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Klinisk Biokemi i Norden

Nordisk Forening for Klinisk Kemi

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INDHOLD

Front page: *Old town of Aarhus. See you soon at the Congress!*

Kanske är framtidens vård enklare än vi tror – den börjar hemma vid köksbordet

Anders Larsson
Klinisk Kemi och Farmakologi
Akademiska Sjukhuset, Uppsala

Vi har ett stort antal patienter som har kroniska sjukdomar som kontrolleras med blodprover. Några exempel är patienter med diabetes, njursvikt, hjärtsvikt och hypotyreos. Många diabetespatienter kontrollerar sitt blodglukos med egenprovtagning i hemmet via kapillärprovtagning. Det fungerar i regel bra, men det borde finnas möjligheter att applicera denna provtagning även på andra analyter. För att det skall fungera så behöver patienten få instruktioner om korrekt provtagning. Det innebär i sin tur att hemprovtagning främst är intressant för patienter med kroniska sjukdomar där utbildningsinsatsen delas på flera provtagningstillfällen. Det är också mest lämpat för monitorering av sjukdom då hemprovtagningen troligen leder till lite längre svarstider (beroende på hur snabb postgången är). I Sverige användes hemprovtagning för HbA1c under många år, där blodproverna applicerades på ett filterpapper och sedan skickades med post till laboratoriet. Detta sker ju i dag i stor skala i neonatalscreeningen för genetiska sjukdomar på tex PKU-laboratoriet i Stockholm.

Hemprovtagning kan appliceras på många olika analyser, men här kommer ett räkneexempel baserat på hemtestning med TSH för monitorering av patienter som står på Levaxin på grund av hypothyreos.

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ifcc International Federation of Clinical Chemistry and Laboratory Medicine

Numera behandlades närmare 500 000 personer med Levaxin i Sverige, en ökning från drygt 300 000 år 2006. För dessa patienter är årsvis uppföljning med mätning av TSH avgörande för att säkerställa rätt läkemedelsdos och god sjukdomskontroll. Traditionellt sker denna provtagning via venösa blodprov på vårdcentral eller sjukhus – en metod som är väl etablerad men som innebär både praktiska hinder och betydande kostnader. Om man ersatte den venösa provtagningen med kapillärprovtagning och placerade provet på ett filterpapper som sedan skickas med vanlig post, så skulle man kunna utföra provtagningen i hemmet.

Ett hemprovtaget test med provtagningsmaterial, skickning av prover med post och den högre analyskostnaden på lab pga. att man behöver extrahera provet ger en totalkostnad på 150-200 kr. Motsvarande kostnad för ett venöst prov taget på vårdcentral är omkring 1 100 kronor per test.

Skillnaden – nästan 1 000 kronor per prov – beror främst på tre faktorer:

- Produktionsbortfall (tid från arbete). Vårdcentralerna är i regel bara öppna under kontorstid vilket innebär att patienten måste ta ledigt från arbetet. Om vi räknar med att patienten behöver ta ledigt 3 tim för att ta sig till vårdcentralen och att personen har en lönekostnad på 300 kr per timme så blir detta en kostnad på närmare 1000 kr. Är patienten t.ex. bilreparatör så blir lönebortfallet betydligt *högre.*
- Resekostnader till och från vårdcentralen
- Kostnader för provtagning inom vården

Själva analyskostnaden är pga. den höga graden av effektivisering på laboratorierna den minsta delen av kostnaden. Eftersom patienter med hypotyreos ofta behöver testa sig minst en gång per år, ibland oftare, blir de samlade kostnaderna betydande. Beräkningar visar att hemprovtagning för Levaxinpatienter i Sverige skulle kunna spara 500 miljoner kronor per år – och sannolikt ännu mer, eftersom många patienter testas flera gånger årligen.

Ökad bekvämlighet och tillgänglighet

Utöver de direkta kostnadsbesparingarna finns tydliga fördelar för patienterna. Hemprovtagning innebär att

Exempel på hemprovtagning. Figuren er genererad med Copilot.

man slipper boka tider, resa till vårdcentralen och vänta på provtagning. I stället kan provet tas vid en tidpunkt som passar individen själv.

Detta är särskilt viktigt för:
- personer som bor långt från vårdinrättningar
- patienter med nedsatt rörlighet
- yrkesverksamma med begränsad möjlighet att ta ledigt

Den ökade flexibiliteten kan också bidra till bättre följsamhet till rekommenderade kontroller, vilket i sin tur kan förbättra behandlingsresultaten.

Minskad belastning på vården

Primärvården i Sverige är i dag hårt belastad, och laboratorieverksamheten utgör en betydande del av arbetsbördan. I Uppsala län analyserades över 120 000 TSH-prover under ett år, vilket illustrerar omfattningen av rutinmässig uppföljning vid hypotyreos.

Genom att flytta en stor del av provtagningen till patientens hem kan:
- köer och väntetider minska
- vårdpersonalens tid frigöras
- resurser omfördelas till patienter med större vårdbehov

Det innebär inte att vården minskar sin roll, utan snarare att den kan arbeta mer effektivt och fokusera på mer komplexa fall. För laboratorierna kommer detta inte innebära minskat arbete utan snarare tvärtom. Det tar lite mer tid per prov då man behöver extrahera provet från filterpapperet och om provtagningen blir enklare för patienten så är det troligt att testningsintervallen kommer att minskas, dvs. antalet analyser ökar.

Utmaningar vid införande

För att hemprovtagning ska fungera optimalt krävs dock vissa förutsättningar:
- tydliga instruktioner till patienterna
- enkel provtagningsutrustning
- smidig integration i laboratoriets arbetsflöden
- fortsatt kvalitetssäkring jämfört med venösa prover

Dessa utmaningar bedöms dock som hanterbara, särskilt i takt med att digitala vårdlösningar utvecklas.

Framtidens provtagning är nära patienten

Sammanfattningsvis så talar det mesta för att hemprovtagning erbjuder en win-win-situation:
- för patienter – enklare, snabbare och mer flexibel vård
- för vården – minskad belastning och lägre kostnader
- för samhället – betydande ekonomiska besparingar

I takt med att antalet patienter ökar och kraven på tillgänglig vård skärps framstår hemprovtagning som en naturlig del av framtidens sjukvård. Att låta patienten ta större ansvar – med rätt stöd – kan både förbättra livskvaliteten för patienten och minska sjukvårdens kostnader.

När man tittar på detta räkneexempel så förefaller det rimligt att vi kommer se mycket mer av detta i framtiden. I Uppsala har man redan inlett forskningsstudier där man skall kontrollera patienter med hemprovtagning. Som jag ser det kommer det att ta några år, eftersom varje analys måste noggrant valideras för att garantera att vi får motsvarande analysresultat med filterpapperprovtagning som med traditionell provtagning. Det gör att det kommer ta tid innan vi ser detta i klinisk rutin, men som jag ser det är det främst en tidsfråga.

Det som en gång krävde ett besök på vårdcentralen kan nu rymmas i ett kuvert – framtiden är snart här!

Ordförandespalten

Per Bjellerup
Chairman of NFKK

Photo: Maj-Britt Bjellerup Franzén.

Maybe August is the "best" month of the year! During the last month of summer, the days are still long, the sun's rays are still warming us nicely, and it can be really hot in the air and swimming in the sea and lakes is often a little warmer. In contrast, the nights are starting to get longer and darker, the starry sky is visible again. The evening air provides a fresh humidity and coolness that enhances the scents of nature. We have had time to disconnect from everyday life and work for a few weeks and recharge our batteries for upcoming challenges. We are filled with a mixture of fond memories and confidence for the challenges of autumn.

Four transformative years!

I have now been chairman of the NFKK for four years and it is time to sum up and hand over the assignment to a new chairman for the coming four years. When I took office in May 2022, we had just escaped the deadly grip of the covid pandemic and Russia had just started its terrible war of terror against Ukraine. During these four years, we have also witnessed and come to understand how ongoing climate change is affecting, and will

The winners of the first NFKK Young Researcher Award (NYRA) and the organizers in 2024. From left: Lasse Back Steffensen (1st prize winner), Emil List Larsen (2nd prize winner), Selma Salonen (3rd prize winner), Lars Melholt Rasmussen and Anders Larsson. Photo: Per Bjellerup.

The Finnish course The Quality Hike was, as its name implies, learning and discussion by walking in the nice autumn weather in the very middle of Finland in 2023.

continue to affect, our lives in profound, and I would argue, negative ways. AI has been introduced and has already powerfully demonstrated its opportunities but also its risks. For NFKK, the pandemic meant that we had to cancel two Nordic congresses, which not only meant that our Nordic exchange was limited, but also a financial strain for NFKK with increased costs and decreasing income. We have also seen that the replenishment of younger clinical chemists and chemists in Iceland continued to shrink to new critical levels.

Four innovative years!

During these years, we have also had great successes. When corporate support for the Astrup Prize was withdrawn, we created NYRA, a modern award for young researchers that is now financed through the Nordic Congress and gives us a more stable situation. NYRA has been a great success and for this year's Nordic Congress in Aarhus in September we have received twelve fine contributions, several describing world-class work. I would like to extend a big thank you to Lars Melholt Rasmussen for driving the work with NYRA in such an exemplary manner!

The Finns have launched their own Nordic course, *The quality Hike*. This exciting "learning by walking" course will be held for the second time in 2027. I would like to extend a big thank you to Anna Linko-Parvinen who initiated the course. We are also happy that the Norwegian *Finsekurset* has been resumed.

KBN has been rolling along nicely with many great articles over the years and now also with more contributions from Finland. From 2027, the journal will become fully digital, a natural step in response to recent developments in the magazine industry. I would like to extend a big thank you to Helle Borgstrøm Hager who has developed KBN for many years in her role as editor-in-chief. I would also like to take the opportunity to thank Henrik Alfthan for his many years of involvement in the KBN and NFKK websites and for all the fantastic nature pictures in the magazine.

We will also remind ourselves of the successful "XXXIX Nordic Congress in Clinical Chemistry" that the Karolinska University Laboratory organised in a constantly sunny Stockholm in September 2024.

NFKK is truly a force to be reckoned with in Nordic clinical chemistry!

Two figurines from Skultuna Brass Mill (founded in 1607) were given to SKKY at its 80th anniversary as a token of the longstanding Nordic friendship in general and between Finland and Sweden in particular. The Swedish lion is made from a clay figure by Lisa Larsson, one of Sweden's most well-known ceramicists. The Finnish Snorkmaiden from the Moomin valley is created by Tove Jansson, Finland's world famous writer and artist. As a coincidence, the Moomin world is also 80 years old. Photo: Per Bjellerup.

Happy Birthday SKKY!

The Finnish Society for Clinical Chemistry (SKKY) turned 80 this year and is the second oldest society in Clinical Chemistry in existence. I do not yet know which society is the oldest one, at least it is not any other Nordic society. The birthday was celebrated with a fantastic banquet in Helsinki on a sunny and warm spring evening in April. As chairman of NFKK, I had the honour of attending and congratulating the society. A fantastic party where the nestor in Finnish Clinical Chemistry, Ulf Håkan Stenman with his wife Ingrid, participated.

The Nordic Congress in Aarhus 2026

Now we are looking forward to the next Nordic Cogress in September in Aarhus. The scientific program looks great, and dancing is promised at the banquet. Read more about the Congress later in this issue. I hope to see you at the NFKK session about analytical interference!

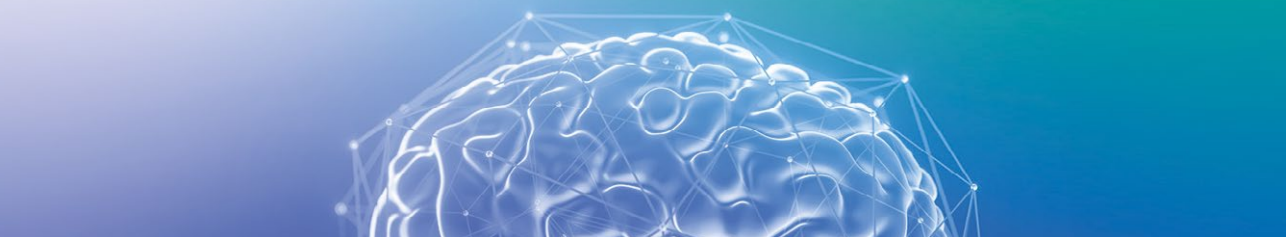
Anna Linko-Parvinen

In connection with the congress, Anna Linko-Parvinen will take over as chair of NFKK. I have had the pleasure of getting to know Anna through our collaboration in NFKK for more than ten years and Anna will be an excellent and extremely competent chair of NFKK. I wish Anna good luck in her work!

With that, dear KBN readers, I would like to thank you for this period and wish you a continued nice late summer! Remember, clinical chemistry is a very important medical specialty, the bridge between chemistry and the clinic!

See you soon in Aarhus!
Bästa hälsningar Per

Professor Ulf-Håkan Stenman and his wife Ingrid were also attending the banquet. Ulf-Håkan has a long history of outstanding research within the fields of hormones and oncology markers. Photo: Per Bjellerup.



