Evaluation of Medicine and Health (EVALMEDHELSE) 2023-2024

Self-assessment for research groups

Date of dispatch: **15. September 2023**
Deadline for submission: **31. January 2024**

Institution (name and short name): Stavanger University Hospital (SUH)
Administrative unit (name and short name): Department of cardiology (Cardio)
Research group (name and short name): Cardiology Research Group (CRG)
Date: 31.01.24
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Content

1. Organisation and strategy

1.1 Research group´s organisation

Describe the establishment and the development of the research group, including its leadership (e.g. centralised or distributed etc.), researcher roles (e.g. technical staff, PhD, post docs, junior positions, senior positions or other researcher positions), the group's role in researcher training, mobility and how research is organised (e.g. core funding organisation verSUH project based organisation etc.).

The Cardiology Research Group, headed by Professor **Alf Inge Larsen (AIL)** and affiliated with the University of Bergen - department of clinical science (UiB), is organized under the Department of Cardiology, which consists of an invasive operative cardiology unit and a clinical cardiology unit. The late **Leik Woie**, former head of the department of Cardiology, was instrumental in establishing research in the former *Central Hospital in Rogaland*, which in the 1980s did not have any university connection. He also founded *Hjertelaget*, a cardiovascular research institution - later renamed *Stavanger Health Research* (SHR). Four subgroups emerged during the early years. The four groups are led by 4 professors focusing on their special areas but with a broad in group interaction.

The group has had and has a considerable cooperation with SHR, where 4 dedicated research nurses are responsible for inclusion and administration of patients in clinical trials. This includes biochemistry, blood sample collection and biobanking. Moreover, there has been a considerable cooperation with the department of biochemistry, headed by PhD **Øyvind Skadberg.** In addition, an extended cooperation with the radiology department regarding research using MRI, CT and nuclear imaging modalities has been established. Finally, there has been a wide cooperation with the physiotherapists at SHR – Hjertelaget in several studies on exercise training in heart disease. This also benchmarked Exercise training (ET) as an intervention. The 2 professors **Kenneth Dickstein (KD)** and **Dennis W.T. Nilsen (DN)**, both affiliated with UiB, have retired from active positions at SUH (2017

and 2020) but are still actively publishing. In 2016, Stein Ørn was appointed professor II at the Dept. of Electrical Eng. and Comp. Science, University of Stavanger.

The four sub-groups are: (A to D)

A. Heart failure research - Kenneth Dickstein (KD) Alf Inge Larsen (AIL)

B. Myocardial infarction - Dennis Nilsen (DN), Stein Ørn (SØ), Alf Inge Larsen (AIL)

C. Exercise training in heart disease – Alf Inge Larsen

D. Response to endurance training in leisure athletes – Stein Ørn

Please also see 1.2. Research Groups Strategy and 2.1 Research Quality

Table 1. List of number of personnel by categories
Instructions: Please provide number of your personnel by categories.
For institutions in the higher education sector, please use the categories used in DBH, https://dbh.hkdir.no/datainnhold/kodeverk/stillingskoder. Please add new lines or delete lines which are not in use.

	Position by category	No. of researcher per category	Share of women per category (%)	No. of researchers who are part of multiple (other) research groups at the admin unit	No. of temporary positions
No. of Personnel by position	Professors	2	0		
	Associate Professors	2	0		
	PhD candidates	11	50%		11
	Research nurses at SHR	3	100%		
	Research nurses		Part time studies		4
	Physicians in clinical work with research integrated in daily work				4
	Retired professors still publishing	2			
	Post Doc (NEEDED)	1		1	

1.2 Research group´s strategy

a) Describe the research group's main goals, objectives and strategies to obtain these (e.g. funding, plans for recruitment, internationalization etc.) within the period 2012-2022.

Please see link to the SUH Cardiovascular Research Group homepage for more information, including a publication list of 400 articles since 2017, with 300 papers in the 5 years period from 2018 – 2022 and the NEEDED program.

Goals: The **general** strategy goals of the cardiovascular research group are to initiate and conduct research, participate in large Randomised Controlled Trials (RCTSs), expand a biological biobank, and

improve international cooperation to improve diagnostics and treatment for patients with cardiovascular disease.

