

Preanalytical variable are an important source of errors on routine coagulation tests. Main pre-analytical errors are clotted samples, underfilled tubes and HIL samples (hemolytic, icteric, lipemic samples). The aim of this study was to evaluate the impact of induced hemolysis out on the CS-5100 and CN-6000 using optical method.

Material and methods

For this study, 14 pools of 10 ml plasma were used to prepare 5 aliquots. A small quantity of plasma was stored with the whole blood and then pooled. Hemolysis was induced by frozen whole blood at −80° for 6 min. Samples were then centrifuged, yielding hemolyzed plasma. Theses hemolyzed samples were mixed at several concentration with the native aliquots to obtain several level of hemolysis. The level of hemolysis was measured thanks to the H index on Cobas 8000. Routine tests (PT, aPTT, fibrinogen and D-dimer) were performed in parallel on CN 6000 and CS 5100. Results of the hemolyzed aliquots were compared to the aliquots without hemolysis and bias expressed in percent (%). Results were compared to the RICOS bias recommendations (PT 2%, aPTT 2.3%, fibrinogen 4.8% and D-dimer 8.8%).

Results
Three levels of hemolysis were selected (H1 = 50–200 mg/dL, H2 = 200 – 400 mg/dL, H3 = 400 – 1300 mg/dL). Regardless the degree of hemolysis and the test carried out no bias exceeded the reference values established by RICOS.

Conclusion
We concluded that there was no significant impact of hemolysis on routine coagulation test whatever the automate used. Comparing the results obtained on the two instruments tells us that the manufacturer has improved the device, making it more effective in eliminating this interference.

H2

CURRENT PRACTICES FOR LUPUS ANTICOAGULANT IN BELGIAN LABORATORIES AND COMPARISON WITH THE UPDATED 2020 INTERNATIONAL SOCIETY ON THROMBOSIS AND HAEMOSTASIS SCIENTIFIC AND STANDARDIZATION COMMITTEE (ISTH-SSC) GUIDELINE

B. Vanhove[1,2], L. van Hoovels[1,3], S. Broeders[4], W. Coucke[4], M. Schreurs[5], C. Bonroy[6,7], S. Schouwers[8], E. Bailleul[1], K. Devreese[6,7]

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Background/Aim
We investigated the practices of lupus anticoagulant (LA) testing in Belgian laboratories and verified these against the International Society on Thrombosis and Haemostasis Scientific and Standardization Committee (ISTH-SSC) Guideline (J Thromb Haemost. 2020;18:2828–39).

Methods
A survey on pre- to postanalytical aspects of antiphospholipid antibodies was distributed by Sciensano to all Belgian laboratories (n=111) certified for autoimmune, coagulation and haematology testing.

Results
Fifty-eight percent (%) of the laboratories (12% private, 69% hospital, 19% university) participated, of which 66% performed LA analysis. Seventy-eight % performed LA analysis on thrombocyte-free citrated plasma. Most laboratories (90%) used 2 test panels: dilute Russell's viper venom time (dRVVT) and activated partial thromboplastin time (aPTT), performing the dRVVT (82%) and aPTT (78%) panel only if the screening test was prolonged. Sysmex, Werfen or Stago devices were the most frequently used, with a variety of reagents. Usually (83%), commercial lyophilised (56%) or frozen (44%) normal pooled plasma was used for mixing tests, mostly (98%) in a 1:1 pool:patient ratio. Interpretation was based on normalized clotting time ratio, using both manufacturers' and own study data as cutoff values. LA with a final conclusion was given by 61% of laboratories. Eight-eight % added a comment, mainly (94%) at a positive result. All laboratories applied a barring period after an initial positive result. Sixty-six % performed LA detection in patients receiving direct oral anticoagulants, 74% after using active charcoal absorption. LA testing for vitamin K antagonists and heparin-treated patients was done by 54%, regardless of international normalized ratio (64%) or anti-FXa results (82%).

Conclusions
Although guidelines are followed by the majority of the laboratories, additional efforts are required to further implement the 2020 ISTH-SSC guidelines, harmonizing LA analysis practices.