Detektion af Alzheimer's patologi i blodet

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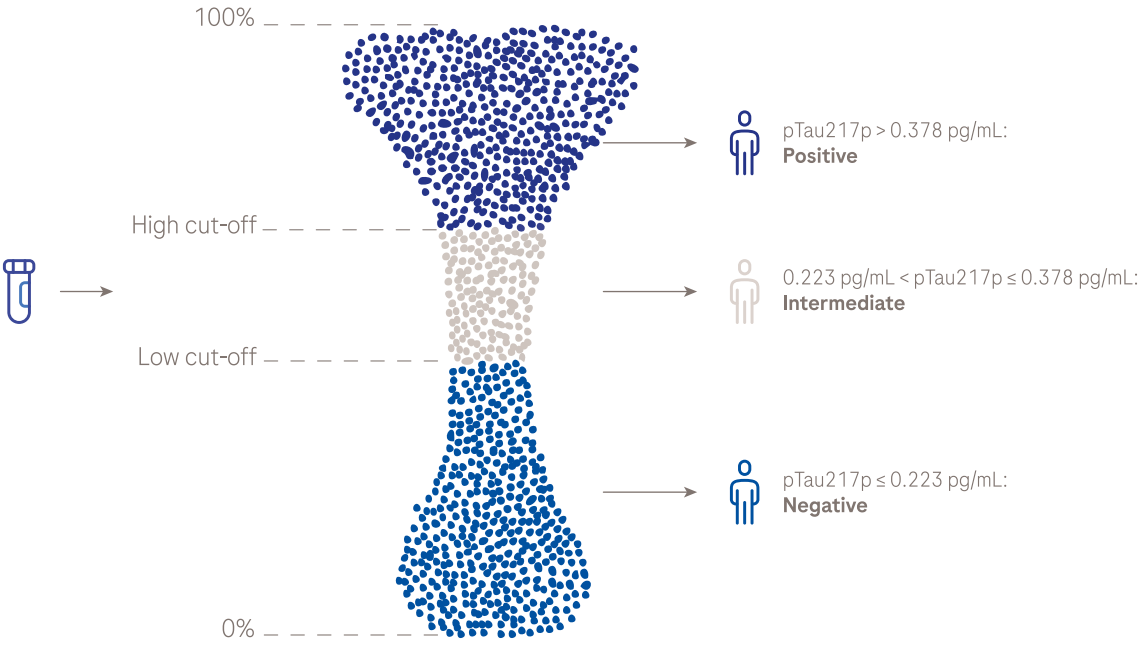

Adapted from Schindler, S. E., Galasko, D., Pereira, A. C., et al. (2024). Acceptable performance of blood biomarker tests of amyloid pathology – recommendations from the Global CEO Initiative on Alzheimer's Disease. Nature Reviews Neurology, 20, 426–439. https://doi.org/10.1038/s41582-024-00977-5

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- Kan anvendes som en del af et diagnostisk udredningsforløb sammen med en kognitiv vurdering for at give en pålidelig Alzheimer's-diagnose.

References:
1. Thijssen EH, et al. Lancet Neurol. 2021;20:739–52.
2. Therriault J, et al. Alzheimers Dement. 2023;19:4967–77.

MC-DK-02901 Roche Diagnostics A/S, Flaskehalsen 17, 4. sal, 1799 København V





Jens Juul Holst *Claus H. Gravholt* *Curtis Huttenhower* *Emma Raitoharju* *Jakob Kjellberg*

See you soon at the 40th Nordic Congress in Clinical Biochemistry 15-18 September 2026!

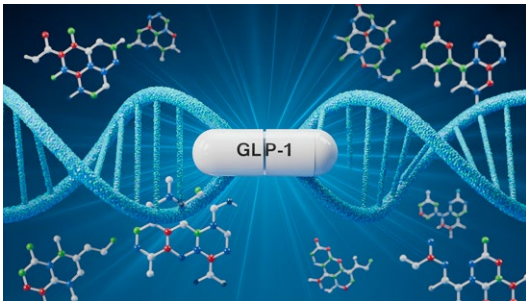
Plenary lectures during the upcoming Congress in Aarhus

TUESDAY 15 September

Gastro-intestinal peptide hormones, from basic research in clinical biochemistry to major public impact

Jens Juul Holst is Professor at the Department of Biomedical Sciences and Senior Group Leader at the Novo Nordisk Foundation Centre for Basic Metabolic Research, University of Copenhagen, Denmark.

His scientific work has focused on peptide hormones of the gastrointestinal tract. Among his major scientific achievements is work on the peptide hormone GLP-1 (glucagon-like peptide 1) and its significance for insulin secretion, food intake, and appetite control. His work has been of major importance for the development of GLP-1 analogue therapeutics now in use around the world to treat type 2 diabetes and obesity.



WEDNESDAY 16 September

Sex, sex differences and biomarkers

Professor ***Claus H. Gravholt***, Department of Endocrinology, Aarhus University Hospital, Aarhus, Denmark.

How do we determine sex? In a clinical setting we determine sex based on chromosomal sex (46,XY or 46,XX), gonadal sex (testis or ovaries), hormonal sex (testosterone or estrogen), and anatomical sex (internal (to have a uterus or not) and external (penis or vagina)). This is usually straightforward in most cases, however in case of disorders of sex development (DSD) there may be incongruency between these different levels of sex and for example we may see an individual with a typical feminine appearance and 46,XY, testis, high levels of testosterone and without a uterus (46,XY female DSD with androgen insensitivity). Patients with DSD typically presents a challenge, when assessing biochemical measures, and this may initially lead to confusion, until a diagnosis is reached. In addition to these levels of sex, which are easily determined clinically, we also talk about the social gender or the perception of oneself, which again may not be congruent with the sex assigned at birth. Some of these individuals choose to change sex – transpersons. In transpersons (female-to-male (FtM), male-to-female (MtF)), many biochemical measures will change in line with the administered sex steroid therapy.

WEDNESDAY 16 September

Next steps for microbiome therapies: mechanism of action

Professor ***Curtis Huttenhower***, Harvard Chan Microbiome in Public Health Center, Harvard University, Boston, USA.

Several microbiome-derived therapies have now received or are undergoing regulatory approval, including both live biotherapeutic products (LBPs) and bioactive small molecules of microbial origin. However, almost none have established mechanisms of action, be they chemical, immune-mediated, ecological, or otherwise. This process is impeded by the extent of microbial "dark matter" even in the well-studied human gut microbiome: some 50-75% of microbial proteins cannot be assigned even putative function from metagenomes alone, and this fraction is above 95% in other environments. We have developed new methods that provide potential pathway assignments for approximately 25% of human gut microbiome proteins, as well as guidelines for extending them to other hosts and environments. Examples include new chemotaxis and B-vitamin metabolism cassettes in Hungatella hathewayi, implicated in inflammatory bowel disease and colorectal cancer, and CRISPR system members in the "anti inflammatory" Faecalibacterium prausnitzii. In addition to metabolic functions, many previously uncharacterized sequences are likely to be viral, and we find perturbations in both DNA and RNA viromes during inflammation (e.g. E. coli phage correlated with increased E. coli abundance) using novel profiling methods. Finally, many ofw these new functions can be linked to small molecule chemistry as well, e.g. putative bilirubin derivatives depleted in IBD. These approaches thus aid in identifying the molecular mechanisms underlying ecological, metabolic, and disease phenotypes and treatments.

Møllestien, Aarhus.

THURSDAY 17 September

The role of epigenetics in mediating health and disease

Academy Research Fellow ***Emma Raitoharju***, Faculty of Medicine and Health Technology, Biomedicine, Tampere University, Finland.

Epigenetic profiles regulate cellular function and gene expression without altering the DNA sequence. These profiles, for example, ensure that daughter cells retain the identity (i.e. cell type) of their mother cells. From an individual's perspective, epigenetic mechanisms enable the body to adapt to environmental conditions and even allow the future offspring to adapt to anticipated conditions already during pregnancy. During lifespan, epigenetic profiles are responsive to external exposures, such as smoking and chronological age and can be used to measure these exposures indirectly, when data is not available. Epigenetic profiles also reflect broader phenotypes, such as rate of biological ageing, but the role of epigenetics in the pathology of non-communicable diseases as well as the clinical utility of these measurements is still under investigation.

FRIDAY 18 September

The future of healthcare – moving closer to the citizen

Professor Jakob Kjellberg, VIVE – The Danish Center for Social Science Research, Denmark.

Professor Jakob Kjellberg – a member of the Danish Health Structure Commission ("Sundhedsstrukturkommissionen") – will share insights from the Commission's work as a starting point for discussing the future development of Nordic healthcare systems. He will examine the necessary shift from hospital-based care towards community- and primary care oriented solutions, addressing the magnitude of change required, the implications for clinical practice and laboratory medicine, and the opportunities and challenges in bringing healthcare closer to the citizen.

Den Gamle By, Aarhus.

Let the Competition Begin!

Scientific Excellence and Awards at the Nordic Congress 2026

When we meet in Aarhus in September 2026, there will be plenty of opportunities not only to share science, but also to celebrate scientific competitive excellence.

One of the highlights will be the **NFKK Young Researcher Award**, chaired by Professor Lars Melholt Rasmussen, Odense. Formerly known as the Astrup Prize, this prestigious award celebrates outstanding contemporary Nordic research in clinical chemistry by researchers under 40. A committee of five senior scientists, representing all five Nordic countries, have selected three finalists to present their work orally at the Congress. And the winners will receive DKK 40,000, 20,000 and 10,000, respectively.

Another major attraction is the **Lorentz Eldjarn Prize Competition for Best Publication**, chaired by Professor Jens Petter Berg, Oslo. Three first authors of highly cited SJCLI papers have been invited to present their research during the Congress. Their scientific work — and their ability to communicate it clearly — will be judged by the Prize Committee. The stakes are high, with prizes of DKK 100,000, 50,000 and 30,000 for first, second and third place.

The Congress will also put the spotlight on Transformative Lab-Enabled Best Practices from the 2026 **UNIVANTS of Healthcare Excellence Award**. Chaired by Tricia Ravalico, Executive Lead of the UNIVANTS programme, the session will showcase winners presenting examples of how laboratory medicine can transform healthcare and improve patient outcomes.

And then there are the **posters**! Awards will recognize the best poster presentations, judged on both scientific quality and presentation.

Finally, for those who prefer their science with a touch of fun, the **Congress Quiz** will offer everyone a chance to compete. Expect questions, surprises and perhaps a few friendly disputes over the correct answer — with a prize awaiting the ultimate clinical chemistry quiz champion.

All winners will be revealed with festivitas at the gala dinner on the evening of September 17.

Scientific program

Tuesday September 15

12:45 -13:00	**Wellcome**		
	OPENING LECTURE by professor *Jens Juul Holst*, Copenhagen, Denmark		
13:00-13:45	**Gastro-intestinal peptide hormones, from basic research in clinical biochemistry to major public impact**		
	Main Hall	**Hall 2**	**Hall 3**
14:00-15:30	***Session 1*** Novel diagnostic opportunities in neurological disease and cognitive decline	***Session 2*** Sustainability in the lab	***Session 3*** Thyroid function tests – past, present, and beyond
15:45-17:15	***Session 4*** What's new: Lipids, lipoproteins, and cardiovascular risk	***Session 5*** ctDNA for early detection and screening	***Session 6*** Establishing Robust Pediatric Reference Intervals
17:30-18:00	**Opening ceremony**		

Wednesday September 16

	Main Hall	**Hall 2**	**Hall 3**
08:00-09:30	***Session 7*** Reproductive biomarkers	***Session 8*** Presentation of working groups in NSMB	***Session 9*** Extracellular vesicles
	PLENARY LECTURE by professor *Claus H. Gravholt*, Aarhus Denmark		
09:45 -10:30	**Sex, sex differences and biomarkers**		
	PLENARY SESSION - PRIZE COMPETITION		
10:45 -12:00	**The NFKK young researcher award**		
12:30 -13:00	Poster walk I		
	PLENARY LECTURE by Professor *Curtis Huttenhower*, Boston, USA		
13:00-13:45	**Next steps for microbiome therapies: mechanism of action**		
	Main Hall	**Hall 2**	**Hall 3**
13:55-14:15	Company session 1	Company session 2	Company session 3
14:30-16:00	***Session 10*** Fibrinogen and fibrinolysis in health and disease	***Session 11*** AI in Diagnostics: Where are we now and what lies ahead?	***Session 12*** Mass spectrometry-based proteomics in clinical biochemistry
16:15 -17:45	***Session 13*** Outcome studies in laboratory medicine	***Session 14*** Updates from Nordic screening and screening pilots (session by SKKY)	***Session 15*** The microbiome and human health

Thursday September 17

	Main Hall	Hall 2	Hall 3
08:00 - 09:30	***Session 16*** Bone turnover markers for monitoring treatment for osteoporosis	***Session 17*** "Illt er í ætt gjarnast". Hereditary diseases in Iceland (session by IFKE)	***Session 18*** Biomarkers of ageing
	PLENARY LECTURE by Academy Research Fellow *Emma Raitoharju*, Tampere, Finland		
09:45 - 10:30	**The role of epigenetics in mediating health and disease**		
	PLENARY SESSION - PRIZE COMPETITION		
10:45 - 12:15	**The Lorentz Eldjarn prize competition for best publication**		
12:45 - 13:15	Poster walks II		
	PLENARY SESSION		
13:20 - 14:50	**UNIVANTS of Healthcare Excellence Award**		
	Main Hall	**Hall 2**	**Hall 3**
15:00 - 15:20	Company session 4	Company session 5	Company session 6
15:25 - 15:45	Company session 7	Company session 8	Company session 9
16:00 - 17:30	***Session 19*** Biomarkers of chronic kidney disease	***Session 20*** From Algorithm to Insight: Practical Applications of AI in Diagnostics	***Session 21*** Platelet function testing: old acquaintances and novel biomarkers

Friday September 18

08:00 - 09:30	***Session 22*** The hidden problem of analytical interference – how to identify, investigate and prevent? (session by NFKK)	***Session 23*** Mass Spectrometry in Myeloma	***Session 24*** ctDNA for guiding treatment decisions
09:45 - 11:15	***Session 25*** Choosing wisely	***Session 26*** Session by YLKB	***Session 27*** Preparedness for war and crisis in laboratory medicine (Session by SFKK)
	PLENARY LECTURE by professor *Jakob Kjellberg*, Copenhagen, Denmark		
11:30 - 12:15	**The future of healthcare – moving closer to the citizen**		
12:15 - 12:30	**Closing ceremony**		

Working groups as a tool for professional development in clinical biochemistry

Ingrid Hokstad[1,2], Mie Hessellund Samson[3,4]
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The organization of professional activities within scientific societies in clinical biochemistry varies across the Nordic countries. In this article, we describe how such work is structured in Norway and Denmark, and ask whether the time is right for more joint Nordic initiatives.