To obtain these goals we seek to:

1) Continue the process of increased and integrated research in clinical work and to make all the professions familiar with this strategy. Every patient should have the opportunity to participate in a study. This will strengthen clinical work and is a prerequisite fundamental to a university hospital.
2) Improve the academic process by building a robust research group based on the physicians with academic affiliations and continuous PhD education with external funding. Improve the in-department research nurse and secretary support.
3) Continue the process of maintaining a high standard of research on an international level based on cooperation and personal exchange with large leading research institutions. CContinue and improve the process of building a ***general cardiological biobank***.
4) Improve the infrastructure with research instruments in or close to the cardiac catheterisation labs.
5) Ensure ***patient involvement***. This is now central, such as in the large national NOREX study. More than 500 patients are now included at SUH in this study.
6) Use ***established registries,*** such as the Norwegian Registry for Invasive cardiology NORIC (Norwegian Registry of Invasive Cardiology (NORIC) (helsedata.no) to perform research.

Clinical main goals

A) **Heart Failure** To characterise patients with heart failure and to reveal treatment options from drug therapy via device therapy to lifestyle interventions such as exercise training. To set up and lead large international studies like the European CRT Survey I and II. To investigate biological mechanisms associated with improvement after intervention – skeletal muscle analyses with assessment of gene expression, nuclear imaging assessment of cardiac neuronal function etc
B) **Myocardial Infarction** To assess strategies for reducing the burden of myocardial infarction in the population, assessing new methods for reducing myocardial injury and to reveal new biomarkers in myocardial infarction. Establishment of special biobanks and a general biobank. Participation in large international RCTs with clinical endpoints. Taking the national lead in large investigator initiated international RCTs like COMPLETE II. Development of new methods for determining myocardial injury and fibrosis employing probability mapping and machine learning to calculate an *Arrhythmical Risk Indicator*, which can predict arrhythmia. The methodology is being patented.
C) **Exercise Training in Heart Disease** Evaluation of training as a treatment option in all aspects of cardiovascular disease, both related to safety and efficacy. In addition, quality of life has been a part of this assessment in cooperation with nursing research at the University of Stavanger (UiS). There is a further focus on quality of life in the large CONCARD study originating from the University of Bergen (UiB) in which the group has a central position.
D) **NEEDED sports-cardiology** The main goal of the NEEDED cardiovascular research program is to develop tools for early diagnosis and monitoring of cardiac disease using biomarkers, sensors, and different imaging modalities to assess the cardiac response to physical stress. The aim is that these tools can be used by all individuals out of the hospital to optimize physical exercise, increasing the benefits and reducing the risk of adverse responses.

b) Please describe the benchmark of the research group. The benchmark for the research group should be written by the administrative unit in collaboration with the research group. The benchmark can be a reference to an academic level of performance (national or international) or to the group's contributions to other institutional or sectoral purposes.

The research strategy outlined above is in concordance with the general research strategy of SUH. The administrative unit expects the research group to conduct internationally recognised research on cardiovascular disease. Key benchmarks for success in the period 2012-2022 are:

Research Group and resources

1) Maintain the number of ongoing externally funded PhDs at approximately 8-10.
2) Prioritise PostDocs to enhance academic continuity following the retirement of academics at the professorial level.
3) Improve the existing research collaborations based partially on MOUs with leading international institutions. This might pave the way for international research fellowships.

Scientific

1) Increase and improve the use of international established bio banks for bio marker analyses in heart failure and acute coronary syndromes.
2) Maintain a high publication, aiming for between 40 and 60 PubMed citations annually.
3) Aim to have at least 1-2 ongoing clinical project in the department initiated by the research group.
4) Take the lead in international RCTs seeking collaboration in Norway.

Guidelines participation

1) Be nominated to take part in the formation of new guidelines and perform research vital to address knowledge gaps identified in the guidelines.

Education

1) Actively contribute to education at all levels, presenting at a minimum of two international conferences and participating in higher education sector programs or initiatives such as PhD programs and local Good Clinical Practices (GCPs) etc. For specific contributions, please see 1.2 c.

Economy

1) Stabilize the number of externally funded PhDs, with a goal of having at least 6-8 ongoing.
2) Improve external funding for local projects and PostDocs.
3) Participate in large NRC and EU projects continuously.

User Involvement

1) Improve user involvement in all kinds of studies and projects locally and externally.

c) Describe the research group`s contribution to education (master´s degree and/or PhD).

