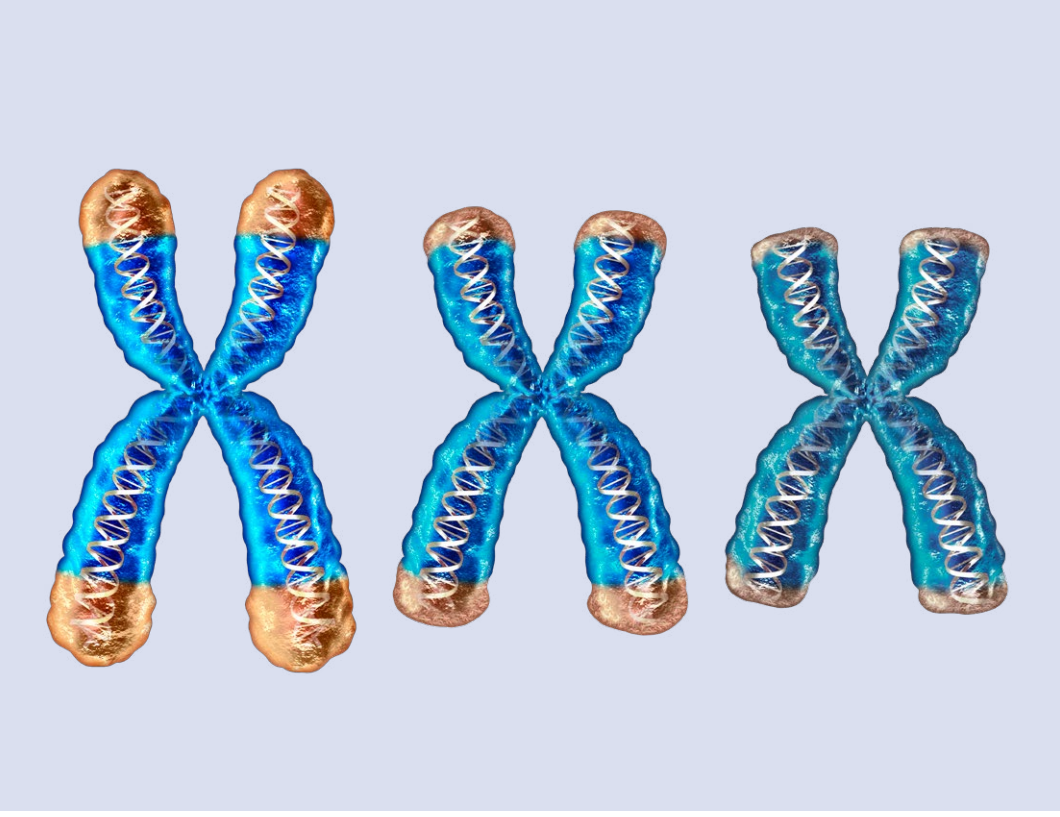
ISSN 1101-2013

Klinisk Biokemi i Norden



Nordisk Forening for Klinisk Kemi

Nr. 4 · vol. 37 · 2025

The NFKK Young Researcher Award, NYRA

Per Bjellerup[1], Lars Melholt Rasmussen[2]
[1] NFKK chairman
[2] NYRA award committee chairman

NYRA
NFKK YOUNG RESEARCHER AWARD

We are delighted to announce the second NFKK Young Researcher Award (NYRA) Competition, which will take place during the XXXX Congress in Clinical Chemistry in Aarhus in September 2026.

Researchers below the age of 40 and who are working in one of the Nordic countries, are invited to submit an abstract of their recent scientific work. In all, there will be three awards at a value of DKK 40 000, DKK 20 000 and DKK 10 000 respectively.
For all details about NYRA, please visit the NFKK homepage (https://www.nfkk.org/) under “stipendier og priser”.

We look forward to receiving your abstract no later than Monday June 1, 2026!

NYRA prize winners in 2024: Emil List Larsen (2nd prize), Selma Salonen (3rd prize) and Lasse Bach Steffensen (1st prize).

INDHOLD

Front page: *Telomere length is a dynamic biomarker of biological aging. You can read more about this in the article "Telomere length – a marker of aging in humans, with focus on cardiovascular aging and disease" on page 14.*

Leder:

The Professional Role of a Clinical Biochemist / Laboratory Doctor:
Erfaringerne fra kurset – set med kursusledernes øjne

Linda Hilsted

Dette kursus I NFKK- regi løb af stablen for 4. gang i september måned. Initiativet til kurset blev oprindelig taget af NFKK's bestyrelse som en strategisk indsats, og overlæge Nete Hornung blev udpeget som Chair for den gruppe der skulle udpeges, og i hvilken de kolleger, der var ansvarlige for speciallægeuddannelsen i de nordiske lande indgik. Nete har være gennemgående kursusleder alle 4 gange kurset har været afholdt, og jeg har haft fornøjelsen af at være med i kursusledelsen de sidste 3 gange. Formålet med kurset er beskrevet her:

The overall topic is to introduce various professional roles in clinical biochemistry – and to discuss what is important when searching for a professional role. Various examples of professional roles of clinical biochemists/laboratory doctors are presented, either by lecturers sharing their personal academic road or by lecturers presenting how they manage important tasks being a specialist in clinical biochemistry. There are 3 sessions with topics within basic clinical biochemistry, laboratory operation and development and leadership and communication. Most lecturers are well known experts within their specific field and will present themselves and their professional role in combination with their specific topic.

Idéen med kurset var netop at undervise i den rolle, som kan være svær at få greb om: rollen som professionel. Og i løbet af de seneste 3 gange, har det været tydeligt at kursisterne ønsker mere tid til gruppearbejde og netværksdannelse. Det har vi prøvet at efterkomme, og da Nete og jeg selv ikke er langtidsholdbare som kursusledere, havde vi denne gang inviteret en nyuddannet speciallæge med i kursusledelsen: Emil List Larsen. Og det var en god idé! Emil bidrog til fornyelsen.

Nogle af underviserne var gengangere fra tidligere, nogle var nye. Vi forsøger altid at få undervisere fra alle de nordiske lande, og det er dejligt, at dem vi spørger, siger ja! Denne gang var der også mange af deltagerne, der ikke var danskere (Kurset holdes i København), idet der var god repræsentation fra Norge, Sverige og Finland. Kurset er åbent for læger i speciallægeuddannelse og for kemikere i Klinisk Biokemi. 35 af de 36 deltagere var læger og 1 var sygehuskemiker.

Hvad oplevede vi kursusledere? Fantastisk engagerede og spørgelystne kursusdeltagere. Mens de tidligere hold nogle gange har været lidt tilbageholdende/generte i forhold til at stille spørgsmål og spille sig selv ind i diskussionerne, var det dejligt anderledes her. Masser af pingpong og undren over hvor forskellig uddannelsen er i de forskellige lande, forundring over alt det, uddannelse i Klinisk Biokemi kan anvendes til, alle de professionelle roller vi har muligheder for at udfylde (forudsat at der er stillinger – hvad der kniber en del i Danmark for tiden). Vi oplevede også (igen) hvor engagerede og velforberedte underviserne er, og stolte af vores "fag! Og vi oplevede (igen) at kursusdeltagerne holder meget af, at der indimellem er nogle undervisere, der ikke anvender power point eller lignende. Men blot fortæller!

LABQUALITY DAYS

50th Anniversary

5-6 February 2026 | Helsinki, Finland

Welcome to the International Congress on Quality in Laboratory Medicine & Health Technology

2026 marks the 50th anniversary of the congress!

In addition to the extensive **two-day scientific program**, the congress includes an **exhibition** of companies in the field of clinical laboratory, IT and health technology, an **ePoster exhibition** where you can share your research and project results, and a **satellite workshop** on patient-based quality control.

Join us in this special anniversary year to hear the latest developments in laboratory medicine and health technology!

Scientific program and registration at

labqualitydays.com

Under the auspices of:

EFLM
EUROPEAN FEDERATION OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE

ifcc
International Federation of Clinical Chemistry and Laboratory Medicine

Når vi skal reflektere over, hvorfor de unge mennesker var så engagerede, kan vi selvfølgelig påstå, at både kursuslederne og underviserne er blevet mere erfarne hen ad vejen, og derfor "leverer en bedre vare" (et citat fra en god kollega: Selvros skal man tro på, den er uden bagtanker!).

Med hensyn til kursisterne, så er der selvfølgelig noget med selve tidsånden, at den unge generation generelt bliver mere og mere vant til at være udadvendte i deres interaktion med andre. Men jeg tænker nu også, at de modtager en bedre og bedre uddannelse i deres klinisk (bio)kemiske hverdag, og derfor føler sig bedre klædt på og bedre tilpas i vores kursussammenhæng, som en forklaring.

Det eneste, jeg kan beklage mig over (og det er jo ikke deres fejl) er, at det med de nordiske sprog og forståelse på tværs af landegrænser er ved at være en saga blot. Jeg har længe vidst, at det talte sprog – især mellem danskere og svenskere - er vanskeligt, men nu siger de unge, at de heller ikke kan forstå de skrevne sprog indbyrdes. Heldigvis er de alle supergode til engelsk, men det er nu lidt sørgeligt.

Kurset er obligatorisk i den danske speciallægeuddannelse i Klinisk Biokemi, men jo ikke i de andre nordiske landes uddannelse. Vi håber at den Danske Sundhedsstyrelse bliver ved med at inkludere kurset i den obligatoriske kursusrække.

Læs om kursusdeltagernes "anmeldelse" af kurset på side 12.

De tre kursarrangører: Nete Hornung, Linda Hilsted og Emil List Larsen.

Ordförandespalten

Per Bjellerup
Chairman of NFKK

Dear KBN reader!

Time flies!
"Time flies" is a dear and truly relevant expression. Our previous issue of KBN, it was the end of August and still summer. The crayfish and surströmming (fermented herring) premieres had just taken place. Now we are in the last autumn month, November, which is also the first winter month, at least in the northern parts of the Nordic region. The lobster season is at its peak, and the oysters are becoming increasingly flavourful, at least if the French have their say.

When in November, it always makes me think of Harry Belafonte. I guess at the most 10% of our readers know about him, a very popular singer during the second half of the 20th century. His records often spun on the turntable at home. Belafonte had a big hit with the song *"Try to Remember"*, and what we should remember is the warm and calm month of September. Now in November, nature has finished preparing for winter, closed the shop, and the darkness dominate the day. November, actually a fine month if you think of it. And, in just a little more time than a month, the daylight will start getting longer again. And not to forget, St. Martin's goose has just been celebrated with black soup, roast goose, and Scanian apple cake. Of course, enjoyed with Burgundy wine of excellent quality!

KBN editorial meeting in Lund in October
Enough about food! In early October, the editorial team of KBN met in Lund, where colleagues Charlotte Becker and Ulf Ekström arranged a nice venue for us to gather. Thank you guys! We saved some money for the benefit of the journal. The weather was as expected in the south of Sweden, warm, not windy and so humid that it was unclear whether it was raining or not. In addition to the usual matters regarding previous and upcoming issues of KBN, we welcomed Ingrid Hokstad to the editorial team as the Norwegian representative. A most valuable and pleasant addition.

Beyond that, a tough question: can we afford to, or do we want to, continue publishing KBN as a printed magazine sending it to all our members? Without the sponsorship that recently was ended for the postal distribution, it will be a substantial deficit in the balance sheet for KBN. Opinions differ on the value of printing and distributing. I am "all for" it as I really like the printed version. But I realize that in the long run, we need new sources of income. However, the most important opinion about it is what you think, dear reader! The different societies will soon email their members to ask whether they still wish to receive KBN in print.

NFKK board meeting in Västerås in November
Of ten members, two from each country, four are brand new at the NFKK's board this year. Therefor we will have an in-person meeting now in November in Västerås. We are staying at the Steam Hotel, a cool

hotel housed in a power plant from the 1920s. Many details are preserved, and on the sixth floor, there is an outdoor pool overlooking Lake Mälaren. The board meeting will be held in the hospital's facilities at no cost. I'll return with a report on what we discussed at the meeting in the next issue of KBN.

Looking back

In the previous issue, I highlighted two major breakthroughs in Clinical Chemistry after the turn of the millennium with great impact on the clinical work. It was PEth, the superb alcohol marker, and the ongoing introduction of blood-based biomarkers for Alzheimer's disease. I asked for a third suggestion and am still waiting. So now I promise a gift card of 100 Euros to whoever helps out!

Posters from NCCC2024 in Stockholm

Did you know that all posters from the Nordic Congress in Stockholm are published in SJCLI? Here's the link: https://www.tandfonline.com/doi/full/10.1080/00365513.2024.2428121

Many thanks to the Department of Clinical Chemistry at Karolinska University Hospital for fixing it, much work and money!

I wish you a pleasant autumn and winter! Next time we meet, the daylight will already be getting longer again!

Meanwhile, do you have an interesting patient case for KBN? Send it to us!