Laboratory medicine is characterized by relatively small professional environments within each healthcare institution. However, many face similar challenges that colleagues elsewhere may already have solutions to. By collaborating across laboratories, healthcare institutions, and national borders, both the capacity and quality of improvement projects may be enhanced.

The Nordic professional communities in clinical biochemistry have a long tradition of collaboration. Although the scientific societies are united under the Nordic Federation of Clinical Chemistry (NFKK), much of the professional work is conducted at the national level. The individual societies have adopted different organizational models to structure activities related to professional development, harmonization, recommendations, and quality improvement. The establishment of scientific committees, as well as working groups and special interest groups, are examples of such models used in, among others, the Norwegian Society of Medical Biochemistry (NSMB) and the Danish Society for Clinical Biochemistry (DSKB).

The aim of this article is to inspire other Nordic countries to establish similar working groups, where such structures are lacking or insufficiently formalized. As a source of inspiration, we provide an overview of how professional activities are currently organized in Norway (NSMB) and Denmark (DSKB). Finally, we discuss whether - in selected areas - it may be appropriate to establish more joint Nordic working groups, given that professional challenges and needs are often shared.

NSMB

NSMB has a long and rich history within the field of medical biochemistry in Norway. The organizations that preceded the current society can be traced back to 1932. Several key institutions in Norwegian laboratory medicine originated from this environment, including the quality organization Noklus and the journal *Scandinavian Journal of Clinical and Laboratory Investigation* (SJCLI). NSMB and its predecessors have also been part of the Nordic collaboration through NFKK, and have actively contributed to the organization of Nordic congresses and courses.

In 2024, the two former specialist societies NFMB and NSMB were merged into a single joint society (1), organized under the Norwegian Medical Association. Most Norwegian specialists in medical biochemistry are currently members of the society. In addition, the organization includes associate members from related professional groups, such as biomedical laboratory scientists and other relevant professions.

Working groups and special interest groups in NSMB

NSMB has both working groups and special interest groups within its organization (2). Working groups are primarily project-based, with a defined mandate and a deadline for delivering a report or professional recommendation. Special interest groups are more permanent structures that bring together professionals with shared interests and carry out ongoing work within a given topic. At present, NSMB has the following groups:

Working groups:

- Choosing Wisely (Chair: Mette Brokner, Vestfold Hospital Trust)
- Recommendations for reporting of monoclonal components (Chair: Sutirtha Chakraborty, Helse Fonna)
- Recommended use of HbA1c in patients with thalassemia or hemoglobin variants (Chair: Eva Camilla Langsjøen, Fürst)
- Which eGFR equations are optimal for Norwegian patients? (Chair: Maria Averina, University Hospital of North Norway)

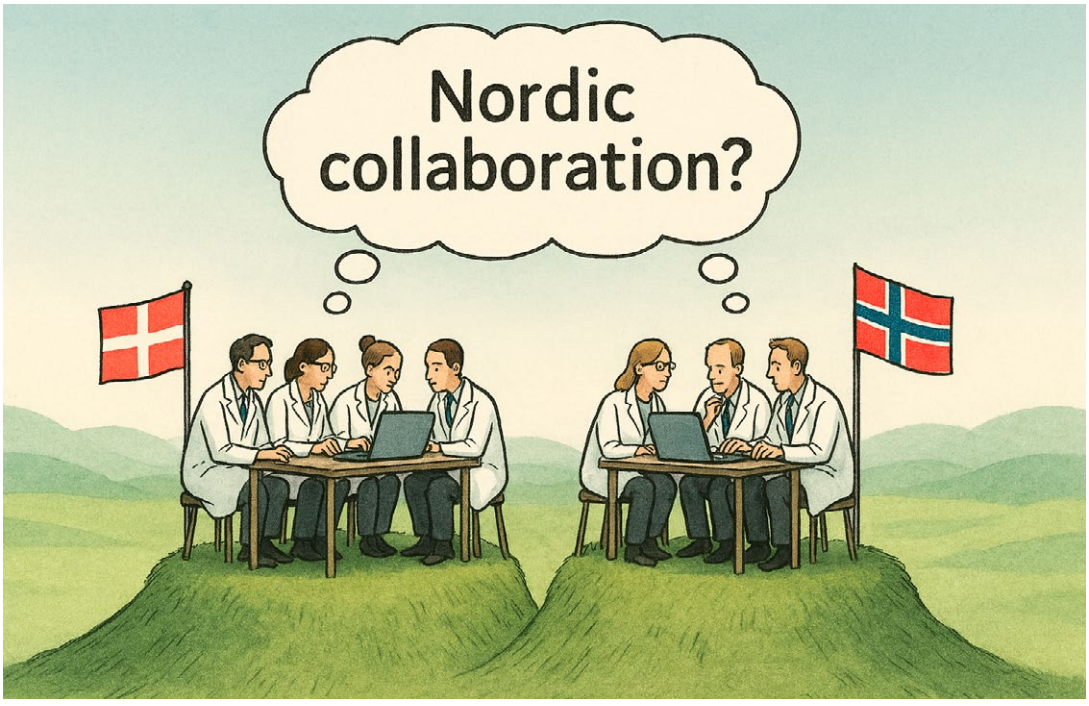
Special interest groups:

- Pediatric reference intervals (Chair: Ingrid Alsos Lian, St. Olavs Hospital)
- Environmental toxins and public health (Chair: Maria Averina, University Hospital of North Norway)
- Reference intervals and clinical decision limits (Chair: Erik Koldberg Amundsen, Oslo University Hospital)

NSMB provides financial support for one in-person one-day meeting per group per year. The board may also, upon assessment, provide financial support for activities beyond meetings, such as publication costs or other expenses arising from the groups' work.

DSKB

On the initiative of Poul Astrup, Per Lous, and Anders Tybjærg Hansen, the Danish Society for Clinical Chemistry was founded at a meeting at Rigshospitalet on Saturday, 27 October 1956. The society was originally named the Danish Society for Clinical Chemistry and Clinical Physiology (SKKKF). Clinical Physiology became an independent medical specialty in 1970, and the society was subsequently renamed the Danish Soci-



Nordic collaboration or separate national working groups (som arbeider på "hver sin tuve"). The illustration was generated using Copilot.

ety for Clinical Biochemistry. From its inception, the purpose of the society has been to promote theoretical and practical advances within clinical chemistry (3).

DSKB is part of the Organization of Medical Societies in Denmark (LVS), and thereby represents the specialty within the Danish healthcare system. The society currently has approximately 400 members, including physicians, biochemists, and biomedical laboratory scientists.

The society's activities include organizing courses and other activities related to both medical and academic specialist training, establishing and supporting working groups and committees, hosting member meetings and scientific congresses, and publishing the society newsletter *DSKB-Nyt*.

Working groups and committees within DSKB

Working groups are continuously established and discontinued under the auspices of DSKB. As in NSMB, they are project-based, with a defined mandate and typically result in the production of a guideline or professional recommendation. Many working groups include representation from medical specialties outside clinical biochemistry or are established as collaborative projects, ensuring that both clinical and laboratory perspectives are addressed. An overview of current groups is available on the society's website (4) and currently includes:

Working groups

- Working group on sample stability (Chair: Christina Munch Jensen)
- Working group for updating the DSKB/DMSG guideline on M-protein testing (Chair: Sigrun Thorsteinsdottir (DMSG))

Like NSMB, DSKB also has more permanent structures referred to as committees. These include one standing scientific committee and two committees for post graduate specialist training (one for physicians and one for biochemists).

Committees

- *Scientific Committee for Quality Assurance (VUK) (Chair: Marianne Benn*). The purpose of VUK is to monitor and develop recommendations within quality assurance. The committee was established in its current form in 1996, although quality assurance activities within DSKB date back an additional 30 years, when the first committee for analytical quality was formed. VUK is a highly active committee that has produced numerous recommendations over the years. Both an overview of recent reports and a historical overview are available on the society's website (5). Today, VUK's recommendations constitute an important tool for quality assurance work nationwide.

- *Committee for Post Graduate Specialist Training for Physicians (UUFL) (Chair: Nete Hornung)*. UUFL develops and organizes courses related to specialist training in clinical biochemistry. In addition, the committee plays an important role in developing the curriculum for the specialist training in collaboration with the Danish Health Authority. UUFL works closely with the Committee for Post Graduate Specialist Training for Biochemists (UUFB).

- *Education Committee for Post Graduate Specialist Training for Biochemists (UUFB) (Chair: Eva Greibe)* UUFB is responsible for postgraduate training of biochemists working in Clinical Biochemistry in Denmark, including ensuring that the training meets the requirements for registration in the EC4 register within the EU. Considerable effort is devoted to planning and organizing courses, both targeted at biochemists in specialist training and joint courses with physicians in specialist training in collaboration with UUFL.

Finally, DSKB is represented in a wide range of permanent national committees and groups, often across specialties and with different institutional affiliations within the Danish healthcare system. An overview of these representations is also available on the society's website (6).

Experience shows that working groups and formal representations are essential tools for developing the specialty of Clinical Biochemistry. However, their impact extends beyond narrow specialty-specific interests and contributes significantly—through cross-disciplinary collaboration—to the broader professional development of the healthcare system in Denmark. For a specialty that spans disease areas and healthcare sectors, the task of ensuring representation in all relevant initiatives and groups is both extensive and challenging.

On this basis, DSKB has a fundamental interest in participating in collaborations that bring together

relevant knowledge and competencies around shared challenges. This naturally also applies at the Nordic level. A good example of such collaboration is the preanalytical working group, which for several years was organized under NFKK.

One important consideration before establishing cross-national groups is whether the task is strictly biochemical, or requires collaboration with other clinical specialties. The latter may be more challenging to manage in a Nordic context. Ultimately, the establishment of future Nordic groups should be based on shared challenges, while also critically assessing whether meaningful synergies can be achieved through collaboration.

Conclusion

Increased collaboration—both nationally and across the Nordic countries—may strengthen the role of laboratories as diagnostic partners, promote harmonization of test results and clinical decision limits, and facilitate the sharing of specialized expertise. We hope that this article may inspire more professional environments to establish working groups and special interest groups within medical biochemistry.

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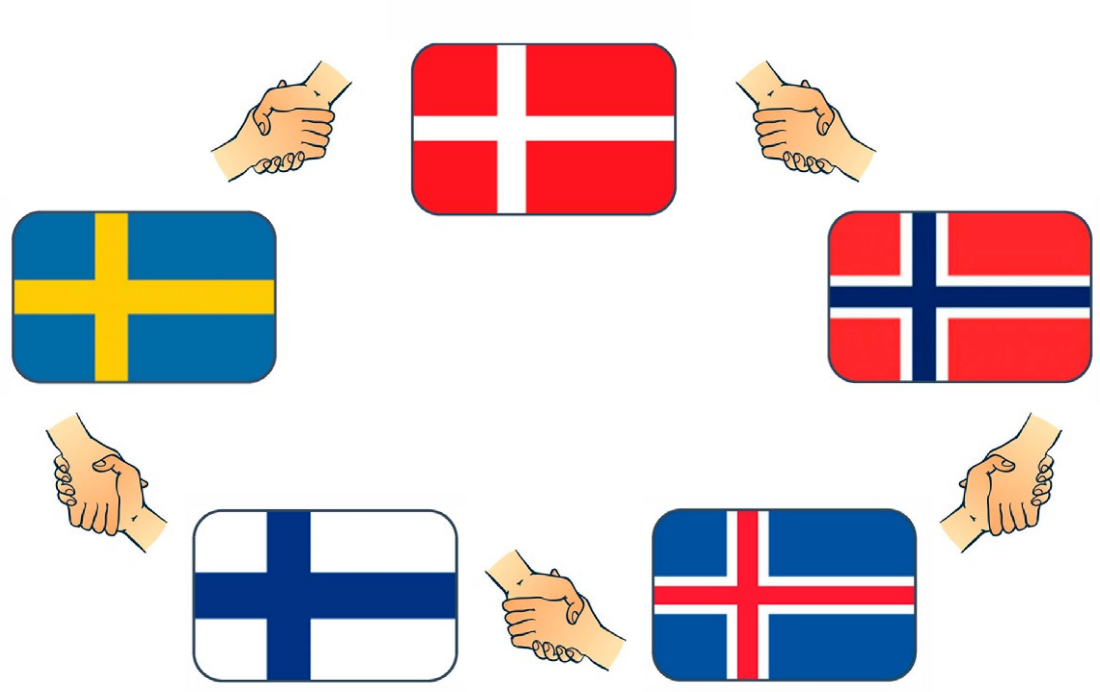

Increased collaboration across the Nordic countries?