Medical Student Education The department has been involved in medical student education in cooperation with UiB since 1999. Until 2017, 5 professors from the research group had a formal connection to the Medical Faculty at the UiB. Kenneth Dickstein oversaw the decentralized education of these students at SUH for many years since the beginning. In addition, Dennis Nilsen, also with a professor affiliation, was central in developing the new educational medical student program at the faculty of Medicine at UiB. Currently Alf Inge Larsen has a prof II appointment with UiB, in addition to Tor Melberg and Kjetil Isaksen, who both are part time employed as associate professors II.

PhD program The group has an extensive PhD program. Research is regularly presented at national and international conferences. The department has 10 cardiologists with a PhD. Over the last 10 years, there has been 11 dissertations associated with the department. Currently the department has 13 externally funded PhD fellows, mostly in a 50% research/50% clinical work arrangement with main supervision from the department. Three dissertations will be held in fall 2024.

Nursing. In addition, members of the group have been involved in the master's and PhD degrees for nurses in the department.

d) Describe the support the host institution provides to the research group (i.e., research infrastructure, access to databases, administrative support etc.).

Our research group benefits from a range of support services provided by the administrative unit, which are essential to our ability to conduct high-quality research. The support includes:

1) **Clinical Research Unit**
    a. Providing infrastructure for collecting processing and storage of biological samples.
    b. Clinical trial and patient administration support from the dedicated research nurses are essential for our research. This is partly paid via external funding, but the host institution administers the activity and gives additional financial support.
2) **Biobanking Services**: Provision of infrastructure and support for biobanking of samples from the group's research projects.
3) **Grant Application Support**: Continuous offer of support and guidance in the application process for external funding.
4) **Medical Statistics**: Advice and active involvement in analyses. Courses in fundamental and advanced statistics.
5) **Training in Good clinical practice (GCP)**: Access to mandatory training in GCP to ensure ethical and quality clinical research practices.
6) **Legal guidance:** The host institution supports administrative and legal advice.
7) **Internationalization:** The host institution has also arranged several study trips to important centres for signing of a of understanding (MOUs) which have been fundamental to further international cooperation in clinical cardiology and in research. This includes MOUs with Aalborg University Hospital DK, Kings College UK and Herrmann Memorial Hospital/University of Texas, US. The large international studies that the research group are involved in are also instrumental to increased internationalization and cooperation. Personal interactions with leading stakeholders in the field improves research quality and magnitude in addition to improving clinical work.
8) **New methods** are evaluated in studies for later implementation in clinical work. The establishment of interventional cardiology, which was fundamental to the PhD of Tor Melberg, is such an example. This was further extended in several international studies on primary PCI in acute myocardial infarction, paving the way for new directions and serving as references in guidelines.

1.3 Relevance to the institutions

Describe the role of the research group within the administrative unit. Consider the research group's contribution towards the institutional strategies and objectives and relate the research group`s benchmark to these.

National and international cooperations and contributions:

1) The research group has represented the administrative unit in several positions internationally, for example, the European Society of cardiology (ESC), both in the leadership (presidency), guideline committees and elsewhere, such as in the formation of international web sites for patients with heart failure: Heart Failure Information for Patients & Caregivers (heartfailurematters.org)
2) Participation in large international studies relevant to new European guidelines in the field of coronary heart disease and heart failure (Prospect II trial, FAME III, Complete II and European CRT surveys.) In most of these SUH has a central role as national PI or sole national centre (FAME III - NEJM 2021).
3) Participation in large multi-site national studies funded partially by RCN.
4) Nationally the research group has been active in the **Norwegian Society of Cardiology**. From this position we have been central in large **Nordic Baltic scientific conferences** and **national meetings.**
    a. The annual meeting of the **Norwegian Society of Cardiology** (NCS) was arranged by the group in 2006, 2016 and 2022 in Stavanger. (AIL board member 2003-2013).

b. Advisory board of several large national mandatory registries and organizations., including the Norwegian Registry of Invasive Cardiology (NORIC) (helsedata.no), Norwegian Cardiac Arrest Registry (NorCAR) (helsedata.no) (AIL) and Norwegian Health Association | Alzheimer Europe (alzheimer-europe.org) (SØ, AIL). KD received the national award in 2016.