Best regards,
Per

Do you have an interesting patient case to share?

In the early 1990s, patient cases were a regular and popular feature in *Klinisk Biokemi i Norden*.
Now, we want to revive this tradition – and we need your help!

We invite our readers to submit manuscripts featuring interesting and educational patient stories. These could include:

- Unusual blood test results
- Atypical disease presentations
- Cases where the laboratory played a key role in diagnosis or clarification

Your manuscript should include a **case description** followed by a **discussion**.

We encourage you to add:

- Reflective questions to stimulate learning and discussion
- Up to 5 key take-home messages at the end

Submit your case and help advance clinical biochemistry across the Nordic region!

The Editorial Team
Klinisk Biokemi i Norden

The 40th Nordic Congress in Clinical Biochemistry 2026 in Aarhus

On behalf of the Nordic Federation of Clinical Chemistry (NFKK) and the Danish Society for Clinical Biochemistry (DSKB), we are delighted to invite you to the 40th Nordic Congress in Clinical Biochemistry. The congress will be held on **15-18 September 2026** and will be located in the heart of Aarhus - Denmark's vibrant and young metropolis.

Registration and abstracts

Early Bird registration:	1 March 2026 - 31 May 2026
Regular registration:	1 June 2026 - 15 August 2026
Late registration:	16 August 2026 - 14 September 2026
Abstract submission:	1 March 2026 - 31 May 2026

Scientific Program

The scientific program is nearing its final form and has been compiled based on input from a number of different environments in all the Nordic countries. We hope we have put together an interesting and relevant program with a mix of current topics and a look to the future.

We plan for 5 plenary lectures, 27 parallel sessions, and, as always, the traditional scientific competitions: The NFKK Young Researcher Award and the Lorentz Eldjarn Prize Competition for Best Publication. We also have the honor of presenting a scientific plenary with the winners of the prestigious UNIVANTS of Healthcare Excellence Award.

We look forward to welcoming you to Aarhus and sharing this exciting scientific experience.

The Organizing Committee

Anne Winther Larsen

Birgitte Sandfeld Paulsen

Holger Jon Møller
Chair of Scientific Committee

Mie Samson
President of Congress

Preliminary PROGRAM NFKK 40th Nordic Congress in Clinical Biochemistry Aarhus, September 15-18, 2026

Tuesday September 15

Afternoon

Wellcome

Plenary lecture

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

Parallel sessions

Novel diagnostic opportunities in neurological disease and cognitive decline	Sustainability in the lab	Thyroid function tests – past, present, and beyond

Parallel sessions

What's new: Lipids, lipoproteins, and cardiovascular risk	ctDNA for early detection and screening	Establishing Robust Pediatric Reference Intervals

Opening ceremony

Wednesday September 16

Morning

Parallel sessions

Reproductive biomarkers	Presentation of working groups in NSMB	Extracellular vesicles

Plenary lecture

Sex and Biomarkers

The NFKK Young Researcher Award

Afternoon

Poster walks

Plenary lecture

Microbiome

Parallel sessions

Fibrinogen and fibrinolysis in health and disease	AI in Diagnostics: Where are we now and what lies ahead?	Mass spectrometry-based proteomics in clinical biochemistry

Parallel sessions

Outcome studies in laboratory medicine	Updates from Nordic screening and screening pilots (session by SKKY)	The microbiome and human health

Thursday September 17

Morning

Parallel sessions

Bone turnover markers for monitoring treatment for osteoporosis	Session by SFKK	Biomarkers of ageing

Plenary lecture

The role of epigenetics in mediating health and disease

The Lorentz Eldjarn Prize Competition for Best Publication

Afternoon

Poster walks

Scientific Plenary:
UNIVANTS of Healthcare Excellence Award

Company sessions

Parallel sessions

Platelet function testing: old acquaintances and novel biomarkers	From Algorithm to Insight: Practical Applications of AI in Diagnostics	LC-MS based immunoglobulin measurement in Clinical Diagnostics

Friday September 18

Morning

Parallel sessions

Choosing wisely	Session by IFKE	ctDNA for guiding treatment decisions
Session by NFKK	to be announced	to be announced

Plenary lecture

Clinical biochemistry in a stressed healthcare system

Afternoon

Closing ceremony

Experiences from the Nordic Course in specialist training 2025 – The Professional Role of a Clinical Biochemist/ Laboratory Doctor

Jennifer Sinead Mack[1], Kirsi Niemi[2], Johanna Dehlsen Wersäll[3], Josefine Bak H. Adelhelm[4]
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[2] TYKS Laboratories, Clinical Chemistry and Hematology Unit, Turku University Hospital, Finland
[3] Avdelningen för Klinisk Kemi, Karolinska Universitetssjukhuset, Sverige
[4] Blodprøver og Biokemi, Odense Universitetshospital, Danmark

I september 2025 deltog 35 hoveduddannelseslæger og én biokemiker i Nordisk kursus i København for at lære om rollen som klinisk biokemiker i de nordiske sygehuslaboratorier. Kurset blev kyndigt faciliteret af lægerne Nete Hornung, Linda Hilsted og Emil List Larsen.

Kursets overordnede temaer var "Goldmining", "Operating and optimizing a Clinical Biochemistry Lab" og "Communication, dialogue, teaching, leadership". Under disse overskrifter mødte vi inspirerende rollemodeller fra specialet, som hver især fortalte om deres karrierevej i klinisk biokemi, og vi blev samtidig bedt om at gennemføre refleksionsøvelser undervejs. Derudover havde vi gruppearbejde om rollen som klinisk biokemiker, poster-præsentation med meget mere. Med afsæt i vore nationaliteters forskelle, følger her beretninger fra kurset fra de fire lande.

En danskers perspektiv (Josefine)

Det var utroligt spændende at mødes med ligesindede fra de øvrige nordiske lande, dele erfaringer og mærke det sammenhold, vi har på tværs af vore lande. De engagerede oplægsholdere satte gang i mine refleksioner over min egen karrierevej inden for klinisk biokemi, og flere pointer har gjort særligt indtryk på mig: Det er afgørende, at vi arbejder tæt sammen med vores kliniske kollegaer, for at sikre faglighed og relevans. Beslutningsstøtte er en uadskillelig del af biokemi nu og i fremtiden – vores rolle er sikre kvalitet og sikker implementering af f.eks. kunstig intelligens. Forskning kan implementeres i vores arbejdsliv på mange forskellige måder – ad de klassiske veje, såsom ph.d. og postdoc, men også ved at anvende data fra den daglige drift. Jeg takker for et yderst givende kursus, som både inspirerede og gav stof til eftertanke.

Et norsk perspektiv (Jennifer)

Jeg er utrolig takknemlig for at jeg fikk delta på kurset, selv om det ikke er en obligatorisk del av utdanningen i Norge. Nete, Linda og Emil, sammen med alle de andre foredragsholderne, klarte å lage et kurs som formidler de delene av faget som er umulig å lære seg fra fagbøker eller litteraturstudie: det som skjer i den daglige jobben vår på jakt etter nye biomarkører, bedre drift eller bærekraftig ledelse; hva dette gjør med oss som mennesker og de utallige veiene å gå videre.

En setning som har gjort spesielt inntrykk på meg var at "vi kan gjøre alt i vår karriere, bare ikke samtidig".

Vi deltakerne fra alle de forskjellige stadiene i spesialistutdanningen fikk høre yrkesbiografier, fortalt av protagonistene selv, og det var gjennom hele kurset en åpen og forfriskende ærlig dialog om utfordringer og løsningsforslag.

På toppen av dette så var utvekslingen med kollegaer fra Danmark, Sverige og Finland veldig givende, og jeg håper å kunne delta på flere nordiske arrangementer fremover. Jeg anbefaler kurset på det varmeste til mine norske kollegaer!

A Finnish perspective (Kirsi, Nikolai and Samuel)
The Nordic Course for MDs in Specialist Training was a deep dive into self-reflection and a career path adventure, where we had the pleasure of meeting our Nordic colleagues. During the course, we had several forward-looking lectures, inspiring discussions about the future of our field (e.g., AI and automation), and even a bit of forecasting along the way. Thankfully, we came to the comforting conclusion that our expertise is still much valued in the future.

As our field of specialty is relatively small, we find it especially important to connect with fellow professionals. In beautiful Copenhagen, our group aimed to learn more about our role as clinical biochemist/doctor in the laboratory. In Finland, clinical chemists also play a crucial role in the daily laboratory work, and it was fascinating to learn about alternative ways of managing laboratory practice across the Nordic countries. Our course also included lectures and group work on leadership and communication, both within and beyond the laboratory. We learned essential facts about the foundations of a well-functioning and reliable laboratory, including pre- and post-analytical factors, as well as how to strengthen the academic part of our work and why research truly matters.

This course was a unique experience for us. Firstly, the leadership lectures guided us to a meaningful introspection (know thyself!). Secondly, it provided us with a platform to meet many of our international peers for fruitful discussions and to share career stories. Lastly, we learned about the newest trends in the field.

We returned to Finland feeling inspired and motivated to continue our work and develop our field.

Et svenskt perspektiv (Johanna)
Jag vill börja med att tacka för en otroligt inspirerande kurs som jag varmt rekommenderar till mina kollegor i Sverige.

Under kursen fick vi ta del av inspirerande berättelser från kliniska biokemister som tagit olika vägar inom yrket men framförallt fick vi tid att diskutera med varandra och skapa kontakter deltagare emellan.

Det finns många likheter mellan våra fyra länder och vår roll som klinisk biokemist men även en hel del olikheter. Vi har kommit olika långt inom olika områden, och därför har vi stor nytta av att mötas och inspireras av varandra.

Framtida samarbeten där vi kan ta del av varandras framsteg och utveckling samt även det som har varit mindre lyckat, vore önskvärt. Jag tror att vår framtid som kliniska biokemister kommer att gynnas av att vi sammarbetar mer, både inom landet och mellan nationerna, för att förbli relevanta och bidra till den största möjliga nyttan för våra patienter.

För att bygga nätverk över nationsgränserna kan kurser som denna lägga en bra grund redan under specialistutbildningen.

Telomere length – a marker of aging in humans, with focus on cardiovascular aging and disease

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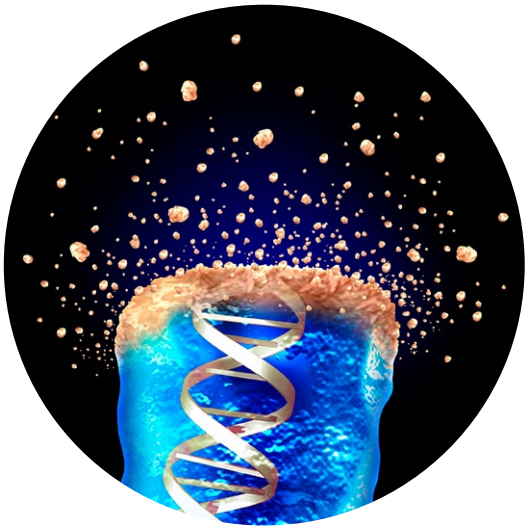
Introduction

The shortening of telomeres, cellular senescence, epigenetic modifications, and mitochondrial dysfunction are key molecular mechanisms of ageing (1). The integrity of genetic stability is fundamental for cellular functions in which telomeres play a crucial role. The present article will focus on mechanisms influencing telomere maintenance and attrition, telomere length in cardiovascular diseases (CVD), and potential interventions that may preserve telomeres and delay the onset of age-related diseases.