Miljøgiftlaboratoriet ved Universitetssykehuset i Nord Norge (UNN)

Et spesiallaboratorium for analyser av organiske og uorganiske miljøgifter i humane prøver

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Oppsummering
Miljøgifter er allestedsnærværende, de inngår i næringskjeden og kan ha betydelige helseskadelige effekter, særlig under fosterutviklingen og i tidlig barndom. Det er stort behov for økt forskning på dette området. De tradisjonelle vitenskapelige miljøer innen medisinsk forskning har begrensede muligheter til å gjøre miljøgiftanalyser i større skala. Miljøgiftlaboratoriet ved Universitetssykehuset i Nord Norge (UNN) ble opprettet for å imøtekomme dette behovet.

Bakgrunn
En miljøgift er et kjemisk stoff som er skadelig for miljøet og levende organismer, selv i små konsentrasjoner og kan være antropogene og/eller naturlige. Det skilles mellom persistente og ikke-persistente miljøgifter basert på stoffets halveringstid. Persistente miljøgifter har tre egenskaper: de er toksiske, akkumulerende og lite nedbrytbare, noe som gjør dem spesielt problematiske. De er giftige for planter, dyr og mennesker, kan hope seg opp i næringskjeden med økende konsentrasjon jo høyere opp man kommer i næringskjeden, og brytes svært sakte ned i naturen, noe som gjør at de kan forbli i miljøet i lang tid (lang halveringstid). Noen eksempler kan være polyklorerte bifenyler (PCBer, antropogen og tidligere brukt i elektrisk utstyr, maling og isolasjonsmaterialer), dioksiner (antropogen og naturlig, og dannes som giftige biprodukter ved forbrenning og visse industrielle prosesser), per- og polyfluoralkylstoffer (PFAS, antropogen og brukt i svært mange applikasjoner, blant annet impregnering, kosmetikk, non-stick-belegg og brannslukningsskum), og tungmetaller (f.eks. kvikksølv, bly og arsen, som er både antropogen og naturlig). Ikke-persistente miljøgifter er kjemiske stoffer som brytes raskt ned og derfor ikke oppholder seg i organismer eller miljøet over lengre tid. Disse stoffene har en kort halveringstid, noe som betyr at de ikke akkumuleres i samme grad som persistente miljøgifter. Eksempler kan være bisfenoler (brukes i produksjon av plast og epoksyharpikser), ftalater (brukes som myknere i plast, spesielt i PVC) eller moderne pesticider (som for eksempel glyfosfat, pyretroider eller neonikotinoider).

Arbeidet med å etablere Miljøgiftlaboratoriet ved Laboratoriemedisin, Universitetetssykehuset i Nord-Norge (UNN) startet allerede i 2005/ 2006. Bakgrunnen var at legene ved avdelingen i økende grad ble oppmerksomme på at miljøgifter finnes overalt, de finnes blant annet i maten vi spiser, i drikkevann, moderne tekstiler, luft og støv. Det er derfor uunngåelig at både mennesker og dyr eksponeres for disse stoffene. Miljøgifter antas å inngå i næringskjeden, med de konsekvenser dette kan medføre (1, 2). Disse stoffene påvises i varierende grad hos mennesker, og flere miljøgifter har dokumenterte svake østrogenlignede egenskaper.

Det har vært, og er fortsatt et stort behov for økt forskning på miljøgifters biologiske effekter, særlig deres innvirkning på menneskers helse, inkludert betydning for sykdomsutvikling og dødelighet. Nyere forskning viser at miljøgifter kan ha uheldig virkning på utvikling av hjerte-kar sykdom, diabetes, kreftforekomst, immunsystemet, hormonbalansen og fertilitet både hos menn og kvinner. Vi kjenner relativ godt til gamle miljøgifters helseskadelige effekt (som for eksempel

Figur 1. *Kunnskapspyramiden for miljøgifter og helseeffekter. Miljøgifter er klassifisert i tre nivåer basert på tilgjengelig kunnskap. Modifisert figur etter Landrigan.*

PCBer, bly og sprøytegiften DDT), men kunnskapen om nyere forurensende stoffer er fortsatt begrenset (Figur1). Små barn og fostre er spesielt sårbare for eksponering for miljøgifter (2). I en publikasjon i New England Journal of Medicine fra januar 2025 settes de siste tiårs økning i forekomst av barnekreft, defekter i reproduksjonsorganer hos mannlige spebarn, defekter i utvikling av nervesystemet, autisme, pediatrisk astma, fedme og diabetes 2 hos barn i sammenheng med eksponering for syntetiske kjemikalier (3). Vi ser også sammenheng mellom PFAS og funn blant norske spebarn med forsinket motorisk utvikling, og tenåringer med tidligere menarke i jenter (4, 5).

Etablering

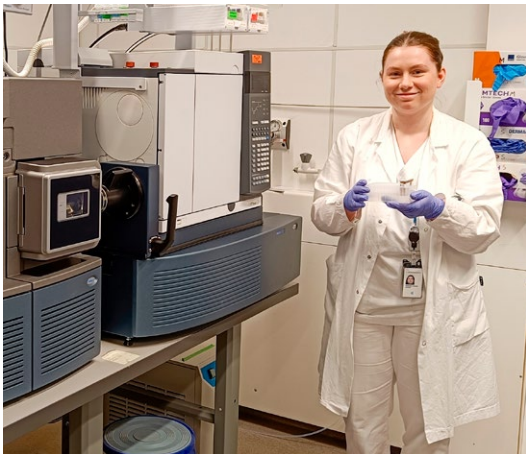
Analysering av miljøgifter er både teknisk og økonomisk krevende. Fagmiljøet ved Laboratoriemedisin ved UNN, i samarbeid med erfarne miljøgiftforskere og deler av ledelsen i Helse Nord RHF, anså det som ønskelig, og i praksis nødvendig, at det ble etablert et spesiallaboratorium for slike analyser. Et slikt tilbud manglet innen det offentlige sykehussystemet og ved universiteter innen medisinsk forskning i Norge og de fleste nordiske land. Laboratoriets primære oppgave skulle være å bidra til forskning, selv om også skulle være mulig å utføre enkelte kliniske analyser.

På lengre sikt vil flere analyser av miljøgifter tas i bruk i klinisk praksis. Dette synspunktet ble støttet av både Det helsefaglige fakultet ved UiT Norges Arktiske Universitet og Helse Nord RHF, og i 2011 kom Miljøgiftlaboratoriet i stand som et samarbeid mellom Universitetssykehuset i Nord Norge, UiT Norges Arktiske Universitet og Helse Nord RHF. Helse Nord RHF informerer på egen hjemmeside om miljøgifter og Miljøgiftlaboratoriet (7). Emnet og Miljøgiftlaboratoriet har også vekket mer allmenn interesse i Nord Norge og er omtalt blant annet i High North News (8).

Ettersom befolkningsundersøkelser er nødvendige for å avdekke miljøgifters helsemessige effekter, må et laboratorium som utfører disse analysene kunne gjøre dette til en noenlunde rimelig kostnad. Samtidig må laboratoriet være i stand til å levere analyseresultater med god kvalitet på en effektiv måte. Det er i hovedsak serum- og fullblodsprøver som analyseres, og både prøveopparbeiding, analyse og resultatbearbeiding må gjennomføres effektivt og uten unødige forsinkelser. Det er også avgjørende å kunne anvende små prøvevolum (mikroliter). I befolkningsundersøkelser er det gjerne mange forskere som har interesse i begrensede prøvematerialer, og det er derfor viktig at analysene ikke krever store prøvevolumer. Tidligere har disse forholdene vært begrensende faktorer ved gjennomføring av store analyseserier. Miljøgiftlaboratoriet har imidlertid utviklet metoder som muliggjør raske og pålitelige prøvesvar, med små prøvevolum, samtidig som kostnadene holdes på et rimelig nivå (9).

Miljøgiftlaboratoriet har samarbeidspartnere lokalt i Tromsø, nasjonalt og internasjonalt, inkludert Norden,

Figur 2. *Ingeniør Mathilde Vik jobber med automatisert prøveopparbeiding.*



Figur 3. *Fagingeniør Margrethe Follesø Perander klargjør prøver for analyse på gass kromatograf koblet til tandem massespektrometer (GC-MS/MS).*

og ønsker samarbeid med flere (10). Vi ser dette som et fagfelt innen medisinsk forskning som er i utvikling og hvor det er ønskelig med flere interessenter.

Infrastruktur

Utstyrsparken består av moderne og avansert instrumentering. For å effektivisere prøveopparbeidingen anvendes automatiserte prøveopparbeidingsmetoder med robot (figur 2). Slik økes prøvegjennomstrømningen, samtidig som operatøravhengig variasjon reduseres.

Selve analysene foregår på ultra-sensitive instrumenter basert på massespektrometrisk deteksjon og koblet til kromatografiske separasjonsenheter som væske-, gass- eller super-kritisk -fluid kromatografer, avhengig av analyttens fysikalsk-kjemiske egenskaper (figur 3 og figur 4). Miljøgiftlaboratoriet har stort oppmerksomhet på bruk av lite prøvevolum for å spare på verdifullt materiale lagret i biobank, slik at et bredt spekter av analyser kan gjennomføres i en og samme prøve – noe som muliggjør en bred kartlegging av miljøgifter, i tillegg til kliniske variabler/markører.

Ved bruk av lavt prøvevolum er ultra-følsomme analyseinstrumenter nødvendige, noe som også gir lave deteksjonsgrenser. Denne kombinasjonen av instrumentering samt skreddersydde prøveopparbeidings- og analysemetoder gjør Miljøgiftlaboratoriet spesialtilpasset i sitt fagfelt. Analysepanelet er under kontinuerlig vurdering og utvidelse, og analysemetodene skreddersys i henhold til problemstillingen i respektivt prosjekt og med hensyn på relevante analytter og prøvematriks. Per i dag kan vi tilby analyser for PCBer (22 analytter), polybromerte difenyletere (PBDEer, 10 analytter), organoklorine pesticider (23 analytter), PFAS (> 55 analytter, under kontinuerlig utvidelse) i serum og plasma. Det jobbes med utvidelse av PFAS metoder for analyser i ny matriks som urin, brystmelk og sædvæske. Analyser for polysykliske aromatiske hydrokarboner (PAHer, 17 analytter) i fullblod og serum/plasma samt hydroksilerte metabolitter (16 analytter) i urin er under utvikling. Analysemetoder for grunnstoffer (33 analytter) er etablert for fullblod, serum, plasma og urin, og for et mindre antall analytter i brystmelk. Tilbudet for analysen i sædvæske kommer mot slutten av året. Nye analyttgrupper implementeres fortløpende og vil inneholde stoffer som er både persistente og ikke-persistente, som for eksempel flammehemmere, moderne pesticider, bisfenoler og andre tilsetningsstoffer i plast.

Lokalitetene er spesialtilpasset miljøgiftsanalyser, med overtrykk på analyselaboratoriene og gode renholdsrutiner for å unngå oppsamling av støv og partikler som kan forurense prøvene og ødelegge analysene.

Personell knyttet til Miljøgiftlaboratoriet består av leger, kjemikere og laboratorieingeniører. Både faglig og analytisk ledelse har samlet en sterk bakgrunn i medisinsk, analytisk og miljø kjemi.

Vitenskapelig aktivitet

Vitenskapelig aktivitet har økt gradvis siden etableringen av laboratoriet. Miljøgiftlaboratoriet initierer og bidrar til mange lokale, nasjonale og internasjonale samarbeidsprosjekter med forskjellige problemstillinger. Det legges blant annet fokus på undersøkelser som kartlegger sammenhenger mellom miljøgifteksponering og kliniske diagnoser og helseeffekter hos mennesker. Videre inngår vurdering av eksponering i arbeidsmiljøer, kartlegging av den generelle befolkningen og i ulike befolkningsgrupper, samt undersøkelser i forbindelse med utilsiktede utslipp av miljøforurensing og eventuell påvirkning på menneskers helse. Flere av prosjektene støtter og bidrar til utdanning av Master og PhD studenter, mest i samarbeid med UiT, men også andre universitet i Norge.

Målsetting og videre utvikling

Vårt mål var at Miljøgiftlaboratoriet skulle utvikles til et akkreditert laboratorium med internasjonal spisskompetanse i miljøgiftsanalyser i humane prøver. Vi

Figur 4. *Spesialingeniør Arntraut Götsch holder på med analyse av tungmetaller og sporelementer på induktiv-koblet-plasma massespektrometer (ICP-MS). På dette instrumentet analyseres både prøver til forskning og klinisk diagnostikk. En del analyser er akkrediterte i henhold til NS-EN ISO 15189:2022.*

kan i dag fastslå at målsettingen er nådd. Samtidig gjenstår det et behov for å øke bevisstheten og kunnskapen om miljøgifter og deres helseeffekter i det medisinske fagmiljøet. Dette gjelder særlig forståelsen og anvendelsen av miljøgiftanalyser som verktøy for kartlegging og vurdering av biologiske og medisinske effekter av miljøgifter i mennesker.