5) Additionally, the group has cooperations with several large research groups internationally and nationally. These include Columbia University (Prof. Gregg Stone). HORIZONS trail and PROSPECT II, TIMI-group, Boston (Prof. David Morrow), Duke University (Dr. Pierlugi Tricoci), University of South Dakota (Prof. Bill Harris), University of Maastricht (Prof. Hugo ten Cate), University of Texas (Prof Gould(Johnson/Smalling), University of Calgary (Prof Anderson), Stanford University (Prof Fallon), Eindhoven (Prof Pijls), Lund University (Prof Erlinge), University of Bergen (Prof. Ottar Nygård), WenBit, WESTCOR, NTNU (Prof. Kåre Bønaa/Wiseth), NORSTENT, NOREX and University of Oslo (Prof. Pål Aukrust and Prof. Thor Ueland) etc.
6) Finally, the group is central to the evaluation of new international guidelines before the approval of the Norwegian Society of Cardiology. (Vernon Bonarjee as leader of "Kvalitetsrådet" in NCS).

The Research Group and Resources

- Through proactive efforts in seeking funding opportunities, we have successfully increased the number of project-based PhD positions from 6 in 2011 to 12 in 2023, contributing to the administrative unit's goal to increase the number of PhD positions.
- We have secured funding to bring state of the art equipment to SUH through well paid studies and applications to central authorities. Several of studies are on a national level, like the NOREX study (NTNU), The SMASH (AHUS/UIO) study and the Concard (UIB) study, in which SUH has central roles and have partly been funded by the RCN. Several PhD positions have been possible though grants from the Western Regional Health Authority. The group was fortunate to get PhD stipends in 2018, 2019, 2021, 2023 and 2024. In addition, a PhD grant was obtained from local industry in Rogaland.

Scientific

- Aligning with the administrative unit's benchmark for quality publication, the active collaborations and extended partnerships as described above have been fundamental to the increase in publications; 300 in the period 2018-2022 (25% in level 2 journals), and 400 from 2017-2023. Most of these are in close cooperation with international high standard environments.
- We have continued international cooperation and have been national PI for several large RCT/Registries like the European CRT registry I and II (KD), the large FAME III trial and the Complete II trial (AIL) etc.
- We have contributed to the administrative unit's goal to increase research-based innovation by establishing new research using a novel method to evaluate coronary flow alterations after a period of training.
- We have arranged the scientific meetings of the Norwegian Society of cardiology in 2006, 2016 and 2022.

Education

- We actively contribute to all levels of education, spanning clinical and university settings. This includes medical student education for UiB students now doing their full clinical education at SUH via Vestlandslegen project. 24 Phds have been facilitated by the group over the last 30 years. 12 candidates are now in process with external funding.
- In line with the unit's expectations, the number of employees with professor competence is 2, but there are 2 associate professors in the group associated with UiB.

- Several projects have been set up to facilitate the master thesis of nurses; please see above 1.2c.
- The European core curriculum for invasive cardiological nurses is translated and implemented at SUH. We have also presented this on national meetings (nurse Mette Skadberg).

Economic

- We have 12 ongoing PhDs funded by external resources, with 5 from the Western Norway Regional Health Authority. Nine of these are under full supervision from the group whereas 3 are in cooperation with external institutions.
- We are currently engaged in 4 large research trials funded by the RCN and several EU studies over the evaluation period. However, there are no ongoing EU studies at present.
- One of the large national RCTs is the NOREX study conducted from NTNU. SUH is in the steering committee and have included 500 patients. In a sub study of this trial, we are evaluating physiological mechanisms including coronary flow measurement employing a novel invasive method.

User Involvement

- We have maintained active engagement with the *Norwegian Health Association* and secured their direct involvement in new patient centred research projects.

1.4 Research group´s resources

Describe the funding portfolio of the research group for the last five years (2018-2022).