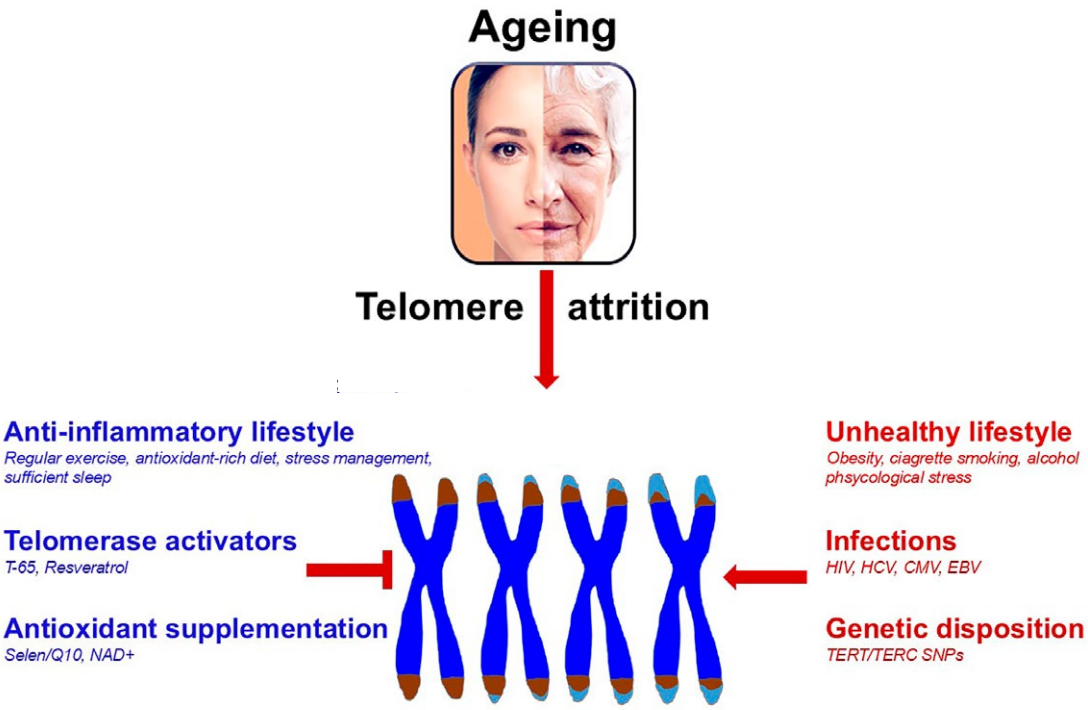
Telomeres are repetitive nucleotide sequences $(TTAGGG)_n$ located at the ends of chromosomes, stabilized by DNA-binding proteins. The telomeric structure prevents genomic instability acting as protective caps - like the plastic tips on shoelaces - preventing chromosome ends from fraying, fusing, or being degraded. The discovery of telomeres and their maintenance stemmed from the pioneering work of Elizabeth Blackburn, Carol Greider, and Jack Szostak in the late 1970s. Their studies in Tetrahymena led to the identification of *telomerase,* an enzyme that extends telomeres. Telomerase was revealed to be a ribonucleoprotein containing both RNA and protein components, which today is known as the catalytic subunit telomerase reverse transcriptase (TERT), the telomerase RNA component (TERC), and the shelterin complex, which includes several accessory proteins (2). Their work was honored with the Nobel Prize in Medicine in 2009 for elucidating how telomeres and telomerase protect chromosomes.



Telomere Shortening and Cellular Senescence

Telomere shortening is a central element of cellular senescence (3). Each time a cell divides, a small portion of its telomeric DNA is lost - a process known as telomere attrition - due to the "end replication problem". Over time, this shortening leads to critically short telomeres, triggering cellular senescence or apoptosis. Telomere attrition is deeply intertwined with genomic instability, and the progressive shortening of telomeres with increasing age, acting as a biological clock, contributes to aging and age-related conditions such as CVD, cancer and neurological disorders (4). Telomere length is regulated by the chromatin structure, telomere-binding proteins, and the enzyme telomerase (5).

In most human somatic cells, telomerase is inactive after birth, except for stem cells and some activated lymphocytes. In contrast, telomerase remains active in germ cells adding telomeric sequences to chromosome ends after cell division (6). Reactivation of telomerase in cancer cells enables them to avoid senescence and proliferate indefinitely.



Measuring Telomere Length

Telomere length is usually measured in isolated DNA retrieved from circulating leukocytes, due to easily accessible blood samples rather than DNA retrieved from solid tissue biopsies. Leukocyte telomere length (LTL) is a widely studied biomarker of biological ageing. LTL can be assessed using quantitative PCR, flow-fluorescence in situ hybridization (flow-FISH), and terminal restriction fragment analysis (southern blot) (7). While LTL has been proposed as a surrogate marker for telomere length in other tissues, its correlation varies significantly across organs (8). Testes, colon and skeletal muscle typically exhibit the longest telomeres, while leukocytes have some of the shortest, with differences of up to 2.5 fold (8). Further research is needed to determine the reliability of LTL as a proxy for tissue-specific telomere length and its role in organ-specific diseases.

Factors that Accelerate Telomere Attrition

Aging and Lifestyle factors

In humans, telomeres covers 10 to 15 kb of DNA, and, approximately 25-200 base pairs are lost with each cell division (5). While aging is the primary driver of this process, several lifestyle and environmental factors contribute to accelerated telomere shortening:

- **Obesity:** Chronic inflammation and oxidative stress associated with obesity, accelerate telomere attrition. Upregulation of telomeric repeat binding factor 1 (TRF1), one of the shelterin complex components, may mediated these effects (9). Recently, a review reported that weigh loss can positively influence telomere length, suggesting it as a potential biomarker in obesity treatment (10).
- **Smoking**: Cigarette smoking mediates an increase in pro-inflammatory factors and pro-oxidants, two factors tightly linked to telomere attrition. A recent meta-analysis confirmed shorter telomeres in smokers and showed an inverse relationship with degree and length of smoking (11). An in-vitro study also revealed *TERT* upregulation and down-regulation of telomere-stabilizing proteins TRF2 and POT1 in smoke-exposed cells (12).
- **Alcohol:** The effect of alcohol on telomere length is unclear. Some data suggest that alcohol consumption may shorten telomere length, particularly in binge drinkers (13, 14). Alcohol-induced oxidative stress and inflammation are likely mechanisms.

Prenatal exposure to alcohol has also been linked to shorter telomeres in newborns (15).

- **Physical Activity**: Moderate physical activity, and physical fitness, appears to protect against telomere attrition possibly by upregulating *TERT*. However, some studies have shown that high-intensity activity in elderly women may shorten telomeres, indicating intensity-dependent effects (16).
- **Psychological Stress**: Chronic stress, including caregiving, socio-economic adversity, childhood trauma, depression, and post-traumatic stress disorder, is associated with accelerated biological ageing. Cortisol responses to mental stress may drive telomere attrition through neuroendocrine mechanisms (17).

Genetics and Viral Influences

LTL is highly *heritable* (18), with both maternal and paternal modes of LTL inheritance. There seem to be a strong correlation between mothers and their newborns, however, the most intriguing observations in telomere biology is the effect of paternal age at conception, with longer LTL in offspring of older fathers, and longer telomere in sperm of older fathers (19). Furthermore, for unknown reasons, offspring of older fathers seem to be relatively resistant to atherosclerosis.

Genetic mutations, especially single nucleotide polymorphisms (SNPs) in *TERT*, *TERC* and *OBFC1* can affect telomere maintenance. Notably *TERT variants* have been linked to clonal hematopoiesis of indeterminate potential (CHIP), which increases cardiovascular risk in the elderly (20). We observed that a frequent SNP in *TERT* increased the risk for major clinical events in patients with coronary artery diseases (CAD) (21). Individuals with very short (or long) LTL at birth are likely to display short and long LTL, respectively, throughout their life (18). We previously showed that LTL were significantly shorter in younger healthy relatives of patients with CHD (22).

Certain viruses (e.g., HIV. HCV, CMV, EBV) can also accelerate telomere loss, likely through inhibition of telomerase and TFR2 and increased oxidative stress, besides a change in cellular composition of the peripheral blood, holding a variety of cellular lengths (16).

Telomeres and Cardiovascular Disease

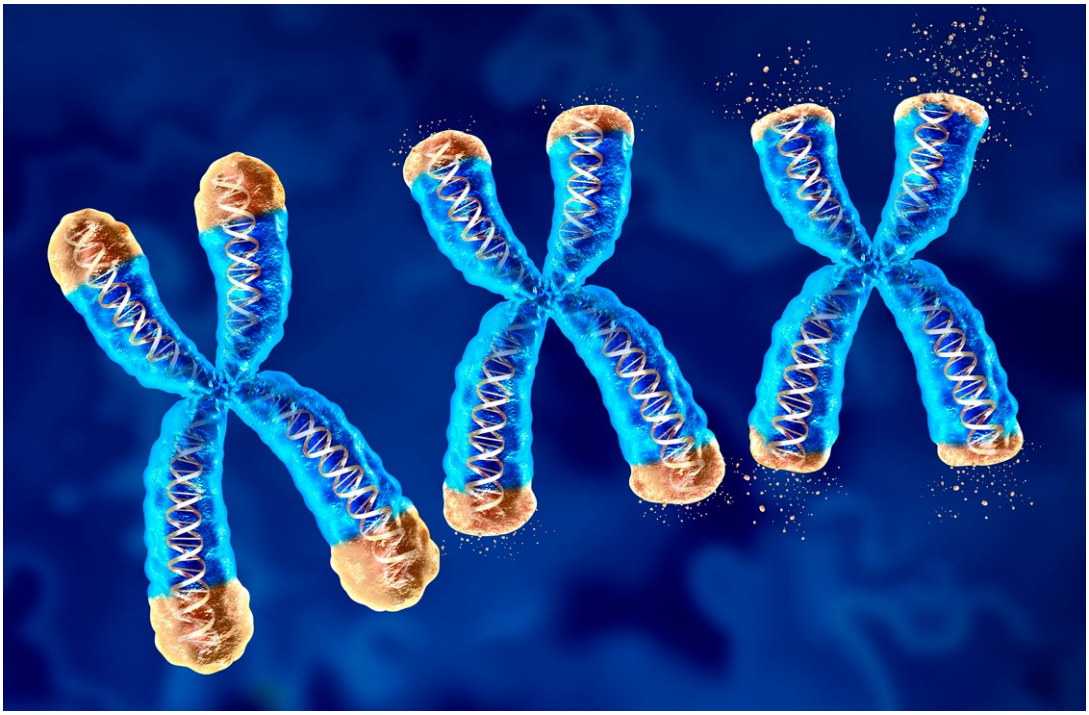
Short LTL in mid-life has been linked to decreased longevity (23) and is associated with increased risk of age-related diseases, particularly cardiovascular conditions, such as atherosclerosis and CAD. Whether telomeres directly participate in the progression of CVD, or are merely a marker of disease, remains unclear. However, Mendelian randomization studies have supported a causal relationship (24-26). Large-scale UK Biobank analyses (>400.000 subjects) found that shorter LTL can decrease lifespan up to 2.5 years (23), and contribute to higher incidence of sudden cardiac death, coronary events and hospitalization due to heart failure (HF) (27).

Hematopoietic and Endothelial Implications

LTL reflects telomere length in hematopoietic stem cells (HSCs), which have low telomerase activity (18). Atherosclerosis is characterized by chronic inflammation and increased oxidative stress, which may harm the endothelium. Shorter LTL in atherosclerosis may be due to an accelerated rate in HSC replication to replace leukocytes consumed in the inflammatory process, and an increase in the loss of telomere repeats per replication due to the sensitivity of GGG triplets in telomeres to reactive oxygen species (ROS) (28). Shorter LTL in atherosclerosis may also be explained by the repair system of endothelial progenitor cells (EPCs) that are present at the site of vascular injury (29, 30). The telomere length of EPSs, descending from HSCs, influences their replicative potential essential for their repair functions.

Cardiomyocytes and Non-dividing Cells

Though cardiomyocytes are post-mitotic, telomere shortening still occurs in diseased hearts. Studies in patients with cardiomyopathy and heart HF have shown telomere attrition independent of cell division (31). In cultured cardiomyocytes, defect expression of the telomere repeat-binding factor *TRF2* led to telomere loss (32). Experiments in mice showed that iPSC-derived cardiomyocytes shortened their telomeres independent of cell division, supporting the idea that stress-related mechanisms, not replication, drive this attrition (31). With aging, the chromosomal structure may change, which epigenetically influences gene-regulatory mechanisms and alter gene expression. Shorter telomeres in cardiomyocytes was shown in patients with HF, probably due to remodeling of the chromatin structure with upregulation of the transcription factor *FOXC1*, which in turn promotes cellular senescence and contractile dysfunction



(31). Despite cardiomyocytes' non-dividing" nature, it seems that telomere shortening occur in diseased post-mitotic myocardial tissue. This feature may also be the case for non-diving cells in other tissues, such as neurons in the brain. As such, shortening of telomeres should be considered also in post-mitotic tissues, contributing to age-related tissue degeneration.

Interventions to Preserve Telomere Length

Telomere attrition is just one of the mechanisms that causes biological ageing (1). Non-pharmacological and pharmacological interventions may counteract cardiovascular ageing, such as caloric restriction, physical activity, antioxidants, sirtuins, anti-inflammatory drugs, epigenetic rejuvenation, and in this context, the prevention of genomic instability and telomere attrition (33).

Pharmacological activation of the telomerase enzyme is possible, however, a re-activation in somatic cells may increase the risk of cancers. A natural derivate antioxidant, resveratrol, and the compound TA-65, which interact with *TERT* and *TERC*, respectively, are promising agents, however, the potential risk of malignancy is a limitation. Recently, we could show that four years of Selenium og Q_{10} intervention preserved the lengths of telomeres in an elderly Swedish population, with association to reduced cardiovascular mortality, mediated via anti-inflammatory and antioxidant mechanisms (34). This treatment also increased circulating Sirtuin1 levels (35), a NAD+-dependent epigenetic regulator involved in DNA repair, inflammation and telomere maintenance (33). NAD+ supplementation, physical exercise, and caloric restriction may increase its activity (33, 36).