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CERT2 and ceramides in cardiovascular risk prediction: Recent advances and clinical implications

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Abstract

Background: Cardiovascular disease (CVD) remains a leading cause of morbidity and mortality worldwide, underscoring the need for prognostic biomarkers beyond traditional lipid measures.

Emerging biomarkers: Ceramides (Cers), a class of bioactive sphingolipids implicated in vascular inflammation, apoptosis, and plaque instability, have emerged as promising biomarkers of cardiovascular risk.

Recent evidence: Growing evidence supports the prognostic value of circulating Cers and their incorporation into lipidomic risk scores, particularly the Cardiovascular Event Risk Tests 1 and 2 (CERT1 and CERT2), which integrate selected ceramide and phosphatidylcholine species.

Clinical performance: CERT2 has shown prognostic value and improved risk stratification in community-based cohorts and in patients with stable coronary artery disease, providing information beyond conventional lipid markers.

Conclusion: This review summarizes recent advances in Cers and CERT risk scores. Overall, ceramide-based scores such as CERT2 appear to improve cardiovascular risk stratification and may complement established clinical and biomarker-based assessment in selected settings.

1. Introduction

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality worldwide (1). Low-density lipoprotein cholesterol (LDL-C) remains central to cardiovascular prevention, yet substantial residual cardiovascular risk persists even among patients who achieve guideline-recommended LDL-C targets (2). In apparently healthy middle-aged and older adults, the prognostic value of LDL-C is weaker than expected, particularly with increasing age (3).

Accordingly, additional biomarkers have been investigated to improve risk prediction. High-sensitivity troponin and natriuretic peptides are established cardiac biomarkers that reflect myocardial injury and cardiac wall stress and are associated with future cardiovascular events (4). Ceramides (Cers) are lipid species that have emerged as potential biomarkers in cardiovascular disease, with specific species and their ratios associated with cardiovascular death independently of traditional lipid markers (5). Experimental and translational studies have linked Cers to endothelial dysfunction, oxidative stress, and pro-inflammatory signalling, sup-

porting their role in cardiovascular pathophysiology (6). Early lipidomic analyses in the Ludwigshafen Risk and Cardiovascular Health (LURIC) cohort identified distinct serum ceramide (Cer) species associated with fatal outcomes in patients with coronary artery disease (7). These findings led to the development of ceramide-based risk scores, including Cardiovascular Event Risk Tests 1 and 2 (CERT1 and CERT2), which integrate selected Cer and phosphatidylcholine (PC) species and have been validated across multiple cohorts for predicting cardiovascular events and mortality (8). Traditional cardiovascular risk models, such as SCORE2, integrate demographic and clinical variables to estimate 10-year cardiovascular risk in primary prevention settings (9). In contrast, ceramide-based scores such as CERT are derived from circulating Cer species and ratios and provide prognostic information beyond conventional risk factors (5,8). This review summarizes recent advances in CERT2 and related ceramide-based biomarkers, with emphasis on their biological basis, clinical prognostic value, and potential implementation in cardiovascular risk stratification.

2. Biological basis of ceramides

2.1 Mechanistic links to vascular pathology

Cers are attractive biomarker candidates because of their mechanistic links to vascular dysfunction. Growing evidence shows that Cers are associated with endothelial dysfunction, reduced nitric oxide bioavailability, and impaired vasodilatation (10). Cers also induce reactive oxygen species (ROS) generation through Nicotinamide Adenine Dinucleotide Phosphate (NADPH) oxidase and mitochondrial pathways, contributing to oxidative stress and endothelial dysfunction, and their chronic accumulation is associated with inflammatory endothelial responses, including increased adhesion molecule expression and macrophage recruitment (6). At the cellular level, Cers may promote cardiomyocyte apoptosis through mitochondrial outer membrane permeabilization and caspase activation, contributing to myocardial injury and cardiac dysfunction (11).

2.2 Functional dichotomy: harmful vs protective ceramides

Disease associations of Cers depend on their chain length (Figure 1). Specific Cer species, particularly Cer (d18:1/16:0), Cer (d18:1/18:0), and Cer (d18:1/24:1), are consistently associated with adverse cardiovascular outcomes, and an increased Cer (d18:1/24:1)/Cer (d18:1/24:0) ratio reflects higher risk. In contrast, the very-long-chain species Cer (d18:1/24:0), used as the reference molecule in CERT scores, has been associated with more favourable outcomes and is selected because of its high plasma abundance and analytical stability (12,13). Thus, these findings highlight that Cers are biologically heterogeneous molecules situated at the intersection of lipid metabolism, vascular inflammation, and cell death, supporting their role as mechanistically informative biomarkers and enabling the clinical translation of ceramide-based risk scores.

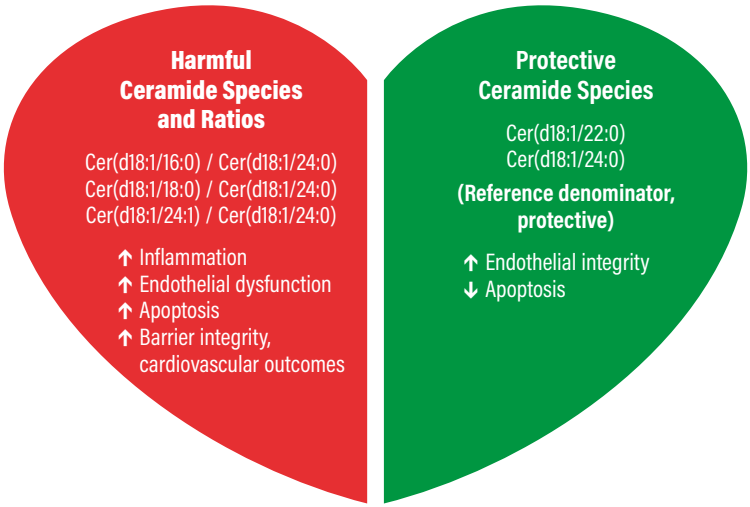

Figure 1. *Functional dichotomy of Cer species relevant to cardiovascular risk. Specific Cer species and their ratios to the reference molecule Cer (d18:1/24:0) are associated with differential cardiovascular outcomes. Ratios involving Cer (d18:1/16:0), Cer (d18:1/18:0), and Cer (d18:1/24:1) relative to Cer (d18:1/24:0) are linked to adverse outcomes, whereas higher levels of Cer (d18:1/22:0) and Cer (d18:1/24:0) are associated with more favourable profiles. This supports species- and ratio-based Cer profiling rather than reliance on bulk Cer measurements.*

3. Development of CERT scores

3.1 CERT1

The use of Cers in cardiovascular risk assessment became practical with the development of ceramide-based risk scores. The original ceramide-based score, CERT1, incorporates three Cer species—Cer (d18:1/16:0), Cer (d18:1/18:0), and Cer (d18:1/24:1)—and their ratios to Cer (d18:1/24:0), which serves as a reference lipid with protective characteristics. CERT1 has demonstrated strong associations with cardiovascular mortality and provides prognostic information beyond standard lipid measurements (5).

3.2 CERT2: refinement with phosphatidylcholines

CERT2 was developed by extending the original Cer panel to include selected phosphatidylcholines (PCs), thereby capturing broader aspects of lipid metabolism and vascular biology. The score comprises one Cer ratio (Cer(d18:1/24:1)/Cer(d18:1/24:0)), two Cer/PC ratios (Cer(d18:1/16:0)/PC(16:0/22:5) and Cer(d18:1/18:0)/PC(14:0/22:6)), and one standalone PC (PC(16:0/16:0)), reflecting integrated lipidomic pathways linked to cardiovascular disease. Studies by Hilvo and colleagues have demonstrated that CERT2 provides prognostic information and improves cardiovascular risk stratification in both primary and secondary prevention (14), as well as in patients with stable coronary artery disease (15).

3.3 Comparison with traditional biomarkers (LDL-C, high-sensitivity C-reactive protein (hs-CRP)

Evidence from meta-analyses and cohort studies indicates that ceramide-based scores such as CERT2 enhance cardiovascular risk prediction compared with traditional lipid biomarkers, including LDL-C (16,17). In contrast to hs-CRP, which reflects nonspecific inflammation, CERT2 incorporates lipid species linked to endothelial dysfunction and plaque vulnerability. Notably, ceramide-based markers have demonstrated prognostic utility in patients with stable coronary artery disease (15). In these contexts, ceramide-based scores such as CERT2 provide improved risk discrimination and help identify high-risk individuals who may not be adequately captured by conventional lipid markers.

4. Clinical evidence

Across community cohorts and patients with stable coronary artery disease, ceramide-based risk scores, particularly CERT2, are associated with major cardiovascular outcomes and improve risk stratification when integrated with conventional clinical factors (14,15). In the FINRISK 2002 cohort, individuals in the highest CERT2 category had substantially higher risk of major adverse cardiovascular events (MACE) compared with those in the lowest category, with a clear gradient across risk groups (14,18). In patients with stable coronary artery disease, CERT2 contributed to risk stratification in combination with prior myocardial infarction, extent of coronary disease, and diabetes mellitus (15). This graded relationship is illustrated in Kaplan–Meier survival curves for MACE in the FINRISK cohort (Figure 2). Similar graded associations between ceramide-based risk categories and cardiovascular mortality have been demonstrated across independent cohorts (Figure 3). As shown in Figure 4, CERT2 was significantly associated with all-cause mortality, cardiovascular death, heart failure, and MACE, with multivariable-adjusted hazard ratios ranging from approximately 1.34 to 1.52 per standard deviation (SD) increase.

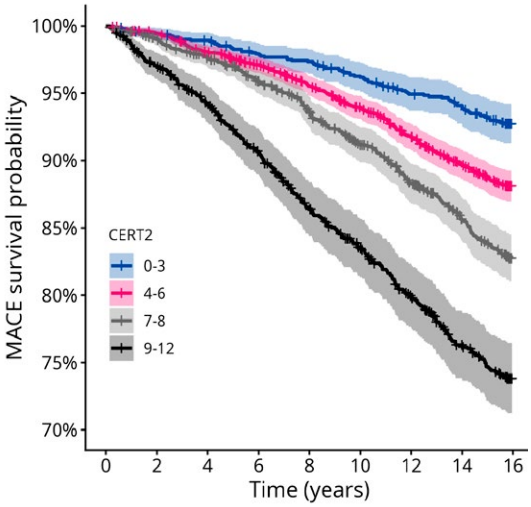

Figure 2. *Kaplan–Meier survival curves for major adverse cardiovascular events (MACE) according to CERT2 risk score categories in the FINRISK 2002 cohort. Patients were stratified into four CERT2 categories: 0–3 (blue), 4–6 (pink), 7–8 (grey), and 9–12 (black). Higher CERT2 scores were associated with progressively reduced MACE-free survival over time.*

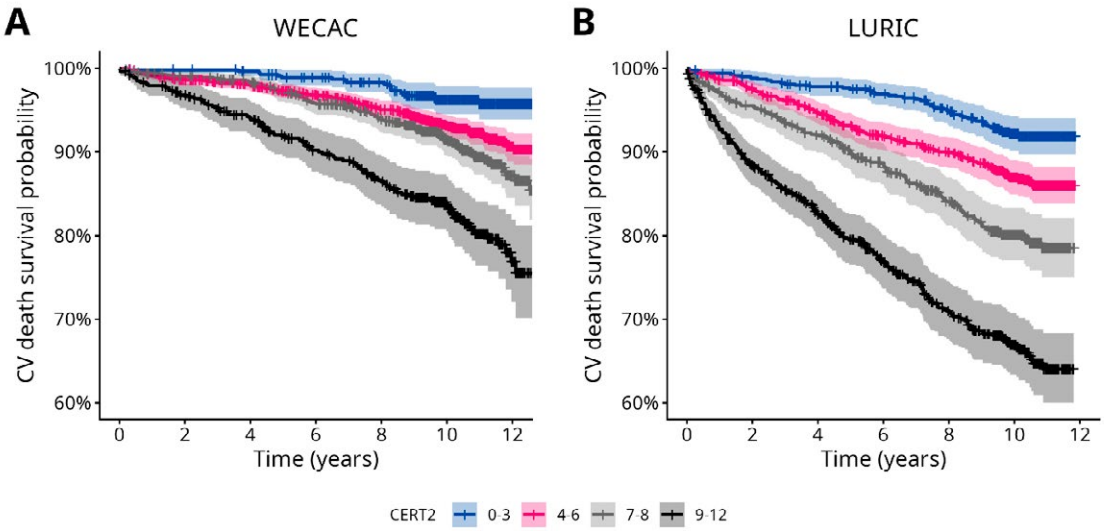

Figure 3. *Kaplan–Meier survival curves for cardiovascular mortality according to ceramide-based risk categories in the Western Norway Coronary Angiography Cohort (WECAC; A) and Ludwigshafen Risk and Cardiovascular Health (LURIC; B) cohorts. Higher risk categories were associated with progressively lower cardiovascular survival. Risk categories are 0–3 (blue), 4–6 (pink), 7–8 (grey), and 9–12 (black). Adapted from previously published cohort analyses (5,8).*