H3

RESULTS OF A 2023 SURVEY ON THE CURRENT PRACTICES ON ANTIPHOSPHOLIPID ANTIBODY TESTING WITH FOCUS ON IMMUNOASSAYS IN BELGIAN LABORATORIES

L. van Hoovels[1,2], E. Bailleul[1], S. Broeders[3], W. Coucke[3], M. Schreurs[4], K. Devreese[5,6], B. Vanhove[1,7], S. Goletti[8], C. Bonroy[5,6], L. Lutteri[9], S. Schouwers[10], M. Vercammen[11,12], X. Bossuyt[2,7]

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Background/Aim
Antiphospholipid syndrome (APS) diagnosis relies on the detection of antiphospholipid (aPL) antibodies, including lupus anticoagulant (LA), anticardiolipin (aCL) IgG/IgM, and anti-beta2-glycoprotein I (aβ2GPI) IgG/IgM. We aimed to evaluate the routine practices of aCL and aβ2GPI testing in Belgian laboratories.

Methods
A survey interrogating aPL diagnostics was distributed by Sciensano to all Belgian laboratories (n=111) certified for autoimmune, coagulation and haematology testing.

Results
Fifty-eight percent (%) of Belgian laboratories [22% primary care, 64% secondary care, 14% tertiary care] responded. Most laboratories (63%) offered aCL and aβ2GPI independently and upon request.

When aPL testing was done, at least aCL IgG testing was performed (77%). The total panel of IgG/M aCL/aβ2GPI testing was analyzed in-house by 42% of the responders, and 36% also offered LA testing. Seventy-eight % of the university hospitals performed all 4 aPL immunoassays. If a laboratory did not perform the full aPL panel, tests were, upon request, outsourced under controlled conditions.

aCL and aβ2GPI tests were mainly performed in autoimmunity departments (77%) using serum samples. Fluorescence enzyme immunoassay (FEIA) and chemiluminescence immunoassay (CLIA) were the most used assay methods. Results were mainly reported quantitatively (70%). Eighteen percent of the laboratories add semi-quantitative interpretations. Within the same assay methodology, the units and cutoff values varied significantly.

Post-analytically, 43% of respondents indicated the use of a barring period, after a first positive result (95%) and to a lesser extent after a negative result (14%) or a second positive result (5%). Only 38% of laboratories added a comment suggesting repeat testing after a positive result.

Conclusion
The survey highlights the need for aCL and aβ2GPI harmonisation in testing practice and between assays, directly impacting the accuracy of APS diagnosis across the country.

H4

A RARE CASE OF YELLOW CRYSTALS IN THE CEREBROSPINAL FLUID

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Objective

The presence of multiple siderophages in the cerebrospinal fluid (CSF) is typically indicative of hemorrhage. Occasionally, remarkable yellow hematoidin crystals are formed. This rare finding alongside numerous siderophages and macrophages with hemophagocytosis is a strong morphological sign of a central nervous system (CNS) hemorrhage.

Methods

We present a case of hemiparesis. Different investigations were performed including neuroimaging with computed tomography (CT) and magnetic resonance imaging (MRI), electromyography (EMG) and electroencephalograhy (EEG). CSF was collected by lumbar puncture at different lumbar levels. Examination of the CSF included cell count with automatic cellular analysis and a differential count by microscopic examination of cytospins stained with May-Grünwald-Giemsa.