Conclusion

Telomere length is a dynamic biomarker of biological aging, particularly relevant in cardiovascular health. Shortened telomeres are associated with increased cardiovascular risk, impaired tissue regeneration, and reduced lifespan. While telomere attrition is a natural part of aging, it is influenced by lifestyle, genetics, and environmental exposures. Promoting an anti-inflammatory lifestyle - balanced nutrition, physical activity, stress reduction, and sleep – may help preserve telomere length and delay the onset of age-related diseases.

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MicroRNAs as novel biomarkers in cardiovascular diseases

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Introduction

MicroRNAs (miRNAs) are short noncoding RNA molecules, approximately 22 nucleotides in length, that play a central role in post-transcriptional gene regulation. They function by binding to complementary sequences on target messenger RNAs (mRNAs), leading to translational repression or mRNA degradation. Through this mechanism, miRNAs fine-tune gene expression in virtually every biological process, such as cell differentiation, proliferation, apoptosis, inflammation, and fibrosis. Furthermore, dysregulation of miRNAs is associated with various disease processes (1, 2). The importance of miRNAs as gene regulators was recently highlighted when Victor Ambros and Gary Ruvkun were awarded the Nobel Prize in Medicine in 2024 for their discovery of miRNAs.

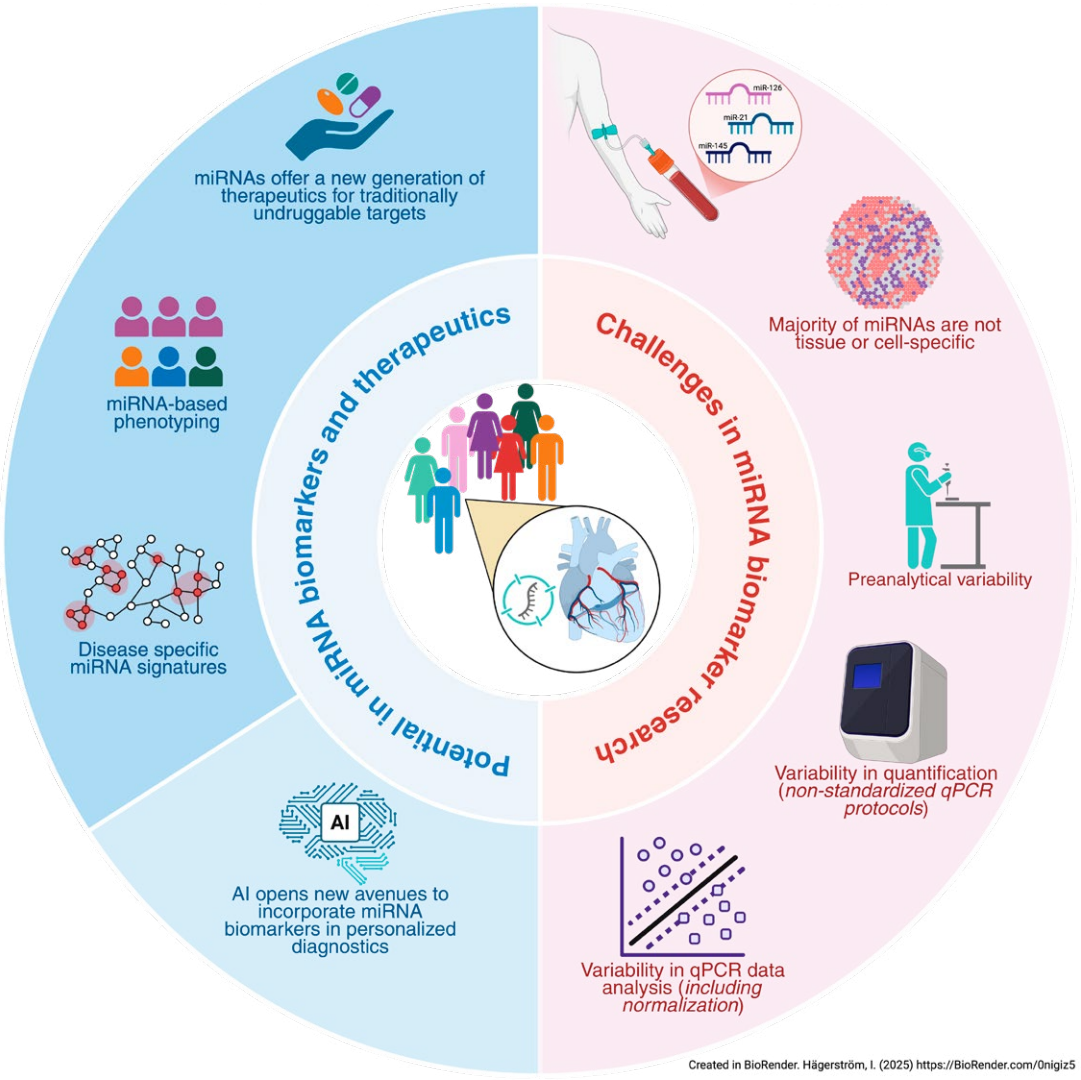
In the cardiovascular system, miRNAs are crucial regulators of myocardial development, vascular integrity, and stress responses. Dysregulated expression of specific miRNAs has been associated with pathological remodelling, ischemia-reperfusion injury, arrhythmogenesis, and heart failure (3). Importantly, many miRNAs are released into the circulation encapsulated in extracellular vesicles, protein complexes (e.g., Argonaute 2), or lipoproteins, rendering them stable and detectable in plasma and serum (3). This stability in biofluids makes miRNAs attractive candidates for biomarkers in cardiovascular diseases (CVD).

MicroRNAs as potential biomarkers and therapeutic targets in cardiovascular diseases

Traditionally, troponins have been used to diagnose acute myocardial ischemia, and natriuretic peptides to diagnose acute heart failure. However, in the era of precision medicine, utilizing novel biomarkers can result in improved diagnosis and prognosis, and better evaluation of treatment efficacy of CVDs and their complications.

Over the past decade, circulating cell-free miRNAs have emerged as promising biomarkers that reflect key pathophysiological mechanisms in CVDs (4). Dysregulated miRNA expression correlates with disease onset, progression, and outcomes, yet translation of miRNA biomarkers into clinical diagnostics remains challenging.

Alterations in circulating miRNA profiles are associated with major cardiovascular conditions, including atherosclerosis, myocardial infarction, and heart failure (5, 6). A recent systematic review on circulating miRNAs as biomarkers for ischemic heart disease identified a panel of five miRNAs (miR-126, miR-21, miR-145, miR-92a, and miR-155) to be most frequently dysregulated across various ischemic heart disease subtypes (5). However, the expression patterns of these five miRNAs varied, for example, in different disease stages (unstable angina, acute myocardial infarction, chronic disease). miRNAs can indeed reflect molecular and cellular stress responses in real-time, including endothelial dysfunction, cardiomyocyte injury, inflammation, and fibrosis. However, when interpret-



ing miRNA results, it is important to note that most miRNAs are not tissue-specific or disease-specific, and they are influenced by disease subtype, stage, patient background, and sample timing, among other factors.

A recent meta-analysis assessed the prognostic performance and risk stratification potential of circulating panels of miRNAs in heart failure with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF) (6). The study identified unique panels of miRNAs that predicted the incidence and severity of heart failure, supporting the clinical utility of miRNA profiling for personalized healthcare and risk stratification in heart failure patients. Combining miRNA signatures with conventional prognostic biomarkers like troponins and natriuretic peptides could improve outcome prediction and medical decision-making towards more personalized treatment of patients.

miRNAs have also demonstrated prognostic poten-

tial in patients with severe cardiovascular disease complications, such as cardiogenic shock (CS). CS is the most severe manifestation of acute heart failure, with the most common etiologies being acute coronary syndrome and worsening of chronic heart failure (7). In CS, a decrease in myocardial pump function can result in circulatory failure and multiple-organ damage. Despite advances in treatments, in-hospital mortality has remained high (approximately 40%) (8). Various scoring systems are used for risk stratification of patients, considering clinical and hemodynamic variables and routine laboratory test values (8, 9). However, there is a need for new biomarkers to classify patients more individually.

We have previously investigated the association between plasma miRNA levels and the clinical picture and prognosis of patients in CS. We used plasma samples collected as part of CardShock study (8) – a multicenter, observational, and prospective study of CS, conducted in nine tertiary hospitals from eight European countries between October 2010 and December 2012. We found that circulating levels of microRNAs miR-21-5p, miR-320a-3p, miR-423-5p, and miR-20b-5p at the time of diagnosis of CS could aid in assessing 90-day mortality (10–12). Cardiogenic shock is a heterogeneous syndrome with significant variation not only in its etiological background but also in the severity of the shock, hemodynamic profile, and degree of organ dysfunction. miRNAs could be used in conjunction with clinical and hemodynamic variables and other biomarkers to help phenotype or classify CS patients into more refined subgroups (13). As miRNAs can mirror the biological processes activated in the disease, their use in the phenotyping of patients could also help in selecting the optimal treatment for the patient (14). A better understanding of activated signaling pathways and biological processes in different phenotypes could, in turn, promote the development of new treatments for CS.

RNA therapeutics are emerging as a new class of drugs with significant potential for the treatment of CVD (15). The best-known examples of RNA therapeutics for CVD are probably small interfering RNA (siRNA) drugs developed for the treatment of different types of dyslipidemias, which are currently in clinical trials. miRNAs are also being developed as therapeutic agents or therapeutic targets. The most advanced clinical example of miRNA therapeutics is CDR132L, which is an antisense oligonucleotide targeting miR-132. In a phase 1b clinical study, CDR132L was shown to be safe and well-tolerated in patients with stable heart failure of ischemic origin, with preliminary improvements in cardiac function and decreased levels of fibrosis- and tissue injury-related biomarkers. CDR132L is currently being investigated in several phase 2 trials, including the large HF-REVERT trial evaluating its effects on post-myocardial infarction and heart failure patients. Other ongoing phase 2 studies are evaluating multiple doses and impact of CDR132L on heart structure and function in patients with heart failure and left ventricular hypertrophy. CDR132L represents the first miRNA-targeting drug to enter late-phase trials for a cardiovascular indication.

Analytical challenges in miRNA biomarker research

There is widespread interest in miRNA biomarkers. At the time of writing this article, October 2025, a PubMed search for "microRNA biomarkers" yielded over 44,000 publications, and a search for "microRNA biomarkers cardiovascular disease" yielded nearly 5,000 publications. Despite promising results, miRNA biomarkers have not yet found their way into clinical

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use. The most widely used technique to quantify circulating miRNA levels is RT-qPCR. Although RT-qPCR is a sensitive and relatively inexpensive method available in almost all laboratories, the lack of standardization and reproducibility of miRNA quantification is currently the major obstacle preventing the translation of miRNA biomarkers into clinical use.

Preanalytical variables comprise the majority (60–70%) of laboratory errors in routine diagnostic testing, and they have major influence on miRNA quantification as well (16). Factors such as the type of anticoagulant used in blood sample collection, hemolysis, sample processing, and storage conditions before and after centrifugation can affect miRNA yield and measured miRNA levels. Choosing blood collection tubes that are compatible with RT-qPCR is important for obtaining reliable results. Heparin tubes should not be used because heparin is known to inhibit enzymes used in RT-qPCR. However, heparin can also originate from patient circulation, as hospitalized patients may have been treated with heparin to prevent blood clotting. In these cases, heparinase treatment of samples should be included in the quantification protocol. Hemolysis, for instance, leads to the release of miRNAs from red blood cells (e.g., miR-451, miR-16), which can confound results. In addition, centrifugation time, speed, and the number of centrifugation steps have a significant effect on the removal of platelets and other cellular components from the sample, thereby influencing miRNA levels. Standard operating procedures and documentation of sample handling are essential in miRNA biomarker research.

RNA concentrations are very low in serum and plasma, bringing further challenges in miRNA quantification. Different RNA isolation methods yield variable recovery rates, and no universal endogenous extraction control miRNA has been established for plasma or serum. Synthetic spike-in controls, such as *C. elegans* miRNA cel-miR-39, are therefore commonly used to monitor RNA isolation step. Moreover, differences in reverse transcription (RT) and qPCR amplification (different kits, different qPCR platforms, etc.) may hinder the comparison of results between different laboratories.

Normalization of RT-qPCR data remains one of the most crucial steps in miRNA quantification to obtain reliable results (16). Currently, there are no universal endogenous reference miRNAs that could be used in normalization and calculation of circulating miRNA expression levels. Thus, stable endogenous miRNAs must be determined separately for each biological condition and experimental setup. Commonly used reference miRNAs (e.g., miR-16) are not always stable in different pathological conditions. Other strategies such as global mean normalization or use of multiple reference miRNAs have been proposed but not standardized. Yet another normalization strategy is synthetic spike-in miRNAs, such as cel-miR-39, which are added in samples during RNA extraction. Main purpose of spike-ins is to monitor technical variation in RNA isolation and RT; however, they are also widely used as exogenous reference genes in normalization of RT-qPCR data. The drawbacks of exogenous reference genes are that manual pipetting can cause technical variation in results and spike-ins do not correct for the variability in sampling and quality of samples. Endogenous miRNAs have therefore been proposed as preferential reference genes in miRNA quantification. In addition to these preanalytical and analytical variables, the analysis of the qPCR data, a final step in miRNA quantification, may also cause significant variation in the results, especially when dealing with possible low expressing miRNAs and missing values (16, 17).