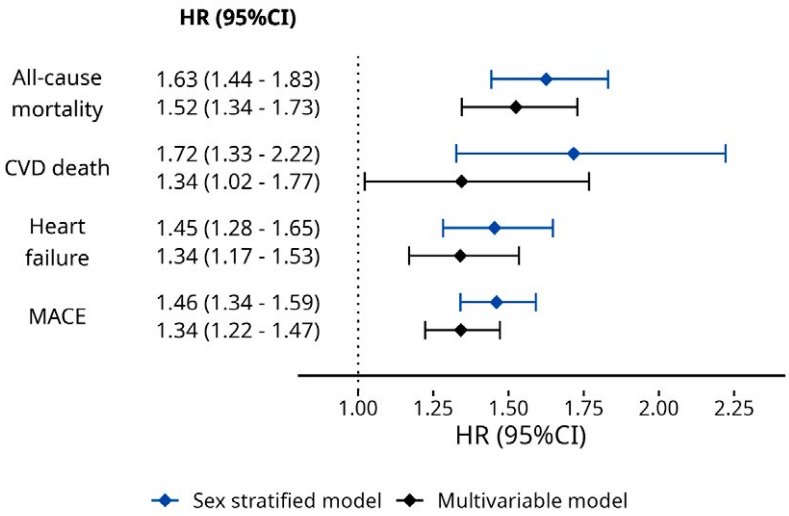

Figure 4. *Forest plot of hazard ratios (HRs per 1 SD increase in CERT2) for major outcomes in the FINRISK 2002 cohort. Univariable models (blue) were stratified by sex and age. Adjusted models (black) were stratified by sex and adjusted for diabetes mellitus type 2, current smoking, body mass index, systolic blood pressure, lipid-lowering treatment, LDL-C, high-density lipoprotein cholesterol (HDL-C) and triglycerides, with age as the time scale. CERT2 was significantly associated with all-cause mortality, cardiovascular death, heart failure, and MACE.*

To further quantify this risk gradient, Table 1 summarizes the distribution of events and non-events across CERT2 categories in the FINRISK 2002 cohort, including risk percentages and relative risks for major cardiovascular outcomes (14). These data demonstrate a clear stepwise increase in 10-year cardiovascular risk across higher CERT2 categories, with substantially higher event rates observed in the highest-risk group.

Outcome	CERT2 Category	Population (%)	No event	Event	Risk (%)	Relative Risk (highest vs lowest)
All-cause mortality	0–3	16.5%	1192	18	1.5%	1.0
	4–6	42.2%	3003	86	2.8%	1.9
	7–8	25.5%	1777	93	5.0%	3.3
	9–12	15.8%	1047	108	9.4%	6.3
Cardiovascular death	0–3	16.5%	1207	3	0.2%	1.0
	4–6	42.2%	3067	22	0.7%	2.9
	7–8	25.5%	1859	11	0.6%	2.4
	9–12	15.8%	1124	31	2.7%	10.8
MACE (composite)	0–3	16.5%	1164	46	3.8%	1.0
	4–6	42.2%	2904	185	6.0%	1.6
	7–8	25.5%	1708	162	8.7%	2.3
	9–12	15.8%	969	186	16.1%	4.2
Heart failure	0–3	16.5%	1189	21	1.7%	1.0
	4–6	42.2%	2998	91	2.9%	1.7
	7–8	25.5%	1807	63	3.4%	1.9
	9–12	15.8%	1059	96	8.3%	4.8

Table 1. *Distribution of events, non-events, risk percentages, and relative risks across CERT2 categories (0–3, 4–6, 7–8, 9–12) in the FINRISK 2002 cohort for 10-year events (14). Outcomes include all-cause mortality, cardiovascular death, MACE, and heart failure. MACE includes myocardial infarction and stroke as component events.*

5. Analytical & practical considerations for clinical chemistry

5.1. Targeted LC–MS/MS and MRM-based quantification

Lipid levels in the FINRISK study were measured using a triple-quadrupole mass spectrometer operating in multiple reaction monitoring (MRM) mode. In this approach, the first quadrupole (Q1) selects ions of interest according to their mass-to-charge (m/z) ratio. These ions are then transferred to the second quadrupole (Q2), where they undergo collision-induced dissociation (CID), producing characteristic fragment ions. The third quadrupole (Q3) subsequently filters a specific fragment ion, enabling detection of a defined precursor-to-product ion transition. Cer and PC species were analyzed using established MRM transitions that target their most prominent or structurally informative fragments. The signal intensity of each monitored transition correlates with the analyte concentration, making accurate quantification possible. To improve reliability, stable isotope-labelled internal standards (SIL-IS) were included to compensate for differences in ionization efficiency, matrix effects, and instrument variability, in line with validated targeted lipidomics methodologies (19).

5.2 Standards, quality control (QC), and inter-laboratory harmonization

Accurate quantification of Cers and PCs requires stable isotope–labeled, analyte-matched internal standards to correct for recovery, ion suppression, and analytical variability. Multicentre studies have demonstrated that the use of authentic matched standards substantially improves inter-laboratory comparability and reduces measurement bias (20). International inter-laboratory ring trials using harmonized LC–MS/MS protocols and standardized reference materials consistently demonstrated that Cer measurements achieve reproducibility comparable to established clinical assays (20). Appropriate calibration strategies, including isotope dilution

and validated reference materials, are essential to ensure accuracy and traceability in clinical implementation (20).

5.3 Pre-analytical and practical considerations

Pre-analytical factors such as blood collection tube, storage conditions, freeze–thaw cycles, and hemolysis may affect lipid measurements; however, in the referenced LC–MS workflow, minimal impact was observed for tube type, storage at −80°C for one year, and up to six freeze–thaw cycles. In contrast, hemolysis had the greatest impact, with changes becoming evident at approximately 0.4%, particularly for phosphatidylethanolamines. In this lipidomics workflow (19), isopropanol (IPA) extraction was selected for sample preparation, automation improved reproducibility, and stable isotope-labelled internal standards with signal correction were used to enhance interbatch consistency. The authors also recommend avoiding reinjection of pierced autosampler plates after 24 h due to compromised sample integrity (19). Key requirements for clinical implementation are summarized in Table 2.

Building upon these analytical requirements, the stepwise laboratory workflow for Cer/CERT2 implementation in clinical chemistry is illustrated in Figure 5.

Step	Requirements	Practical Consideration
Sample collection	EDTA plasma	Stable under standardized storage (e.g., −80 °C); robust to freeze–thaw cycles and long-term storage
Extraction	Organic solvents (chloroform-free preferred, e.g., isopropanol/ethyl acetate	Automatable for high-throughput workflows
Internal standards	Stable isotope-labeled ceramides and phosphatidylcholines (e.g., Cer(d18:1/16:0)-d7, PC(16:0/16:0)-d9)	Needed for recovery correction and accurate quantification of both ceramides and PCs in CERT2
Chromatography	LC separation of chain-length/unsaturation	Prevents isobaric overlap
Detection	LC–MS/MS in MRM mode	Enables targeted, sensitive, and rapid analysis
Quality control	Pooled plasma, calibration curve, external QC	Maintain CVs <10 %
Inter-lab validation	Participation in ring trials	Ensures reproducibility across laboratories
Reporting	CERT2 score, percentile ranking, risk category	Integration with laboratory information systems (LIS/EHR)

Table 2. *Analytical checklist for Cer/CERT2 implementation in clinical chemistry. Quality control, inter-laboratory validation, and integration into laboratory information systems are essential to ensure reproducibility and facilitate clinical translation of ceramide-based risk scores.*

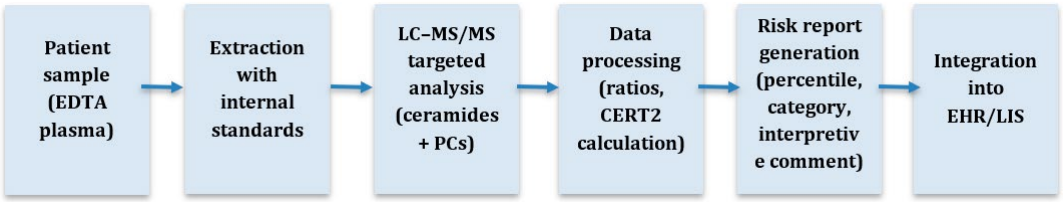

Figure 5. *Workflow diagram for Cer/CERT2 implementation in clinical chemistry. Stepwise workflow from patient plasma collection to clinical reporting of CERT2 results. Abbreviations: EDTA, ethylenediaminetetraacetic acid; LC–MS/MS, liquid chromatography–tandem mass spectrometry; PC, phosphatidylcholine; CERT2, Cardiovascular Event Risk Test 2; EHR, electronic health record; LIS, laboratory information system.*

6. Conclusions

In summary, recent advances suggest that Cers and composite Cer/PC scores such as CERT2 are emerging clinical chemistry tools. Across different clinical settings, they show consistent, independent associations with major cardiovascular outcomes and provide additional information beyond LDL-C, troponin, natriuretic peptides, and hs-CRP. Importantly, targeted LC–MS/MS methods, combined with analyte-matched isotope-labeled internal standards, allow reliable quantification in clinical settings. Reporting Cer panels as a numeric CERT2 score with risk categories also facilitates clinical interpretation.

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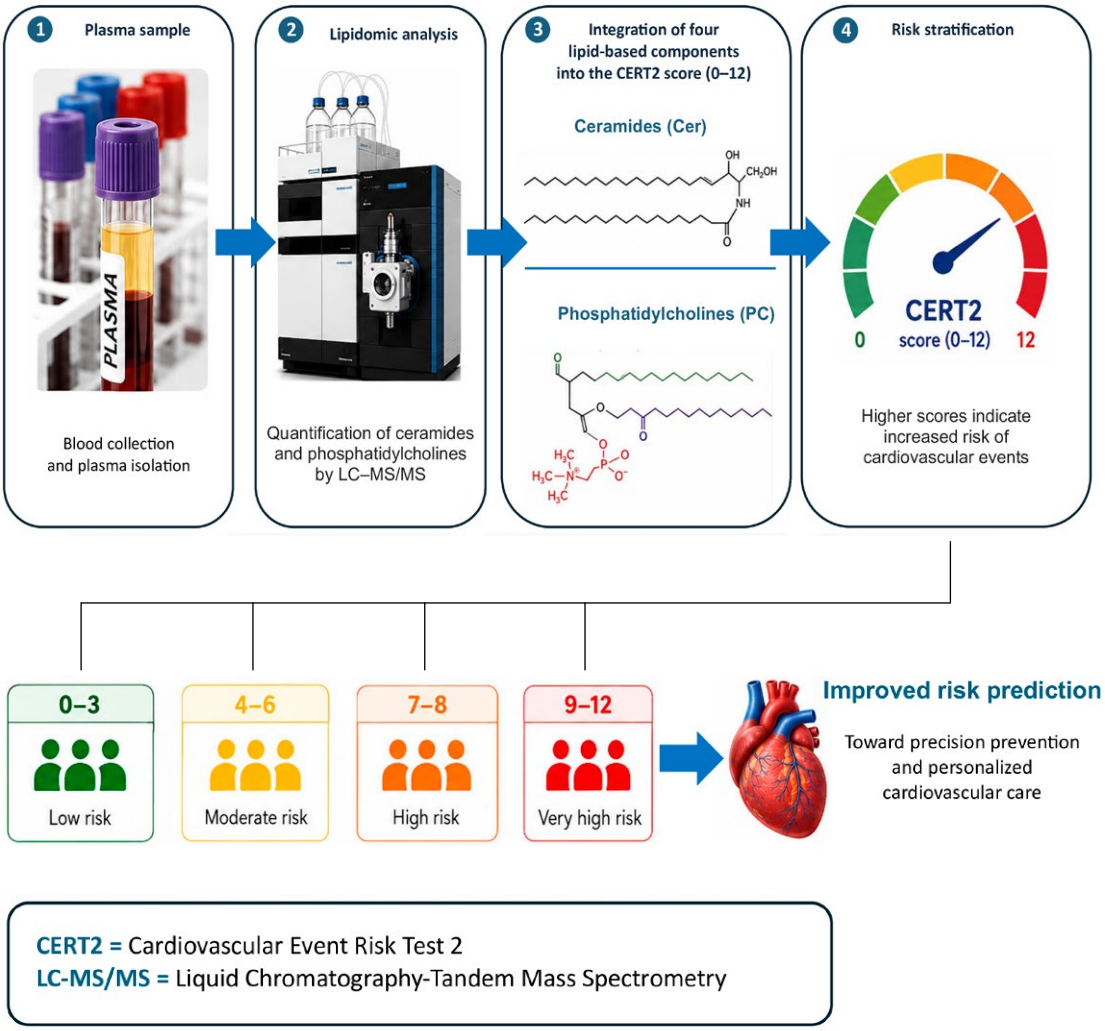