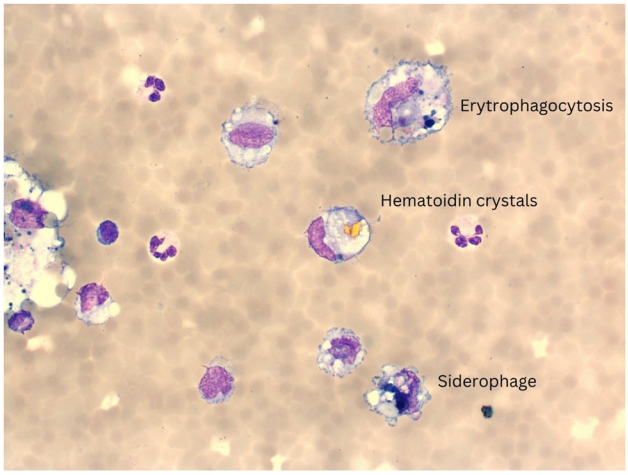
Results

A 70-year-old man, under anticoagulation therapy with apixaban, presented with right-sided wake-up hemiparesis. Clinical examination showed paresis and hypesthesia of the right arm and leg, along with intermittent confusion. MRI revealed extensive hyperintensities over the cervical myelum, suspicious of an intramedullary hemorrhage or ischemia. To exclude a traumatic tap being the source of the bloody CSF, more than one lumbar puncture was performed after interruption of anticoagulation therapy.

Automated cell count revealed 9760 white blood cells/µL and 1989 red blood cells/µL. Microscopic examination of the white blood cells showed a differentiation of approximately 70% monocytes. Numerous erythrophages, hemosiderin-laden macrophages as well as multiple clear yellow crystals were observed. These intracytoplasmic rhomboid crystals, so-called hematin or hematoidin crystals, are an end product of the breakdown of heme from the hemoglobin in red blood cells.

Conclusion

Both neuroimaging studies as examination of CSF were suspicious of CNS hemorrhage in this anticoagulated patient with hemiparesis. In CSF siderophages can persist for months following hemorrhage. The combination of siderophages, hemophagocytosis and hematoidin crystals, strongly suggest a chronic or prolonged CNS hemorrhage.



H5

FLOW CYTOMETER DXFLEX EVALUATION AND COMPARISION WITH FACSCANTO II

J. Beaucarne[1], M. Keldermans[1], J. Dumortier[1], C. Loosen[1], J. Brauner[1], P. Nguyen[1]

[1]Epicura, Boussu, Belgium

1. **Objective**
This study aimed to evaluate the novel DxFlex 13 colors cytometer (Beckman Coulter = BC) compared to the FACSCanto II 8 colors cytometer (BD).

2. **Material and Methods**
38 samples (blood, bone marrow, lymph nodes) (4 healthy, 18 non-Hodgkin lymphoma (NHL), 18 patients with circulating blasts (PB) or plasma cells (PP)) were selected. Studied surface antigen (Clearlab LS tube (BC)): CD45, CD10, CD3, CD4, CD8, CD56, CD19, CD5, CD20, kappa, lambda, CD34, CD38. Using similar gating strategies, the percentages (%) of positive cells were compared between cytometers. In all patients, % of neutrophils (PNN), lymphocytes (Ly), monocytes, and T, B, NK ly were compared. In NHL patients, % of clonal B cells and their expression of CD5, Kappa/Lambda were compared. In PB and PP, % of CD34+ blasts and CD38++ plasma cells were compared. Median fluorescence intensity (MFI) ratios were also compared for all patients and NHL (CD19, CD20, CD5, kappa, lambda on B cells, CD10 on neutrophils) Paired Wilcoxon, Spearman correlation, Passing-Bablok, Bland-Altman tests were used.

3. **Results**
In all patients except NHL, medians were statistically different for %PNN, %LyB CD19, %LyT CD4, %LyT CD8, and %NK but similar for other parameters (p-value threshold at 0.05). Differences could be explained by wash/lysis protocols and reagents. % of monoclonal B cells, PB, and PP were statistically similar. Spearman's test showed high correlations. Passing-Bablok and Bland-Altman tests revealed no significant bias or deviation from linearity. CD10 and lambda MFI ratios were significantly higher in DxFlex. In NHL, CD5 and lambda MFI ratios were higher in DxFlex, CD20 lower. Both cytometers produced similar results with two exceptions: DxFlex detected an additional pathological B-cell population.

4. **Conclusion**
DxFlex showed good performance overall. DxFlex's additional fluorescence channels improved sensitivity in detecting pathological cells in some cases by using one screening LS tube.

H6

PERFORMANCE EVALUATION OF THE SYSMEX DI-60 (CELLAVISION) BODY FLUID APPLICATION

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Objectives
Cytological evaluation of body fluids is crucial for differentiating between numerous potential disease processes and monitoring effectiveness of treatment. In this study, the performance of the Sysmex digital cell imaging analyzer DI-60 (CellaVision) Body Fluid (BF) application was evaluated at the department of Laboratory Medicine of the University Hospital Leuven, Belgium.