How to move forward to overcome challenges related in miRNA quantification? Substantial efforts are needed to standardize protocols for miRNA biomarker research in order to incorporate the most promising miRNA biomarkers into clinical practice in the future. Inter-laboratory comparison trials, or ring trials, could play a pivotal role in identifying the most critical sources of variation in different phases of miRNA quantification (preanalytical, analytical, and postanalytical) (18). A ring trial could help establish guidelines on the best practices to improve the quality and reproducibility of miRNA quantification. Furthermore, the development of specific miRNA biomarker guidelines analogous to MIQE (Minimum Information for qPCR Experiments) and dMIQE (the Minimum Information for Publication of Digital PCR Experiments) could improve transparency and comparability across studies, facilitating the integration of miRNA biomarkers into clinical practice (19, 20).

Conclusion

miRNAs are promising novel biomarkers in cardiovascular diseases and their complications. The potential of miRNAs to represent pathophysiological mechanisms beyond traditional biomarkers, along with

advancements in RNA therapeutics, renders miRNAs attractive as novel tools for personalized diagnostics and prognostics of CVD. The application of miRNAs in personalized diagnostics could be further enhanced by artificial intelligence (AI) and machine learning tools. The main reason hampering the clinical use of miRNA biomarkers is the lack of standardization and reproducibility. Addressing these issues require determined collaborative efforts from the miRNA research community.

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Riktig bruk av laboratoriet:

Minste retestingsintervaller og inspirasjon til kvalitetsarbeid inkludert i nasjonal brukerhåndbok

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Unødvendig bruk av laboratorieanalyser utgjør en økende utfordring i helsetjenesten. Vi har tatt initiativ til et nytt kapittel i norsk nasjonal brukerhåndbok for medisinsk biokjemi med overskriften «Riktig bruk av laboratoriet». Her har vi samlet forslag til minste retestingsintervaller og aktuelle problemstillinger knyttet til bruk av enkelte analyser. I følgende artikkel vil også erfaringer med innføring av minste retestingsintervaller ved sykehuset i Vestfold bli omtalt.

Unødvendige blodprøver

Unødvendig laboratorietesting fører til uhensiktsmessige kontroller, utredninger og behandlinger og er en utfordring for helsevesenet (1). Det medfører også økte kostnader, merarbeid for laboratoriene og rekvirentene, forsinkede svar på viktige prøver og ubehag for pasientene. Blodtapet fra en enkelt prøvetaking er som regel ikke stort, men særlig for intensivpasienter og barn kan volumet under en innleggelse bli betydelig og øke faren for transfusjonskrevende anemi. Blodtransfusjoner øker sykelighet og er derfor uheldig (2,3). Laboratoriene er storforbrukere av kjemikalier og engangsplast og står for en betydelig andel av spesialisthelsetjenestens utslipp av CO_2, og overforbruk øker laboratorienes klimaavtrykk ytterligere (4,5).

Over flere år har man sett en vesentlig økning i antall blodprøver som rekvireres, uten at antall pasienter har økt i samme grad (6). Den internasjonale kampanjen «Choosing wisely» har satt søkelys på overdiagnostikk og overbehandling som ikke medfører bedre helse og i verste fall kan skade pasientene (7). Inspirert av dette har vi tatt initiativ til et nytt kapittel *om riktig bruk av laboratoriet* i vår nasjonale brukerhåndbok i medisinsk biokjemi (8). Brukerhåndboken er tilgjengelig på nett, https://metodebok.no/index.php?action=book&book=biokjemi og som en app i appstore/google play under «Metodebok».

Det nye kapittelet inneholder bl.a. veiledende retestingsintervaller for noen analyser (Tabell 1) og aktuelle problemstillinger som kan inspirere til kvalitetsarbeid (Tabell 2). Informasjonen er også samlet i egne avsnitt under de aktuelle analysetekstene.

Retestingsintervall

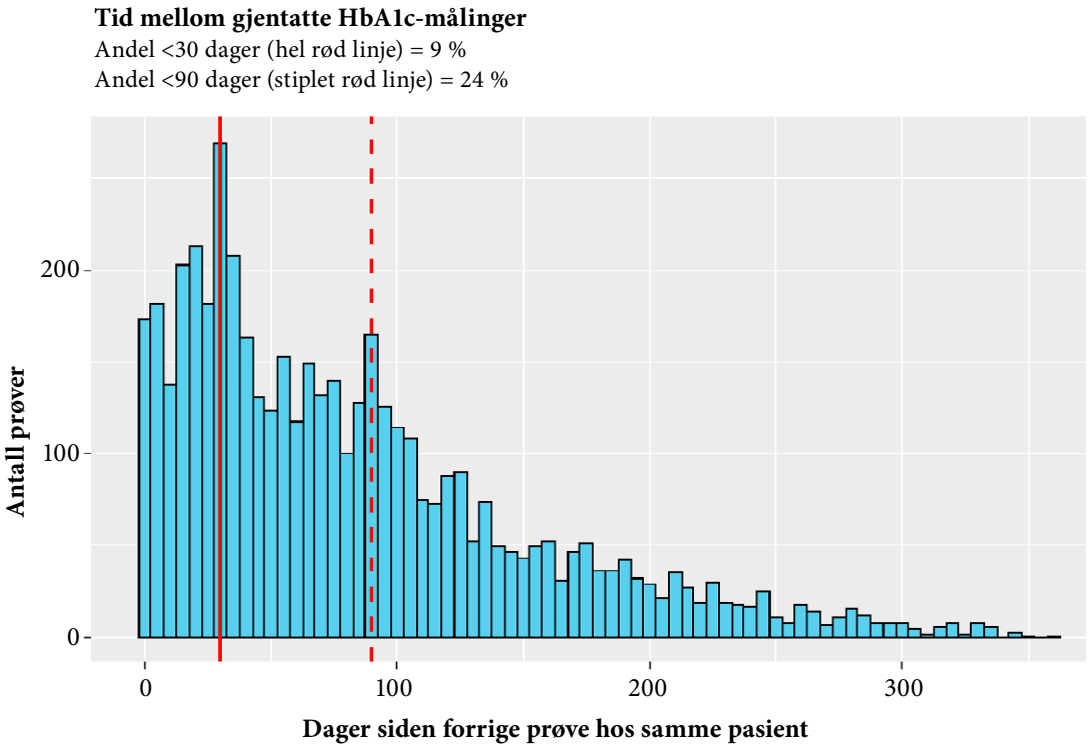
Minste retestingsintervall er et forslag til den korteste tiden som bør gå dersom man har behov for å gjenta en test hos samme pasient. Intervallet er avhengig av testens biologiske egenskaper og kan variere med ulike problemstillinger. For eksempel vil TSH vise full effekt av doseendring av levotyroksin først etter 6–8 uker. Dersom man velger å endre dosering basert på en test tatt tidligere, kan det føre til feilbehandling. Ved hypertyreose kan det derimot være behov for hyppigere kontroller. Nasjonale anbefalinger for minste retestingsintervall ble publisert i Storbritannia allerede i 2011 (9).

For laboratoriene kan innføring av sperrer i elektronisk rekvireringsmodul når en test rekvireres for ofte, være et godt virkemiddel for å redusere andelen unødvendige prøver (10,11). I tabell 1 har vi lagt inn forslag til tidsintervall for sperrer i rekvireringssystemer for noen analyser. Vi anbefaler imidlertid at det gjøres lokale tilpasninger, særlig da journalsystemene ofte er lite utviklet på dette feltet.

Erfaringer med sperrer for rekvirering og minste retestingsintervall fra Sykehuset i Vestfold

Sentrallaboratoriet ved Sykehuset i Vestfold har i løpet av de siste ni årene innført sperrer i elektronisk rekvireringsmodul for noen utvalgte analyser for sykehusets interne rekvirenter. Dersom en analyse rekvireres med for kort intervall hos samme pasient vil det komme opp et varsel om at analysen bestilles for tidlig; enten i form av ett «hardt stopp» - rekvirenten må kontakte laboratoriet for å få gjennomført analysen - eller «mykt stopp» - rekvirenten kan velge å ignorere varselet og likevel bestille analysen. Eksempler på analyser med «hardt stopp» i Vestfold er HbA1c, vitamin D, kolesterol og proteinelektroforese, mens TSH og fritt T4 har «mykt stopp». Alle sperrer er lagt inn etter høring hos rekvirenter fra aktuelle fagspesialiteter.

Totalt 9 % av alle HbA1c-analysene utført på innlagte og sykehusets polikliniske pasienter ved Sykehuset i Vestfold ble tatt med mindre enn 30 dagers intervall før innføringen (Figur 1). Dette til tross for at gjeldende retningslinjer anbefaler minst 90 dager mellom målingene for de fleste pasienter (12). Etter innføring av minste retestingsintervall med 30 dagers sperre og «hardt stopp», gikk andelen prøver med kortere intervall ned til ca. 3 %. Dette samsvarer med internasjonale erfaringer, blant annet fra Storbritannia og Canada, som viser betydelig kostnadsbesparelse ved innføring av minste retestingsintervall (10,11). Det er få studier som har sett på kliniske utfall etter innføring av sperrer i rekvireringssystemer, men enkelte har vist at dette ikke fører til økt morbiditet eller mortalitet (10). For analyser der Sykehuset i Vestfold har lagt inn «mykt stopp» var det ingen eller liten nedgang i antall prøver tatt med kortere intervall. Varsler som rekvirentene kan velge å ignorere og trykke seg forbi, har altså vist seg å ha liten effekt.



Figur 1. *Fordelingen av tiden mellom repeterte HbA1c-analyser hos samme pasient i løpet av et år. Tallene er hentet fra inneliggende og sykehusets polikliniske pasienter ved Sykehuset i Vestfold noen år før innføring av minste retestingsintervall på 30 dager for HbA1c.*

Tabell 1. Veiledende retestingsintervaller (8).

Analytt	Veiledende retestingsintervall *	Spesielle kliniske problemstillinger	For lab**
HbA1c	-Ikke stabilt/ønsket nivå: **3 mnd** -Velbehandlet diabetes: **6 mnd** -Pasienter *uten* diabetes (HbA1c < 42 mmol/mol) bør ikke screenes oftere enn hvert **1. til 3. år** avhengig av risikoprofil -Repetert måling innen **2 uker** kan være aktuelt for å stille diagnose hos asymptomatiske pasienter	-Hyppigere kontroll for barn/unge med type 1 diabetes, diabetikere som planlegger å bli gravide, gravide og pasienter med rask endring i blodglukose -HbA1c er ikke pålitelig ved endret levetid for RBC (f.eks. graviditet, nyresvikt og anemi)	**30-90 dager**
SR	-Arteritis temporalis og polymyalgia rheumatica: **3 mnd** (oftere initialt) -Rheumatoid artritt: **1 mnd** (inntil sykdomskontroll)		**7 dager**
TSH	-Hypotyreose: **6-8 uker** etter endring i medisinering -Velbehandlet hypotyreose: **1 år** -Subklinisk hypotyreose (Høy TSH, normal fT4): Første kontroll etter **3-6 mnd,** videre oppfølging avhenger av anti-TPO -Hypertyreose behandlet med tyreostatika: **4-6 uker**, oftere initialt -Hypertyreose på vedlikeholdsdose: **3 mnd**	-Alvorlig hypertyreose, gravide, barn/ungdom: **2-4 uker** -Immunterapi: Økt risiko for tyreoiditt (2-6 uker)	
TPO-antistoff	**-Ikke nødvendig å gjenta** ved kjent forhøyet TPO-antistoff hos voksne (>20 år)		Voksne: >100 kIU/L (metodeavhengig verdi): ∞
TRAS	-Graves hypertyreose: Ved diagnose og før seponering av behandling	-Gravide med aktiv Graves eller tidligere forhøyet TRAS krever tettere oppfølging	**3 mnd**
25-OH Vitamin D	-Igangsatt behandling ved påvist mangel og samtidig underliggende sykdom og/eller medisiner som kan gi nedsatt absorpsjon/endret metabolisme: kontroll etter **3 mnd**	**-Unngå å bestille analyse av vitamin D hos personer uten økt risiko for vitamin D-mangel**	**3 mnd** (<50 nmol/L) **6 mnd** (≥50 nmol/L)
Vitamin B12	-B12-mangel: **Ikke nødvendig å gjenta** (kontrolleres med andre parametre) etter igangsatt behandling (unntak: Dersom manglende retikulocytose eller vedvarende anemi eller nevrologiske symptomer) -Livslang terapi: **Ev. årlig kontroll**	-*Uttalt megaloblastær anemi eller alvorlig nevrologi*: Hb, MCV/MCH, retikulocytter, og ev. MMA etter 14 dager og 8-12 uker (ev også folat og ferritin) -*Uten alvorlige symptomer*: Hb, MCV/MCH, folat og ferritin, og ev. MMA etter 8-12 uker	**3 mnd**
Genanalyser (kimbane)	**-Sjelden nødvendig å gjenta**		∞
Proteinelektroforese	-MGUS: **12 mnd** (**6 mnd** initialt) -Aktiv myelomatose: **4-6 uker** under behandling, **2-3 mnd** i stabil fase		4 uker