Ivar Asbjørn Følling – oppdageren av fenolketonuri

Helle Borgstrøm Hager
Sentrallaboratoriet, Sykehuset i Vestfold

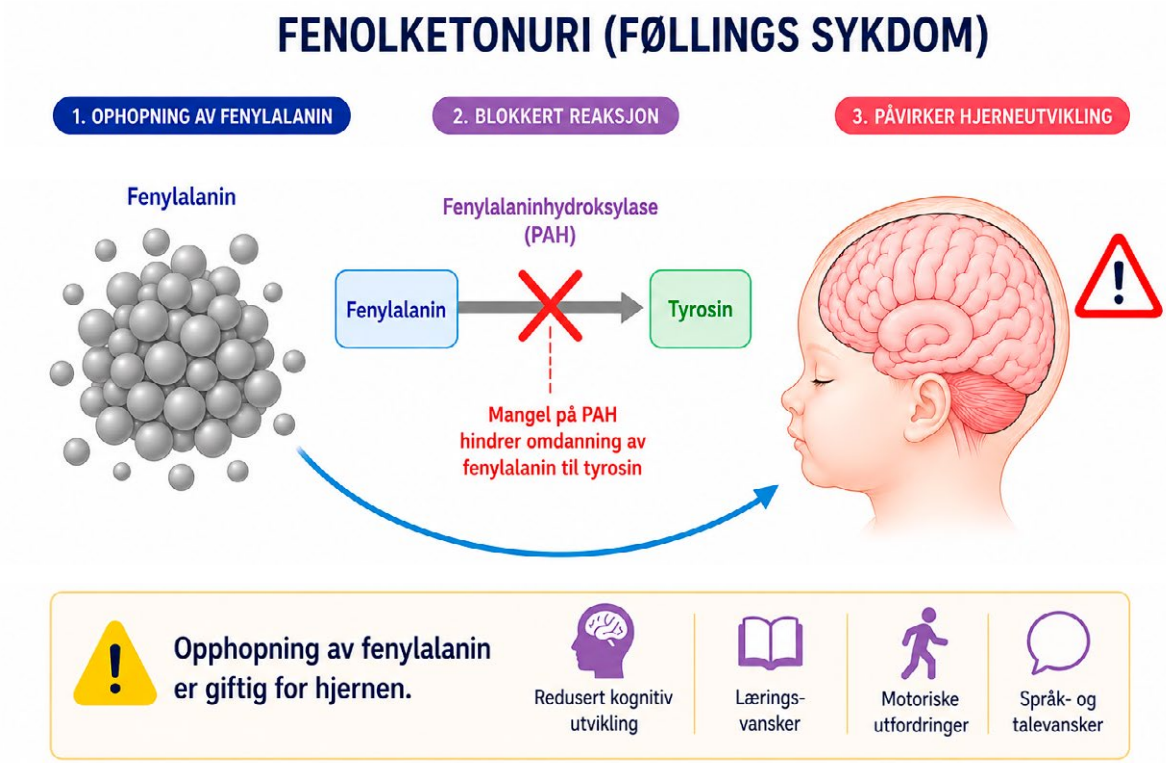
Ivar Asbjørn Følling (1888–1973) var en norsk lege og kjemiker som oppdaget stoffskiftesykdommen Føllings sykdom, i dag kjent som fenylketonuri. Urin med gjennomtrengende lukt og grønnfarge ved Gerhards prøve dannet grunnlaget for hans oppdagelse av en spesifikk biokjemisk årsak til psykisk og fysisk utviklingshemming.

Følling var bondesønn fra Nord-Trøndelag og vokste opp som yngstemann i en søskenflokk på fire. Etter videregående skole begynte han i 1910 på kjemistudier ved Norges tekniske høyskole i Trondheim. I 1916 ble han sivilingeniør, men han fortsatte studiene og begynte på medisinstudiet i Kristiania (nå: Oslo). Som ferdig utdannet lege arbeidet han de første årene som stipendiat ved medisinsk avdeling på Rikshospitalet, der han bygde opp et klinisk laboratorium. Han var professor i ernæringsfysiologi ved det medisinske fakultet ved Universitetet i Oslo fra 1932 til 1935. Fra 1935 til 1953 var han professor i fysiologi/biokjemi ved Norges Veterinærhøyskole i Oslo og i perioden 1953–1958 professor i biokjemi ved Rikshospitalet.

Den store oppdagelsen gjorde Følling i 1934. Han ble oppsøkt av en familie som hadde to mentalt retarderte barn. Barna hadde utviklet seg normalt de første levemånedene, men viste så økende tegn på hjerneskade. Ingen leger hadde kunne hjelpe familien, men foreldrene var overbevist om at det var noe helt spesielt med barna. De hadde merket en påfallende stram lukt av urinen deres. Professor Følling sa seg villig til å undersøke barna og ba dem ta med urinprøver.

Bondegutten Følling la etter sigende merke til at urinen hadde en lukt som minnet om silo eller maursyre. På laboratoriet utførte Følling en såkalt Gerhards prøve, der man dryppet jernklorid i urinen for å påvise syrer som normalt ikke skal være der, som ketoner og aceton. Ved tilstedeværelse av slike syrer, fikk man et fargeomslag til dyp fiolett. Urinen til disse to barna ble imidlertid ikke fiolett, men dyp grønnfarget, før fargen forsvant etter noen minutter. Dette hadde ingen beskrevet tidligere. Følling forsøkte å isolere substansen som ga den grønne fargen. I 1930-årene fantes ikke kromatografiske teknikker og bare fellingsreaksjoner kunne benyttes i renseprosessen. Følling greide å vise at den aktive substansen som ga grønnfargen var fenylpyruvat, et stoff som høyst sannsynlig kom fra aminosyren fenylalanin. Parallelt med rensesarbeidet begynte han å undersøke urinen til flere såkalt åndssvake barn. Han fant den samme grønne jernkloridreaksjonen hos 10 av 430 barn. Følling publiserte sitt arbeide i et nordisk og et tysk tidsskrift (1,2).

Ivar Asbjørn Følling.



Figuren ble generert med ChatGPT.

Det ble snart vist at sykdommen skyldes mangel på et enzym som omdanner aminosyren fenylalanin til tyrosin, fenylalanin-hydroksylase. Fenylalanin hoper seg opp i kroppen og det dannes ulike metabolitter (fenylketoner) som skader hjernens utvikling. Dermed hadde han påvist en sammenheng mellom kroppens stoffskifte og hjernens utvikling. Andre verdenskrig må ta sin del av skylden for at det tok så lang tid før oppdagelsen kunne brukes til nytte for pasienter. Forskning på utviklingshemmede var ikke akkurat prioritert av tyske akademikere under Hitler. Det tok 20 år før den første rapport om diettbehandling ble publisert (3), og først i 1960-årene ble det vist at nyfødte med sykdommen som ble satt på fenylalaninfattig kost fikk normal utvikling.

Følligns oppdagelse la grunnlaget for den metabolske screening av nyfødte som utføres i alle industrialiserte land i dag. En høy konsentrasjon av fenylalanin i blodprøve hos nyfødte gir mistanke om Følligssykdom. Hvis diagnosen bekreftes, vil en proteinfattig diett som inneholder svært lite fenylalanin medføre tilnærmet normal vekst og utvikling for barnet. Fenylketonuri arves autosomalt recessivt, og forekomsten i Norge er ca. én av 12 000 nyfødte.

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PhD avhandling:

Bruk av kunstig intelligens for diagnose, prognose og subgruppering av infeksjonssykdommer

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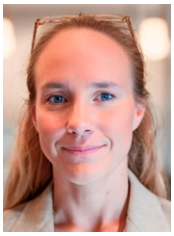


Å stille diagnose og prognose for pasienter med infeksjonssykdommer

Pasienter som innlegges i akuttmottak med mistanke om infeksjonssykdommer eller sepsis kan ha betydelig nytte av rask diagnostikk, slik at adekvat behandling kan iverksettes så tidlig som mulig. Tidlig identifisering av pasienter med høy risiko for dårlig prognose kan også forbedre risikostratifisering og bidra til mer målrettet behandling.

Sepsis er et heterogent syndrom. Til tross for omfattende forskning de siste tiårene, inkludert en rekke studier av immunmodulerende behandling, har det ikke blitt oppdaget ny behandling som forbedrer prognosen ved sepsis. En mulig forklaring kan være den betydelige interindividuelle variasjonen i symptomer, kliniske funn, etiologisk agens, komorbiditet, grad av skrøpelighet og immunrespons. Denne heterogeniteten kan medføre at behandlingseffekten varierer mellom ulike pasientgrupper, og dermed blir vanskelig å påvise i studier av uselekterte sepsispopulasjoner. En sentral hypotese er derfor at identifisering av biologiske eller klinisk definerte subgrupper av sepsispasienter kan legge grunnlaget for mer persontilpasset behandling (1).

Bruk av laboratoriedata og kunstig intelligens

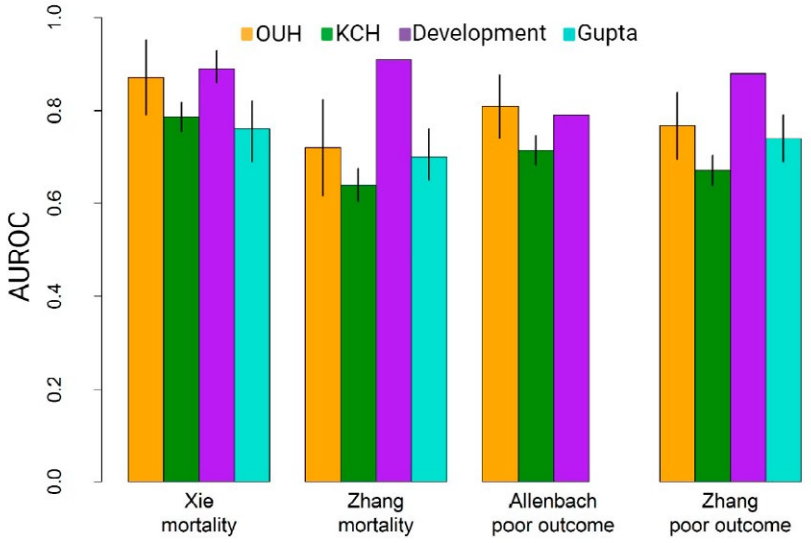
Det utføres årlig millioner av analyser ved laboratoriet, og resultatene lagres i laboratorienes informasjonssystemer. Disse dataene representerer en verdifull ressurs for klinisk forskning. Bruken av helseopplysninger til forskningsformål er i Norge regulert av lovverk og etiske retningslinjer. I enkelte tilfeller kan forskning gjennomføres etter godkjenning av Regional komité for medisinsk og helsefaglig forskningsetikk (REK) med dispensasjon fra pasientenes samtykke. Laboratoriedataene kan potensielt benyttes til å utvikle prediksjonsmodeller basert på kunstig intelligens for diagnostikk og prognostisering, som videre kan brukes som beslutningsstøtte i akuttmottaket.

I våre prosjekter fikk vi, etter søknad til REK, dispensasjon fra taushetsplikten og tillatelse til å bruke dataene. Vi benyttet data fra to prospektive registre, et for pasienter med covid-19 og et for pasienter med sepsis. Registrene inkluderte voksne pasienter innlagt via akuttmottak og inneholdt kliniske variabler registrert ved innleggelse. Laboratorieanalyser rekvirert i akuttmottaket ble koblet til de kliniske dataene. Endelig diagnose ble fastsatt av infeksjonsmedisinere i etterkant av innleggelsen, basert på en samlet vurdering av journalopplysninger samt laboratorie-, radiologiske og mikrobiologiske funn.

Datasettene dannet grunnlaget for utvikling av multivariable modeller for prognostisering, diagnostikk og subgruppering blant pasienter med infeksjonssykdommer i akuttmottaket. Multivariable modeller kombinerer informasjon fra flere variabler for å estimere en sannsynlighet for bestemte diagnoser eller kliniske utfall. Dersom det allerede foreligger publiserte modeller for samme problemstilling, anbefales ekstern validering av disse med andre kohorter, før utvikling av nye. Modellene kan baseres på tradisjonell statistikk som multivariat logistisk regresjon, eller maskinlæringsmetoder som random forest, naïve Bayes og nevrale nettverk.

Prognose hos covid-19-pasienter

Ved utbruddet av covid-19-pandemien i 2020, var det et stort behov for mer kunnskap om sykdommen for å forbedre tidlig diagnostikk og identifisere pasienter med risiko for et alvorlig sykdomsforløp. Flere multivariable prognostiske modeller var publisert, og vi ønsket å gjennomføre en ekstern validering av aktuelle modeller basert på data fra 307 voksne covid-19 pasienter innlagt i akuttmottaket fra Oslo og en kohort fra Oxford på 1295 pasienter. Ved en litteraturgjennomgang fant vi fire aktuelle modeller, tre fra Kina

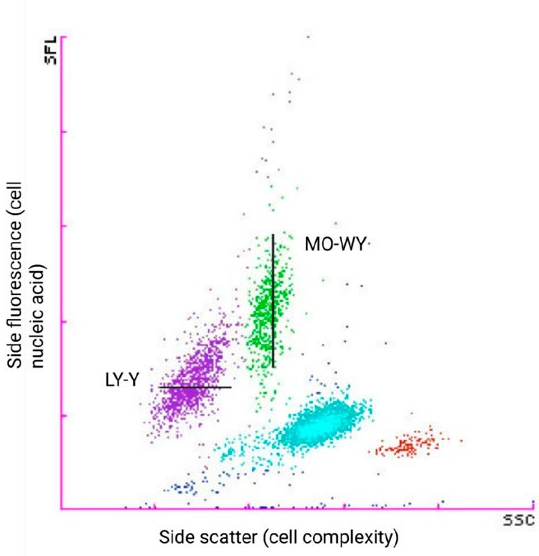


Figur 1. *Diskriminering av de fire modellene ved ulike kohorter. Area under the receiver operating characteristic curve (AUROC) fra de fire modellene ved validering ved Oslo University Hospital (OUH), Kings Cross Hospital (KCH), de originale AUROC-verdiene i utviklingskohortene, samt resultater fra ekstern validering i en engelsk kohort i Guptas studie (5). Figur fra Wickstrøm et al. (6).*

og en fra Frankrike som hadde utfallene mortalitet eller alvorlig sykdom (innleggelse på intensivavdeling (2, 3, 4). Modellene var basert på multivariat logistisk regresjon og inkluderte ulike kombinasjoner av kliniske variabler og prøvesvar. Ved ekstern validering i våre kohorter fant vi at modellenes prestasjon var gjennomgående lavere ved validering enn for de opprinnelige kohortene (Figur 1). Den best presterende modellen for prediksjon av mortalitet inkluderte alder, laktat dehydrogenase (LDH), arteriell oksygenmetning og lymfocytter, og hadde en AUC på 0.87 (0.79-0.95) i kohorten fra Oslo og 0.79 (0.76-0.82) i kohorten fra Oxford. En tilsvarende studie av Gupta et al. validerte de samme modellene i en engelsk kohort og de rapporterte også varierende resultater (5). Våre funn viser viktigheten av ekstern validering før prognostiske modeller implementeres i klinisk praksis (6).