Materials and methods
In this study, 161 May-Grünwald Giemsa-stained cytocentrifuge preparations of body fluids were retrospectively analyzed. The results of the digital imaging system DI-60 were compared with those obtained through manual microscopy. Both methods were performed independently by two study investigators. The manual microscopic evaluation consisted of

classifying 200 white blood cells (WBC) in four cell classes (lymphocytes, monocytes/macrophages, neutrophils and eosinophils). The DI-60 system pre-classified 200 cells into the same different cell classes, resulting in a pre-classification. The study investigator subsequently verified and adjusted this pre-classification (if necessary), resulting in the post-classification. In addition, the study investigators independently classified each body fluid sample as malignant (including hematological and non-hematological), suspicious for malignancy or non-malignant.

Results

Out of the 161 cytospin slides, 39 could not be processed by the DI-60. This resulted in 122 remaining samples, including 11 cerebrospinal fluids, 47 peritoneal fluids, 37 pleural fluids and 27 synovial fluids. Passing-Bablok analysis showed an excellent correlation coefficient (r) between the manual differential count and the DI-60 count for all WBC types: neutrophils (r = 0.985), lymphocytes (r = 0.966), monocytes/macrophages (r = 0.934), and eosinophils (r = 0.908). Scatterplots, Passing-Bablok analyses and Bland-Altman analyses, revealed that the DI-60 tended to slightly overestimate the number of monocytes/macrophages while underestimating lymphocytes. Despite these discrepancies, the total count of mononuclear cells, including monocytes/macrophages and lymphocytes remained consistent. Regarding the morphological assessment, the majority of the analyzed samples were classified as non-malignant by both manual microscopic examination and the DI-60 (n=102). Additionally, malignancy was more distinctly observed in four body fluids through manual examination compared to the DI-60 system.

Conclusion

In conclusion, the Sysmex DI-60 BF application is a valuable tool for automating and standardizing the cytological examination of body fluids. However, it remains the user's responsibility to screen for malignancies and to ensure accurate WBC differentiation.

H7

EVALUATION OF FEATHERED EDGE TOOL IN DIGITAL MICROSCOPY FOR DETECTION OF PLATELET AGGREGATES IN PERIPHERAL BLOOD SMEARS

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Objective

In hematology laboratories digital imaging (microscopy) is routinely used for white blood cell differential. Recently, a novel digital microscopy tool was designed to scan the feathered edge of peripheral blood smears for the detection of platelet aggregates in order to diagnose pseudothrombocytopenia. Thrombocytopenia is a common laboratory finding requiring correct diagnosis as it can have major therapeutical consequences. In vitro, EDTA-induced pseudothrombocytopenia results in falsely low platelet counts due to platelet aggregation and requires accurate detection.

We studied this novel digital microscopy tool in evaluating the presence of platelet aggregates.

Material and Methods

A retrospective study was conducted at University Hospitals Leuven, analyzing 100 peripheral blood samples with suspected platelet aggregates from both ambulatory and hospitalized patients. Platelet aggregates were assessed by manual microscopy (10X and 50X magnification) on May-Grünwald-Giemsa-stained peripheral blood smears (SP-50, Sysmex) and compared to digital microscopy evaluation (10X magnification) with the DI-60 system using the feathered edge tool. Results were classified into categories based on aggregate presence (0, 1+, 2+, 3+, 4+) [1]. Manual microscopy served as the reference standard. Sensitivity and misclassification rate were calculated, with misclassification defined as a discrepancy of more than one category between both methods. Categorical agreement of semi-quantitative results between the methods was evaluated using the Weighted Cohen's Kappa coefficient (κ).