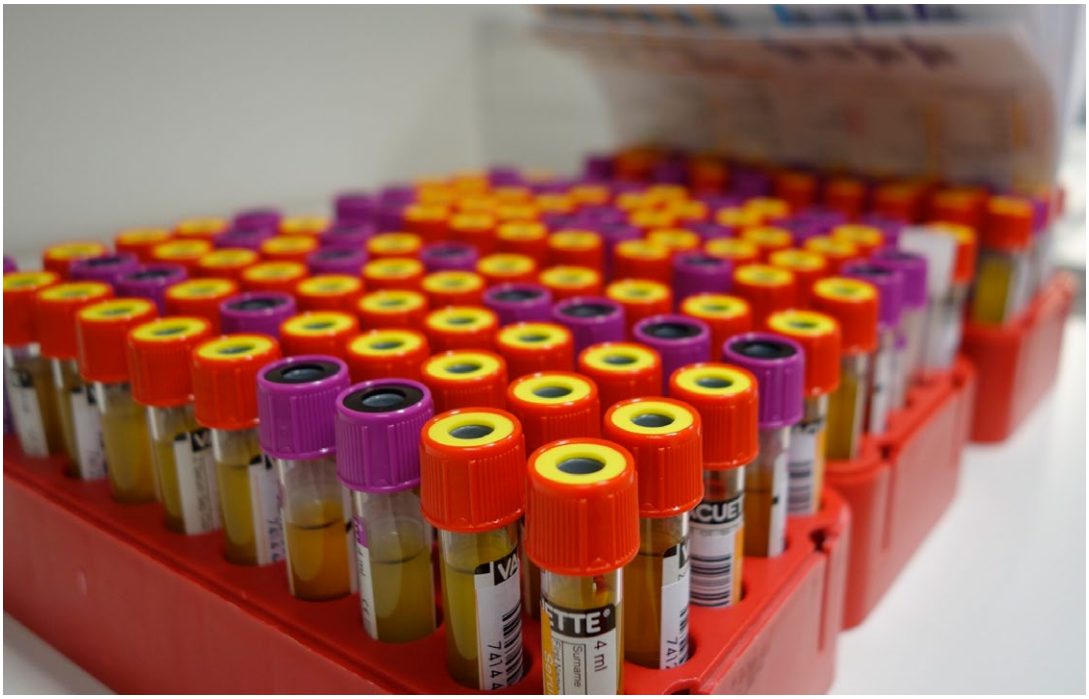
***Retestingsintervallet** indikerer den *korteste* tiden som bør gå *dersom* man har behov for å gjenta en analyse og vil være avhengig av problemstilling. Anbefalingene er veiledende og skal ikke erstatte klinisk skjønn. **Forslag til tidsintervall for varsler og sperrer i rekvireringssystemer. Lokale forhold bør hensyntas.

Dessverre kan vi ikke i vårt rekvireringssystem (DIPS Arena) lage ulike lengder på intervallene avhengig av forrige analyseresultat eller hvilken avdeling som bestiller analysen. Ordlyden i varslene er dessuten standardiserte uten opplysning om når forrige prøve ble tatt eller resultatet av denne. Det er derfor et stort behov for bedre funksjonalitet i bestillingssystemene for å kunne utnytte dette verktøyet best mulig.

I Norge har det pågått et nasjonalt prosjekt der en gruppe med representanter fra alle helseregionene har utarbeidet forslag til tiltak for å redusere overforbruk av laboratorietjenester. I sin rapport til Helsedepartementet har de blant annet anbefalt å legge bedre til rette for bruk av minste retestingsintervall i elektroniske rekvireringsmoduler (13). Dette gir håp om at systemutviklerne i større grad må forbedre brukervennligheten i fremtiden.

Utfordringer ved bruken av enkelte analyser - inspirasjon til kvalitetsarbeid

I litteraturen finnes det mange eksempler på studier som har sett på problematisk bruk av vanlig rekvirerte analyser. Vi har samlet noen av referansene under overskriften «Overforbruk av blodprøver» og håper at disse kan inspirere til målrettet kvalitets-



Tabell 2. Aktuelle problemstillinger. Her er listet referanser som kan danne utgangspunkt for diskusjoner om riktig bruk av laboratoriet.

Analytt	Referanser
HbA1c	En europeisk studie fant at > 1/3 av multimorbide eldre ble behandlet med for strenge behandlingsmål for HbA1c (18). I en annen artikkel tar forfatterne til orde for kritisk gjennomgang av diabetestesting på sykehjem etter at de fant at < 1% av HbA1c-resultatene var over aksjonsgrensen hos sykehjemspasienter som ble screenet for diabetes (14).
NT-proBNP	En studie som så på hvordan tilgjengelighet påvirker etterspørsel, fant 374% økning i rekvirering av NT-proBNP etter at analysen ble gjort lettere tilgjengelig for rekvirering (19).
Laktat, ANA, Magnesium, Troponin, APTT	De fem testene med mest problematisk bruk (basert på kostnad, lav andel unormale svar og stor variasjon mellom rekvirenter) i en europeisk studie på pasienter innlagt ved indremedisinske avdelinger (20).
INR og APTT	Choosing wisely Canada har gjennomført kvalitetsprosjekter for å redusere unødvendige blodprøvetakninger på intensivpasienter, med fokus på bl.a. repeterte koagulasjonsanalyser (21). Kun en liten andel av koagulasjonsanalyser på intensivpasienter var unormale i en australsk studie, og de fleste forble normale under oppholdet (15).
SR	Et kvalitetsprosjekt reduserte samrekvirering av SR og CRP med 33% (22). Choosing Wisely Canada har laget en anbefaling om bruk av SR (23).
TSH	Ettersom TSH er mye mer fininnstilt enn fT4, er det ofte tilstrekkelig å måle TSH (24). Ved Diakonhjemmet Sykehus har man automatisk etterrekvirering av frie tyroideahormoner når TSH er utenfor referanseområdet mens ved Sentrallaboratoriet i Vestfold har man en algoritme tilpasset utredning av tyroideasykdom (25).
25-OH vitamin D	Rapportert stort overforbruk, en enkel intervensjon reduserte rekvirering med nesten 30% (26). Anbefaling om rekvirering fra «Kloke valg»-kampanjen (27).
Vitamin B12	«Best practice»-pop-up reduserte rekvirering med ca 50% i en amerikansk studie (28).
PSA	Rutiner for PSA-testing på eldre menn varierte betydelig blant klinikere i en amerikansk studie (16). Hos menn >75 år er testing for tidlig diagnose omdiskutert. Rundt 40% av mannlige norske 75-åringer testes årlig (17).

Forkortelser: ANA; Antinukleære antistoff. INR; Internasjonal normalisert ratio. APTT; Aktivert tromboplastintid. SR; Senkningsreaksjon. TSH; Tyreoideastimulerende hormon. PSA; prostataspesifikt antigen.

arbeid på laboratorier i samarbeid med rekvirenter (Tabell 2). Eksempler er uhensiktsmessig bruk av analysen HbA1c hos pasienter på sykehjem (14), at kun en liten andel av koagulasjonsanalyser på intensivpasienter er unormale (15) og at rutiner for PSA-testing på eldre menn varierer betydelig blant klinikere (16). Hos menn >75 år er testing for tidlig diagnose av prostatakreft omdiskutert, og det er et paradoks at rundt 40% av mannlige norske 75-åringer testes årlig (17).

Konklusjon

Vi håper kapittelet Riktig bruk av laboratoriet i vår nasjonale brukerhåndbok kan bidra med nyttig informasjon om rekvireringsintervaller og inspirere til kvalitetsarbeid. Innføring av minste retestingsintervall i form av «harde stopp» ved blodprøvebestilling reduserer effektivt overrekvirering, men krever god dialog mellom laboratoriet og rekvirentene. For å utnytte verktøyet bedre må imidlertid rekvireringsløsninger optimaliseres for bruken. Erfaringer bør deles på tvers av laboratorier for harmonisering og best mulig praksis.

Vi tar gjerne imot generelle tilbakemeldinger på kapittelet, samt konkrete forslag til analyser som kan legges til i tabellene.

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De viktigste 20 referansene er med her, de øvrige kan ved behov fås ved å kontakte redaksjonen eller forfatterne.

On the importance of documenting achievements, successes, and failures

Documentation and dissemination determine how discoveries are remembered – or forgotten

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Early professional contacts

Long ago, in the 1940s and 1950s, when clinical chemistry emerged as a distinct medical discipline, central laboratories began appearing in hospitals - both large and small - like mushrooms in moist soil. During this time, national societies were established, with the professional association Nordic Federation of Clinical Chemistry (NFKK) as an "umbrella organization" to coordinate and stimulate development. Committees with specialists from the national societies carried out the work of NFKK. Some NFKK recommendations were pioneer projects with international implications, e.g. the Nordic Enzyme recommendations finally settled the measuring temperature to 37 ºC. Committee work was regularly published in the Scandinavian Journal of Clinical and Laboratory Investigation (SJCLI). Committees formed one pillar of NFKK's activities; the organization of biennial Nordic congresses was the other. In the beginning, these meetings attracted 25 - 50 participants and were hosted by a local laboratory. Many participants will recall them as occasions for making friends and establishing collaborations as much as for scientific discussion. Laboratories prepared their own reagents and designed their manual analytical procedures, so methodology and quality improvement were recurring topics. Often, but not always, proceedings of the meetings were published as "supplements" to SJCLI.

Over the decades, as the field and its institutions matured, the congresses evolved into the modern format we recognize today, comprising four tiers: oral and poster presentations, a commercial exhibition, and social activities. Their size and financial turnaround now exceed the capacity of routine laboratories. Almost all oral presentations are by invited

established scientists. There may be several reasons why specific speakers were chosen, for instance, their ability to skillfully explain their own research in a broader context, their relevance to the congress theme and the organizers´ interests, or more rarely, to present new findings. Some congresses publish abstracts of oral presentations, but it's all volatile; once the event is over, memory fades, and performances are soon forgotten. A given lecture rarely appears as a distinct entry on a person's CV.

International information exchange

Research and development are competitive, but collaboration and information exchange are fundamental for progress. It is important for the individual or research group to document new achievements – and to claim priorities. Early on, letters, personal notes and books were the only means of documentation and the remnants are invaluable sources to understand the development of science. The first regularly published scientific journals occurred in 1665: "The Philosophical Transactions of the Royal Society" (https://royalsocietypublishing.org/loi/rstl/) and the French "Journal des sçavans (scholars) (https://archive.org/details/s1id13378460).

Lymf and oxygen

The history of science contains many interesting and informative controversies. To illustrate how the recognition of scientific discoveries often depends on documentation, timing, and communication, let us recall two Nordic stories that have gained international recognition.

The famous Danish scientist Thomas Bartholin Jr described his observations of lymph in dogs in the autumn of 1652. The discovery of the lymphatic system, however, has been attributed to the Swedish polymath Olof Rudbeck Jr., following long and heated discussions. Is that fair? Yes, maybe. The Swedish, curious, and science-interested Queen Christina of Sweden visited Uppsala and Rudbeck in the spring of 1652. An autopsy, probably of a dog, and a demonstration of the circulation of lymph performed by Rudbeck was on the program and described in the Royal reports but not formally published until Rudbeck's "Nova exercitatio anatomica, exhibens ductus hepaticos aquosos, & vasa glandularum serosa" became available in 1653. The original observation was before the Bartolini publications; thus, the discovery has been internationally attributed to Rudbeck. As a side note, Bartolini was born a Dane in Malmö, but became a Swede after the Peace of Roskilde in 1658.

Another classic story is the discovery of oxygen. The Swedish pharmacist Carl Wilhelm Scheele, a largely self-taught scientist working in Köping, had previously worked for Professor Torben Bergman in Uppsala, who studied the affinity of substances. Bergman's famous "De attractionibus electivis" (On Elective Attractions) is a 400-page description of known and characterized substances and their reactions, translated to English in 1785. It was a source of inspiration for generations of chemists, although it embraced the phlogiston theory. A digitized copy is available that also includes all intricate


Carl Wilhelm Scheele's
d. Königl. Schwed. Acad. d. Wiſſenſchaft. Mitgliedes,
Chemiſche Abhandlung
von der
Luft und dem Feuer.
Nebſt einem Vorberichte
von
Torbern Bergman,
Chem. und Pharm. Prof. und Ritter; verſchied.
Societ. Mitglied.
Upſala und Leipzig,
Verlegt von Magn. Swederus, Buchhändler;
zu finden bey S. L. Cruſius.
1777.