Prediksjon av infeksjon hos pasienter med mistenkt sepsis ved hjelp av Sysmex cell population data

Cell population data (CPD) er parametre som genereres fra hematologiske scatterplot samtidig med analyse av leukocytter i hematologiinstrumenter. Variablene er tilgjengelige, og omfatter mellom 20-30 variabler som beskriver lymfocytter, nøytrofile granulocytter og monocytters morfologiske egenskaper som størrelse, grad av aktivering og intracellulært innhold (Figur 2). CPD brukes ikke i rutinen i dag, men enkelte er foreslått som biomarkører for infeksjon og sepsis. Vi ønsket å undersøke om CPD kunne benyttes til å predikere infeksjon hos pasienter innlagt i akuttmottaket med mistenkt sepsis. Basert på en utviklingskohort ble flere multivariable modeller vurdert, hvorav den mest optimale modellen benyttet fem CPD variabler kombinert med maskinlæringsmetoden multilayer perceptron.

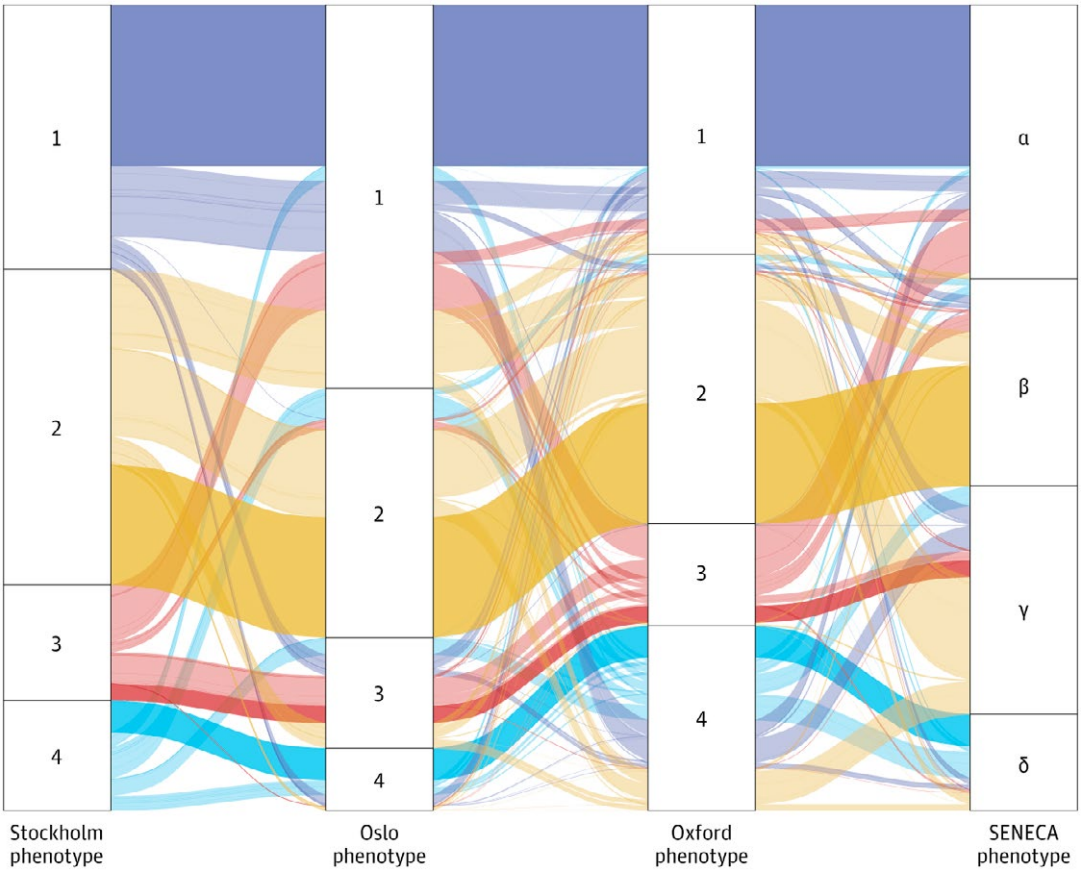


Figur 2. *Hematologisk scatterplot med to CPD variabler vist; LY-Y og MO-WY. Variablene genereres for hver av de ulike cellene og utgjør verdier på X-, Y-, Z- aksen (for eksempel LY-Y). LY-Y er median av lymfocyttpopulasjonen på Y-aksen og beskriver innhold av nukleinsyre og grad av aktivering. Distribusjonen av de ulike X, Y og Z variablene er også generert (for eksempel MO-WY som viser distribusjon av MO-Y). Modifisert figur fra Sysmex.no med tillatelse.*

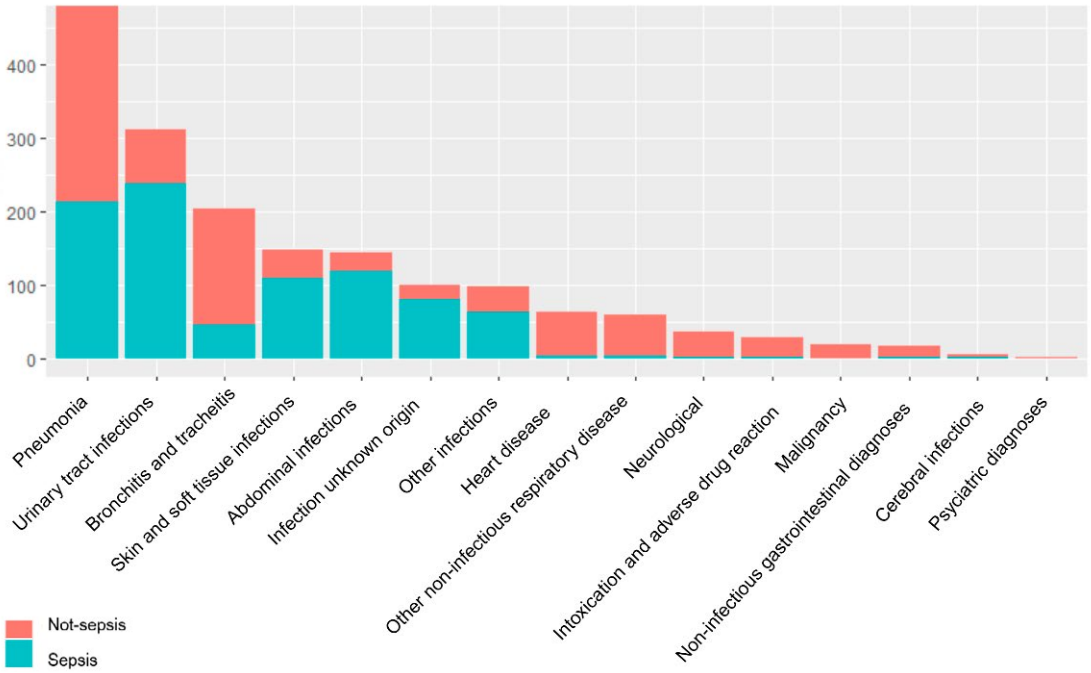
Modellen viste god diskrimineringsevne med AUC på 0,86 (95 % KI 0,85-0,87) i utviklingskohorten og 0,78 (95 % KI 0,74-0,82) i en intern valideringskohort, samt tilfredsstillende kalibrering (7).

Fire subgrupper hos sepsis pasienter kunne ikke valideres

I en høyt sitert publikasjon i JAMA fra 2019 identifiserte Seymour et al. fire distinkte subgrupper blant pasienter med sepsis ved hjelp av ikke-veiledet maskinlæring (1). Ikke-veiledet maskinlæring brukes til å identifisere skjulte mønstre og undergrupper i komplekse datasett uten bruk av forhåndsdefinerte utfallsmål. Subgruppene var klinisk gjenkjennbare, og forskerne kunne vise til forskjellig respons på behandling mellom gruppene. Vi ønsket å validere disse subgruppene i tre internasjonale kohorter fra Oslo (n=1806), Stockholm i Sverige (n=30865) og Oxford i England (n=15575), med samme metodikk og inklusjonskriterier. Inklusjonskriteriene i SENECA kohorten fra Seymourartikkelen var voksne pasienter innlagt i akuttmottaket som hadde startet med antibiotika, kroppsvæske for mikrobiologisk undersøkelse var tatt og pasientene hadde to eller mer Sequential Organ Failure Assessment (SOFA) poeng. Etter analysering kunne vi ikke reprodusere de samme subgruppene i våre kohorter eller finne likheter mellom fire subgrupper fra kohortene (Figur 3) og funnene illustrerer viktigheten av å eksternt validere subgrupper før klinisk bruk (8).



***Figur 3**. Fenotypetilhørighet for pasienter fra Stockholm. Første kolonne til venstre viser resultatet fra klusteranalysen i Stockholm-kohorten, og de øvrige kolonnene viser hvordan de samme pasientene er klassifisert til sentroider fra de ulike stedene (Oslo, Oxford og SENECA). Fargene beskriver Stockholm-fenotypene. SENECA= Sepsis Endotyping in Emergency Care. Figuren er fra Yoon et al. (8).*



Figur 4. *Inkluderte sepsispasienter i Oslo kohorten med SENECAs inklusjonskriterier. Oslo-kohorten har samme inklusjonskriterier som SENECA for sepsis; pasienter som har startet antibiotika, tatt en «kroppsvæske» til mikrobiologiske undersøkelser samt mer enn 2 SOFA poeng. Sepsisdiagnosen er også vurdert retrospektivt av en infeksjonsmedisiner ved journalgjennomgang. Figuren viser at kun 54 % av pasientene med SENECAs inklusjonskriterier for sepsis, får diagnosen sepsis i en retrospektiv ekspertvurdering.*

Åtte subgrupper av sepsis med en nøye utvalgt kohort av sepsis pasienter

I Oslo-kohorten ble sepsisdiagnosen fastsatt i etterkant av infeksjonsspesialister på grunnlag av journalopplysninger. Under valideringen med de tre kohortene som beskrevet i forrige avsnitt, ble SENECA-kriteriene brukt for inklusjon. Da vi anvendte disse kriteriene i Oslo-kohorten, fant vi at kun 54% av pasientene oppfylte sepsisdiagnosen slik den var vurdert av infeksjonslegene (Figur 4). Vi gjorde dermed en ny analyse basert på et snevrere utvalg av pasienter med kun ekspertvurdert sepsisdiagnose. De samme metodene for ikke-veiledet maskinlæring ble utført, men med en statistisk mer robust håndtering av manglende data. I motsetning til Seymour et al. fant vi da at åtte subgrupper ga den beste beskrivelsen av pasientgruppen. Disse subgruppene representerte en bedre fordeling av kliniske fenotyper og kunne karakteriseres som en yngre mild gruppe, en eldre mild gruppe, en gruppe med mild respirasjonssvikt, en gruppe med alvorlig respirasjonssvikt, en inflammatorisk gruppe, en gruppe med nyre- og multiorgansvikt, en gruppe preget av cytopeni og en gruppe med leversvikt. Subgruppene må valideres i eksterne kohorter før de kan vurderes for klinisk bruk.

Konklusjon

Multivariable modeller basert på laboratoriedata kan bidra til bedre diagnostikk og prognostisering hos pasienter med infeksjonssykdommer. Før slike modeller implementeres i klinisk praksis, er ekstern validering viktig for å sikre at de er robuste og generaliserbare.

Ikke-veiledet maskinlæring kan benyttes til å identifisere subgrupper av pasienter med sepsis. Også slike subgrupper er viktig å validere eksternt før klinisk bruk.

Sepsis er et heterogent syndrom og en sentral hypotese er at ulike subgrupper kan respondere forskjellig på behandling. Identifisering av subgrupper kan derfor legge grunnlaget for persontilpasset behandling i fremtiden.

Takk til veiledere Erik Amundsen, Valeria Vitelli og Christian Prebensen, samt Unilabs Laboratoriemedisin, Ullevål Universitetssykehus og Universitetet i Oslo.

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