Results

Out of the 100 samples, 77 samples were positive for platelet aggregates (Table 1). The Weighted Cohen's kappa coefficient (κ) for detecting platelet aggregates was 0.73 (95%, confidence interval 0.63–0.83), indicating a good agreement between the two methods [2]. However, in 10% of our samples, the DI-60 evaluation resulted in a misclassification. Misclassification was observed in samples classified as 3+ or 4+, when the feathered edge was inadequately visualized by a scanning artifact, with aggregates predominantly concentrated in this region. The system's overall sensitivity was 85%. When samples in the 1+ category (n=9) were excluded from false negatives due to their limited clinical significance, the sensitivity increased to 97%.

Conclusion

The DI-60 automatic feathered edge tool demonstrated high sensitivity and substantial concordance with manual microscopy in detecting platelet aggregates. However, further optimization of the scanning area is needed to reduce the misclassification rate.

References

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Table 1 Overview of the categorical agreement between manual and digital microscopy.

		Manual microscopy					
		0	**1+**	**2+**	**3+**	**4+**	**Total**
Digital microscopy	**0**	23	9	0	0	2	34
	1+	3	12	6	2	5	28
	2+	0	0	6	0	1	7
	3+	0	0	0	6	1	7
	4+	0	0	0	0	24	24
	Total	26	21	12	8	33	**100**

O1

CYTOKINE PROFILE IN PATIENTS WITH POST-ACUTE SEQUELAE OF COVID-19

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The enduring impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its disease manifestation, COVID-19, on public health remains significant. Post-acute sequelae of SARS-CoV-2 infection (PASC) affect a considerable number of patients, impairing their quality of life. While the role of the cytokine storm in acute COVID-19 is well-established, its contribution to the pathophysiology of PASC is not fully understood. This study aimed to analyze the cytokine profile of PASC patients following *in vitro* stimulation of Toll-Like Receptor (TLR) pathways, comparing them with a healthy control group.

From October 2020 till March 2021, the Brugmann University Hospital's clinical research unit included PASC patients in the study. Whole blood samples were collected from 50 patients and 25 healthy volunteers. After *in vitro* stimulation under five different conditions, cytokine levels were measured using a multiplex method.

Significantly decreased cytokine levels were observed in PASC patients compared to healthy volunteers, particularly after TLR4 (IL-1α, IL-1β, IL-2, IL-10, INFα, IFNγ, IFNω and TNFα) and TLR7/8 (IL-1α, IL-1β, INFα, IFNω, IFNγ and TNFα) pathways stimulation. Principal component analysis identified two distinct clusters, suggesting a likely dysregulation of immunity involving TLR4 and TLR7/8 pathways in PASC patients.

Our study suggests that TLR4 and TLR7/8 pathways play a role in the pathophysiology of PASC. Continuous basal activation of immunity could explain the high basal concentrations of cytokines described in these patients and the decreased amplitude of response of these signaling pathways following specific stimulation.

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Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

O2

REALIZING A JOINT LABORATORY INFORMATION SYSTEM

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Objective(s)
Realize a joint laboratory information system (LIS) for three laboratories (Catharina Hospital, Anna Hospital, Maxima Medical Center) by merging the Glims systems from two laboratories (Catharina Hospital, Anna Hospital) and transitioning the third laboratory (Maxima Medical Center) from Labosys to the merged Glims system. Prepare for the transition, by establishing a comprehensive roadmap, which takes all challenges into account.

Material and Methods
Literature on how to approach such transitions is surprisingly scarce, therefore advice was scavenged from various resources (literature, colleagues, vendors, consultancies, etc.).

Results
Realizing a joint LIS is challenging endeavor, requiring careful consideration of many factors. Just to name a few: Synchronizing procedures (across laboratories), establishing communication (with analyzers and healthcare systems), ordering tests (from various systems), printing (using various protocols), tracking samples (within and across laboratories), reporting results (to various systems), logging actions (from users and analyzers), invoicing (to various parties), complying (to privacy regulation), training (technicians and maintainers), preserving historic results (conversion), contacting manufactures (strict appointments), standardizing (naming conventions), freezing (impossible to map mutating systems), testing (while maintaining daily operations).