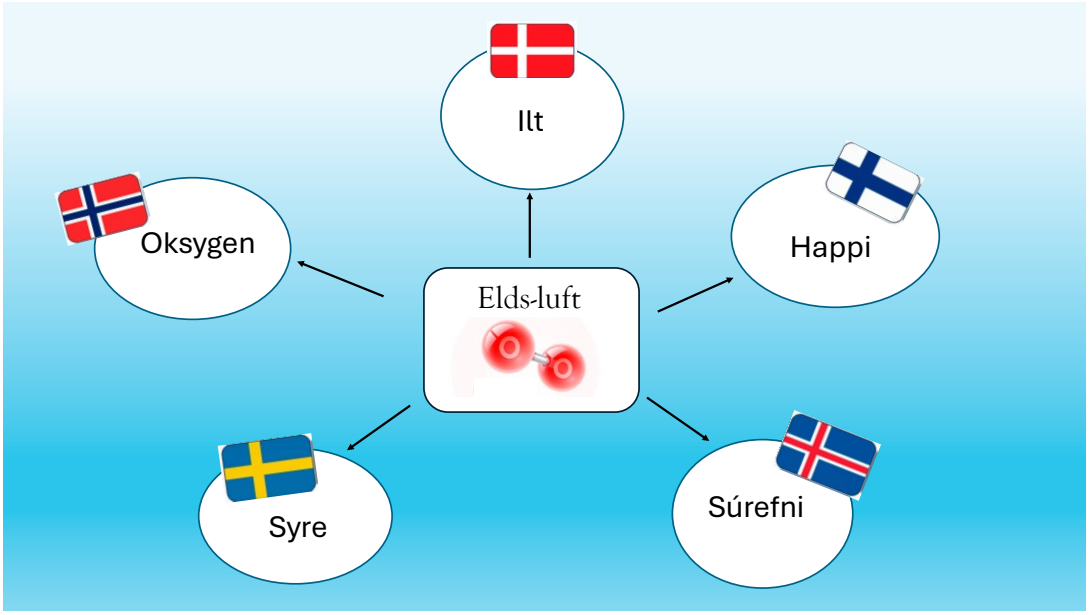
The first Swedish pharmacopoeia was published in 1686, the second in 1775. Among all the recipes, they prescribed a standard set of instruments for pharmacies; those illustrated on the cover of Scheele's "chef-d'oeuvre" are mainly of his own design.

symbols for chemical substances used before the Berzelii system became widely adopted. With our present knowledge of the substances available to Scheele, and the dominating Phlogiston theory of fire and heat it is not simple to understand Scheele's reasoning in setting up the experiment. Scheele added Vitriol oil, i.e., concentrated sulfuric acid, to saltpeter (potassium nitrate). He found that the stronger sulfuric acid decomposed saltpeter, producing a gas. This gas was called Vitriol air. Scheele heated manganese oxide and several other metal oxides and isolated a gas that enhanced combustion and shared other properties with Vitriol air. He renamed it "Fire air". These experiments were described in "manuscript number 52" from 1770-1772, which was not formally published until 1777 in Scheele's major work, "Chemische Abhandlung von der Luft und dem Feuer". Scheele described his experiments in a letter to the Royal Swedish Academy of Sciences and also communicated with Lavoisier in France. Meanwhile, Joseph Priestley, still in England, isolated and described "dephlogisticated air" in a report to the Royal Chemical Society (1775). Therefore, the discovery of oxygen is generally credited to Priestley, but even internationally, often also acknowledged to Scheele.

Naming of elements

At this point, it might be justified to explore the etymology of the element's name. We know from various letters and reports that Scheele preferred "elds-luft," whereas Priestley called it "dephlogisticated air". The phlogiston theory became increasingly hard to defend, and Antoine Lavoisier in Paris ultimately proved it wrong. Based on his experiments, Lavoisier named the gas described by Priestley and Scheele Oxygène in 1787. The name comes from the Greek OXY, meaning sharp or acid, and we recognize "GEN" from "generate," meaning create. The story goes that Lavoisier observed that when non-metals burn in air, they form acidic products – oxides – usually soluble in water. He initially thought this was an effect of "vital air," but later changed it to "oxygène." Chemistry responded with irony: when metals are heated in air (oxygen), the emerging metal oxides will be basic and rarely soluble in water!

Berzelius accepted Lavoisier's name in "Essai sur la nomenclature chimique" 1811, and local translations soon appeared: Sauerstoff (DE), happi (FI), súrefni (IS), and syre (SE). Norway and the Anglo-Saxon languages, along with many others, copied Lavoisier directly, e.g., oksygen (NO). The Danes diverged, guided by Hans Christian Ørsted, who invented "ilt" derived from ild, meaning fire, in 1814 and brent for hydrogen from brend. Thus "brent over ilt" represent an important compound (*Ørsted, H. C. 1814. Ten-*



tamen nomenclaturae chemicae omnibus linguis Scandinavico-Germanicis communis). Danish is one of the few languages that still preserve a direct link to Scheele's original observation and terminology. Hans Christian Ørsted – the renowned physicist who discovered the connection between magnetism and electricity (1822) – was also a notable philosopher. Among his many pursuits was the promotion of a scientific approach to the naming of substances and natural phenomena. This same principle, I believe, later inspired René Dybkaer and Henrik Olesen in their dedicated efforts to bring greater clarity to the nomenclature of clinical chemistry.

IUPAC now authorizes the naming of new elements. The latest element synthesized is Oganesson (2015), named after the Russian nuclear physicist Yuri Oganessian (still alive), and preferred over Berzelium. The next heavy element, number 119, is still hypothetical, and the name Ununennium is thus preliminary. It is an unholy mixture of Greek and Latin numerical roots that fits the IUPAC rules. If ever synthesized, a unique name will be selected based on suggestions from the IUPAC members.

Documentation of conference contributions: posters

Currently, scientific achievements are mainly documented in journals or monographs. However, many important ideas and information are shared during congresses that often don't reach a wider audience. New and revolutionary discoveries are rarely presented in oral sessions; instead, they are published in peer-reviewed journals, and there is limited space for oral presentations during the conferences. To include more presentations or "food for thought", poster sessions are organized. These often highlight new ideas and findings that authors want to discuss, and this makes poster sessions particularly interesting and important. Traditionally, posters were only sheets mounted on-site, but now they are produced in PowerPoint or PDF formats, which raises the question: Why do physical posters at all?

The first time I experienced a digital posters' exhibition was at the Labquality Days in Helsinki in 2023. Instead of physical posters, those accepted were displayed on several large screens. The posters were constantly visible, and the audience could call them up one by one. The authors stood nearby. It was certainly not the first-time posters were digitized at conferences, and it will become increasingly established.

Posters have often been short-lived, like dragonflies, and have never appeared outside the conference (unless displayed locally at the original laboratory) or in people's CVs.

Posters have usually not been particularly encouraged, appreciated or taken seriously by the scientific community. I am of another opinion. I believe that posters are valuable channels for presenting new ideas and discussion of projects that may not yet be sufficiently developed for formal publication. The digitized format invites information exchange with the authors, even after the poster session is closed.

The Diskussionforum project

The Diskussionsforum decided to give congresses the opportunity to share posters with all followers, not just the congress participants, and to ensure that the posters are archived on a suitable homepage. This allows readers to review and consider the message at their own pace. The proposed plan involves circulating a table of contents, the original abstracts sent to the scientific committee, and a link to a repository of the actual posters on a stable homepage where they can be accessed.

We have completed some poster projects, e.g., the Vilnius EFLM congress in 2024, (https://llmd.lt/lt/renginys/xvii-baltijos-saliu-laboratorines-medicinos-kongresas) the Labquality days in 2025 and 2026 and the SFKK congress in Eskilstuna in 2025 (https://www.dropbox.com/scl/fo/69zgtetgbsan82avsuq2s/APKQgoj_Fl8P3QFKPYDuDwY?rlkey=hgx0dc-9nhoylhb0uztiy699uo&dl=0). We are negotiating upcoming congresses in Denmark and Norway.

Diskussionsforum has about 700 followers in the Nordic and Baltic countries; the scheme would thus provide considerable exposure of the laboratories' interests, research, and development. It is our hope that it will also stimulate the submission of more posters and higher-quality posters.

Diskussionsforum aspires to be the collective memory and mind of clinical chemistry – a forum and marketplace for exchanging ideas. We take this opportunity to encourage all of you to look your colleagues in their eyes and ask, "Have you joined Diskussionsforum – yet?". There are simple application forms on the national societies' homepages and on the NFKK homepage. You can also write directly to me, anders.kallner@ki.se.

Oväntat låga folatvärden med Roche Folate III-metod

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Serum/plasma folat analyserat med Roche Folate III-metod har under en period uppvisat anmärkningsvärt låga folatnivåer. Förhoppningen är dock att detta åtgärdats under oktober 2025.

Folatbrist är kliniskt betydelsefull och kan leda till megaloblastanemi och neuropatier. Serumfolatanalys är därför en vanlig laboratorieundersökning i Sverige och andra europeiska länder som inte har någon obligatorisk folsyraberikning. I icke-berikade populationer, såsom den svenska, är flera grupper – till exempel äldre, patienter med malabsorption, anemi, graviditet eller antiepileptisk behandling – särskilt utsatta för folatbrist, med en uppskattad prevalens på 8–25 %. Därför är riktad folatanalys motiverad [1]. Inget av de nordiska länderna har ännu infört obligatorisk folsyraberikning, till skillnad från t.ex. USA, Kanada och Australien, där detta sedan länge har minskat förekomsten av neuralrörsdefekter. I motsats till de svenska förhållandena har folatbrist i länder med folsyraberikning, exempelvis Nordamerika, minskat till 0,1–1 %, vilket gjort rutinmässig screening med serumfolatanalyser mindre kostnadseffektiv [1,2].

Roche Diagnostics Elecsys® Folate III-analys används på många kliniskt kemiska laboratorier. År 2016 restandardiserades metoden mot WHO:s internationella standard (NIBSC 03/178), vilket ledde till lägre patientresultat [3]. Tillverkaren angav en minskning på cirka –20 % och upp till –50 % vid lägre koncentrationer. Flera oberoende studier har rapporterat ännu lägre nivåer och visat på att Roche:s reviderade nedre referensgräns (från 10,4 nmol/L till 8,8 nmol/L) inte fullt ut kompenserar för den observerade sänkningen [4,5]. Senare studier har också visat en negativ bias på –8,3 % jämfört med WHO-standarden, trots uppgiven spårbarhet [6].

Folate III-analysen används på Cobas e 801-instrument i både Region Stockholm och Region Uppsala. I oktober 2023 introducerade Roche en ny version med förbättrad biotin-tolerans för att minska interferens från biotin-rika patientprover [7]. Verifiering med patientprover visade ingen signifikant bias i Stockholm, men en genomsnittlig negativ bias på –9 % i Uppsala. Liknande resultat rapporterades även av andra svenska laboratorier och inom Equalis externa kvalitetssäkring (EQA) för folat. Roche har informerats om dessa observationer.

Implementeringen av den nya metoden skedde vid olika tidpunkter: mars–april 2024 i Stockholm och oktober 2024 i Uppsala. Kort därefter kom kommentarer om oväntat låga patientresultat och fler värden under den nedre referensgränsen (NRG). För att utreda detta analyserades trender i patientmedelvärden. Medianvärden från laboratoriedatasystemet (LIS) ger ett robust verktyg för metodövervakning och kompletterar traditionell kvalitetskontroll (QC) [8].

Vid början av 2023 låg medianvärdena för serumfolat kring 16,6 nmol/L i båda regionerna. Därefter noterades en successiv nedgång, först i Stockholm och senare i Uppsala – i takt med att den nya versionen infördes. I oktober 2024 var medianen cirka 13,5 nmol/L, motsvarande en minskning med 19 % jämfört med början av 2023, vilket överstiger den verifierade –9 % biasen. Detta tyder på att en ytterligare kalibreringsförskjutning kan ha inträffat.

Andelen provresultat under nuvarande nedre referensintervallsgräns (7,0 nmol/L) ökade från 4 % till nästan 15 %. Om Roche:s föreslagna gräns 8,8 nmol/L används, skulle motsvarande andel stiga till cirka 25 %. Denna utveckling speglar inte en verklig ökning av folatbrist, utan hur prevalensuppskattningar påverkas av val av referensgräns och kalibrering.

Skillnaden mellan analysens kalibrering och Roche rekommenderade nedre referensintervallsgräns, som först uppmärksammades efter restandardiseringen 2016 [4], förefaller nu ha ökat. Detta leder till att fler

patienter klassificeras som folatbristiga. Tillverkaren bör därför antingen justera kalibreringen eller revidera referensintervallet. Metoden bör kalibreras i enlighet med WHO:s internationella standard. I avvaktan på detta kan laboratorier behöva överväga att anpassa sina egna referensgränser.

Nyligen gjorde Roche en rekalibrering av Folatmetoden som skall ha medfört högre Folatvärden vilket då bör förbättra överensstämmelsen mellan referensintervallsgränser och kalibreringen av metoden.

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Summary of an evaluation organised by SKUP

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Elisabet Eriksson Boija, on behalf of Scandinavian evaluation of laboratory equipment for point of care testing (SKUP)
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Figure 1.
Capitainer B sampling card.

Capitainer B

A sampling card for self-sampling of capillary blood. Performance evaluated by measurement of haemoglobin A1c (HbA1c).

Background

Capitainer B is a sampling card (figure 1) for the collection of a volumetrically defined dried blood sample. The product is intended for use by health care personnel and lay persons. The capillary blood samples can be collected both in and outside of clinical settings with Capitainer B by the intended users and subsequently transported to a laboratory via regular mail, where measurement of numerous measurands is possible. For this evaluation, SKUP and the manufacturer agreed to use HbA1c as the measurand to assess the analytical performance of the capillary blood samples collected with Capitainer B.

The Capitainer B sampling card was launched on the Scandinavian market in February 2020. A SKUP evaluation was carried out in 2024 at the request of Capitainer AB in Sweden. After the completion of this evaluation, the manufacturer made changes to the pre-analytical procedure and shortened the recommended stability time of the Capitainer B sampling card from 14 to 5 days after sampling, in response to poor accuracy. These modifications led to a second evaluation.

The aim of the evaluation

The aim of the evaluation was to assess the analytical performance of Capitainer B for the measurement of HbA1c, when sample collection was performed by intended users; health care personnel and lay persons, and to assess the user-friendliness of both sample collection and pre-analytical procedures. The measurements of HbA1c were performed by biomedical laboratory scientists (BLSs) at a hospital laboratory.

Materials and methods

In the first evaluation, 113 participants were recruited at a hospital laboratory, and 92 participants were recruited from primary health care centres (PHCCs). In the second evaluation, only the self-sampling part by lay persons was performed, and 115 participants were recruited from PHCCs. Duplicate samples were collected by healthcare personnel at the hospital laboratory, while participants at the PHCCs performed duplicate sample collections themselves. The Capitainer B sampling cards were sent via regular mail to the hospital laboratory, where the blood was extracted, eluted and haemolysed followed by measurement of HbA1c on Roche cobas pro c 503 (Roche Diagnostics), using the Tina-quant hemolysate application (application code number (ACN) 851). These results were compared to HbA1c results from venous EDTA-samples collected from the same participants, measured on the comparison method Tina-quant on cobas pro c 503 whole blood application (ACN 881).

The analytical results and user-friendliness were assessed according to pre-set performance specifications for HbA1c. The analytical performance specification (APS) for precision was a repeatability (coefficient of variation, CV) of ≤3,0 %, and for accuracy, that at least 95 % of the results should be within ±3,0 mmol/mol of the results from the comparison method at HbA1c concentrations <35,3 mmol/mol and within ±8,5 % at HbA1c concentrations ≥35,3 mmol/mol.

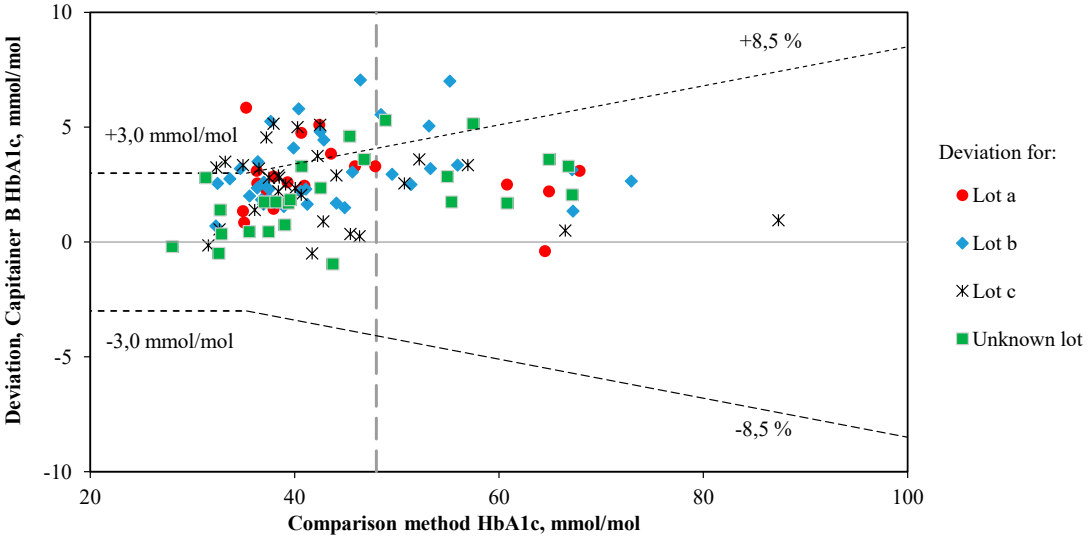

Figure 2. *Accuracy of HbA1c results from Capitainer B samples when the samples were collected by health care personnel in the first evaluation. The x-axis represents the mean HbA1c result of the comparison method. The y-axis represents the HbA1c deviation of a single Capitainer B sample measurement from the mean result of the corresponding sample of the comparison method. The vertical line at 48 mmol/mol HbA1c illustrates the diagnostic threshold value for diabetes. The different lots of Capitainer B are illustrated with the symbols ● (Lot a), ♦ (Lot b), ✳ (Lot c) and ■ (Unknown lot, i.e., a, b or c). Stippled lines represent the allowable deviation limits according to the APS. Number of results (n) = 111.*

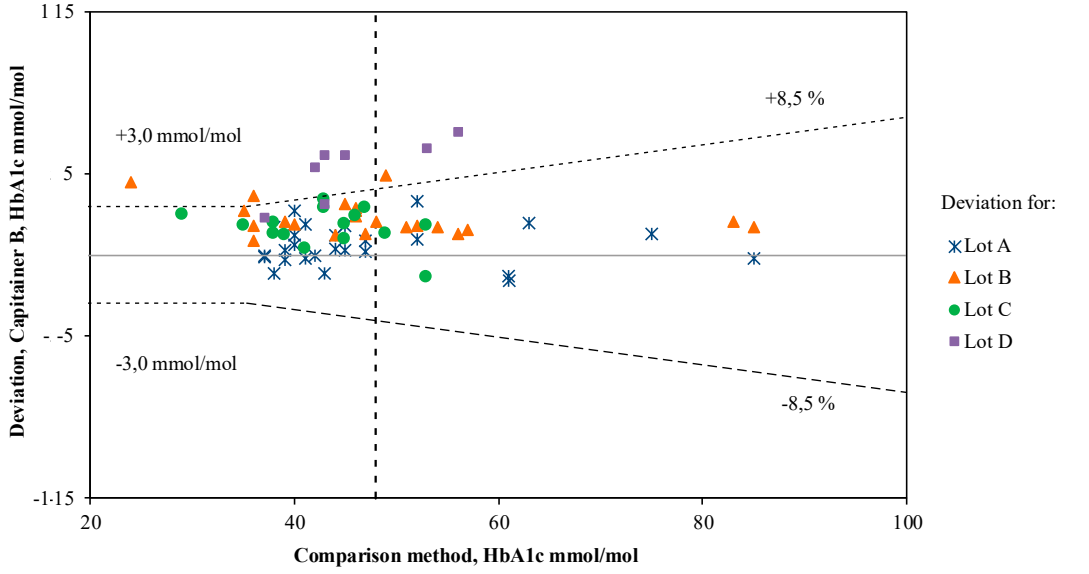

Figure 3. *Accuracy of HbA1c results from Capitainer B samples when the samples were collected by lay persons in the second evaluation. The x-axis represents the HbA1c result of the comparison method. The y-axis represents the HbA1c deviation of the first Capitainer B sample measurement from the result of the corresponding sample of the comparison method. The vertical line at 48 mmol/mol HbA1c illustrates the diagnostic threshold value for diabetes. The different lots of Capitainer B are illustrated with the symbols ✳ (Lot A), ▲ (Lot B), ● (Lot C) and ■ (Lot D). Stippled lines represent the allowable deviation limits according to the APS. Number of results (n) = 70.*

The user-friendliness was assessed using two questionnaires: one for sample collection (lay persons), and one for extraction and elution of samples (laboratory personnel). Three ratings were used: satisfactory, intermediate and unsatisfactory. To achieve the overall rating "satisfactory", the tested equipment had to receive a total rating of "satisfactory" in all subareas.

Results

The repeatability achieved when samples were collected by health care personnel at a hospital laboratory was a CV between 1,4 and 2,8 % (table 1). The repeatability achieved when samples were collected by lay persons at PHCCs was a CV between 1,5 and 2,0 % in the first evaluation (not shown) and 0,8 and 1,3 % in the second evaluation (table 2). When samples were collected by health care personnel the accuracy was 74 % (figure 2). When samples were collected by lay persons the accuracy was 27 % in the first evaluation (not shown) and 89 % in the second evaluation, following the introduction of a new preanalytical procedure and shortened stability time (figure 3). Overall, the user-friendliness of the Capitainer B for both the sample collection and the pre-analytical procedures before measurement was rated satisfactory by the lay persons and the laboratory personnel, respectively. However, some intermediate and unsatisfactory ratings were also reported.

Conclusion

The APS for repeatability was fulfilled both when samples were collected by health care personnel and by lay persons. The APS for accuracy was not fulfilled by either party. However, the accuracy clearly improved after the manufacturer introduced changes to the pre-analytical procedure and shortened the recommended stability time. The performance specification for user-friendliness was fulfilled.

The complete evaluation report as well as summaries in Danish, Norwegian and Swedish is available at www.skup.org.

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Table 1. *Repeatability (CV) of Capitainer B samples measured for HbA1c. Results achieved when the samples were collected by health care personnel in the first evaluation.*

Level	n*	Excluded results (statistical outliers)	Mean value HbA1c, mmol/mol	CV (90 % CI), %
1	24	1**	35,6	2,8 (2,3 – 3,8)
2	66	0	45,1	2,5 (2,2 – 2,9)
3	16	1**	67,6	1,4 (1,0 – 2,0)

** The given number of results (n) were counted before the exclusion of statistical outliers. Mean and CV were calculated after the exclusion of statistical outliers.*
*** Two samples were statistical outliers according to Burnett's model [1] and therefore excluded.*

Table 2. *Repeatability (CV) of Capitainer B samples measured for HbA1c. Results achieved when the samples were collected by lay persons in PHCCs in the second evaluation.*

Level	n*	Excluded results (statistical outliers)	Mean value HbA1c, mmol/mol	CV (90% CI), %
1	11	0	36,2	1,3 (1,0 - 2,1)
2	39	1*	46,0	0,8 (0,6 - 0,9)
3	8	0	69,6	1,0 (0,7 - 1,7)

** The given number of results (n) were counted before the exclusion of statistical outliers. Mean and CV were calculated after the exclusion of statistical outliers.*
*** One sample was a statistical outlier according to Burnett's model [1] and therefore excluded.*

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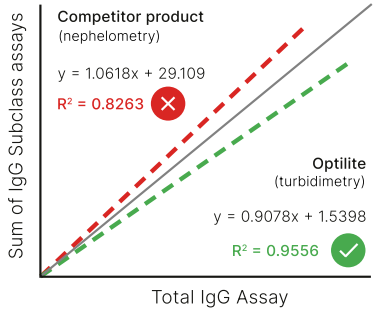

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Journal article with more than three authors:

2. Fiechtner M, Ramp J, England B, et al. Affinity binding assay of glycohemoglobin by two-dimensional centrifugation referenced to hemoglobin Alc. Clin Chem 1992;38:2372–9.

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Book chapter:

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Online source:

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See also NFKK's and KBN's homepage: www.nfkk.org

The Nordic Federation of Clinical Chemistry (NFKK)

NFKK's purpose is to promote the advancement of clinical chemistry, with a particular focus on Nordic collaboration in research, professional development and education. It comprises members from the national societies for clinical chemistry in Denmark, Finland, Iceland, Norway, and Sweden. The activities of NFKK are carried out through various project groups and working groups. The federation has scientific responsibility for the *Scandinavian Journal of Laboratory and Clinical Investigation (SJCLI)*, publishes *Klinisk Biokemi i Norden*, and organizes the Nordic Congresses in Clinical Chemistry together with the national societies – a key event for professionals in the region.

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