Conclusion(s)
Firstly, the functionalities of the existing LIS should be thoroughly documented. All kinds of functionalities are easily overlooked, and implementing those last-minute is quaranteed to cause delays. Secondly, establish conventions at the start, and stick to thosse conventions. Thirdly, strive for synchronization across laboratories, and avoid laboratory-specific routines whenever possible. Deviating from conventions and building laboratory specific routines makes things much harder (in the long run).

Presentation
We love to share our mistakes!

O3

MISPL CODE IN GLIMS SYSTEMS (MAPPING THE CIRCLE OF INFLUENCE)

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Objective(s)
Custom functionality can be added to most laboratory information systems (LIS). Typically this is done via chunks of code (snippets). These snippets are crucial for core functionality (such as conversions) and useful for optimizations (such as handling exceptions). However, these snippets are also notorious for increasing LIS complexity, and hampering LIS maintainability.

Typically, snippets are written in a proprietary programming language. For example, GLIMS uses MISPL for its snippets. Essentially, GLIMS can show where snippets might be triggered, but GLIMS cannot show what snippets might influence, which hampers maintainability.

Our goal was to build a piece of software, which interprets all snippets within a GLIMS system, and shows their circle of influence.

Material and Methods
Snippets were exported from our GLIMS system, and analyzed by our software (created from scratch in the R environment). Our software features a MISPL tokenizer and MISPL interpreter (which is key determining the circle of influence of GLIMS snippets).

Results
For each snippet, our software shows three things. Firstly, how it might be triggered (for example at confirmation or authorization). Secondly, what it might do (for example: add tests to orders, stop tests within orders, add comments to tests, add attributes to patients, etcetera). Thirdly, what it might use as input (for example: results from other tests, text variables, etcetera).

Our software also works the other way around. For example, for each test, our software can list the snippets that use it as input variable (for example for calculations), and can list the snippets that influence it (for example adding or stopping it based on conditions).

Conclusion(s)
Our in-house non-commercial software greatly improved the maintainability of our GLIMS system, by automatically analyzing our snippets, and showing their circle of influence.

Presentation
Show how we maintain our GLIMS system with hundreds of interacting snippets.

SPO1

OXYGEN ATTACHMENT DISSOCIATION (OAD) MS/MS FOR THE STRUCTURAL IDENTIFICATION OF DOUBLE-BOND POSITIONS IN POTENTIAL LIPID BIOMARKERS OF PANCREATIC DUCTAL ADENOCARCINOMA

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Objective(s)

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive cancer with one of the lowest survival rates due to late diagnosis and high resistance to treatment. To aid early detection, potential lipid biomarkers of PDAC have been identified in human serum using untargeted LC-MS/MS with collision induced dissociation (CID). Since the architecture of lipids is directly related to biochemical function, it is essential to structurally characterise lipids to understand their biological roles. Lipid class and chain length can be identified using CID, however alternative fragmentation is required to localise double bonds. In this study, Oxygen Attachment Dissociation (OAD) has been applied to provide C=C specific fragmentation to structurally characterise lipids significant in PDAC.

Material and Methods

Healthy and PDAC patient serum extracts were analysed using LC-OAD-MS/MS (LCMS-9050, Shimadzu Corporation). The OAD Radical source I was used to introduce gas phase O/OH radicals into the collision cell to enable C=C specific fragmentation. Spectra were acquired with simultaneous OAD and CID-MS/MS in ESI+ and ESI- ion mode. Data were analysed using MS-DIAL, which incorporates the OAD database for automated annotation of data acquired using OAD-MS/MS. The research project was approved by the Pancreatic Cancer Research Fund Tissue Bank (PCRFTB) Access Committee.

Results

Untargeted LC-MS/MS analysis of serum samples from PDAC patients and healthy controls revealed significant alterations in lipids putatively identified as PC(18:1_18:2), PC(18:2_18:2), PC(18:2_20:4), LPC(18:2) and LPE(18:2). OAD-MS/MS spectra revealed that all these potential lipid biomarkers of PDAC specifically contain omega-6 linoleic acid (18:2(n-6,9)).

Conclusion(s)

The use of OAD aims to enhance pancreatic cancer research by providing more comprehensive identification needed to understand the biological roles of the lipids identified as potential markers of PDAC.