Alf Inge Larsen has a part time 20% professorship at the Department of Clinical Science, Faculty of Medicine, UiB and SUH provides additional 20% research time. Tor Melberg (TM) and Kjetil Isaksen (KI) have associate professorships at the same faculty (20%). In addition, Stein Ørn has a position at UiS. Currently 12 PhD candidates are affiliated with the department. The PhD candidates HH, CS, ER, VF have 50% *research funding* from the *Western Norway Health Trust*. SHR provides administration and research nurse work funded by external investigator-initiated studies (IIS). Nurses in the department of invasive cardiology are also funded part time by external resources associated with IIS. Research activities are presented and coordinated during research meetings and continuous internal communications. Funding is mainly provided by external sources, based on grants and project applications. The group is engaged in 4 national RCTs partly funded by RCN (PRADA II, BETAMI, NOREX, SMASH II)

The research group's activities are funded by 2 main sources:

1. Basic funding of permanent research positions (including technical/administrative staff) by Stavanger University Hospital. (Stavanger Health Research, study nurses, statisticians)
2. Project-based external funding from the private and public sector. Mostly Western Norway Health Authority but also RCN in the large national CRTs named above in addition to EU studies.

Table 2. Describe the sources of R&D funding for the research group in the period 2018-

	2018 (NOK)	2019 (NOK)	2020 (NOK)	2021 (NOK)	2022 (NOK)
Basic funding	500 000	500 000	500 000	500 000	500 000
Funding from industry and other private sector sources	5 000 000	5 000 000	5 000 000	5000 000	5000 000
Commissioned research for public sector	0	0	0	0	0
Research Council of Norway	500 000	500 000	500 000	500 000	500 000
Grant funding from other national Sources	1 000 000	600 000	2000 000	4500 000	3600 000

International funding e.g. NIH, NSF, EU framework programmes					
Other Belønningsmidler helsevest					150 000

1.5 Research group´s infrastructures

Research infrastructures are facilities that provide resources and services for the research communities to conduct research and foster innovation in their fields. These include major equipment or sets of instruments, knowledge-related facilities such as collections, archives or scientific data infrastructures, computing systems communication networks. Include both internal and external infrastructures.

a) Describe which national infrastructures the research group manages or co-manages.

a. The Norwegian Society of Cardiology (escardio.org) is affiliated with the European Society of Cardiology. The group has been represented in the board for many years, implying the arrangement of national and international scientific congresses and the establishment of national and international research collaborations. The SUH CRG also hosted the annual meetings in 2006, 2026 and 2022. The group has been represented in the leadership of ESC for many years in this period.
b. Norwegian Registry of Invasive Cardiology (NORIC) (helsedata.no). The group is represented in the advisory board. All cardiological invasive procedures have to be registered in this registry which is a part of the About the Norwegian Cardiovascular Disease Registry - NIPH (fhi.no) . This is owned by the Norwegian Institute of Public Health - NIPH (fhi.no). Data collection started in 2012. The registry makes it possible to assess treatment strategies for patients with coronary artery disease and aortic stenosis. Furthermore, demographics and mortality might be assessed.
c. Norwegian Cardiac Arrest Registry (NorCAR) (helsedata.no). The group is also represented in the advisory board of this registry that is fundamental to understanding the treatment and prognosis in sudden cardiac arrest. We are currently in the process of combining data from NORIC and NorCAR with SUH CRG as PI.
d. Norwegian Myocardial Infarction Registry (NORMI) (helsedata.no); fundamental to the NOREX study [Norwegian]
e. Norwegian Health Association | Alzheimer Europe (alzheimer-europe.org)

b) Describe the most important research infrastructures used by the research group**.**

The research group actively utilises a range of research infrastructure, including internal technical hospital facilities, Clinical Research Unit and biobank infrastructure. Locally, collaborative lab facilities at both the hospital and the University of Stavanger are available. Noteworthy is the partnership with "Hjertelaget Physiotherapy," serving as an exercise training site vital for cardiovascular disease studies. Internationally, collaborations extend to renowned institutions such as Kings College, Mount Sinai US, and Eindhoven accessing various assessments, from myocardial contractile biomarkers to plaque burden and new methods for coronary flow measurements. Additionally, our research benefits from data processing platforms and networks, including NorCRIN, a collaboration involving all six university hospitals in Norway.

1.6 Research group´s cooperations

Table 3. Reflect on the current interactions of the research group with other disciplines, non-academic stakeholders and the potential importance of these for the research (e.g. informing research questions, access to competence, data and infrastructure, broadening the perspectives, short/long-term relations).

Interdisciplinary (within and beyond the group)	Interdisciplinary cooperation aims to facilitate the continuous improvement of the group. This includes cooperation between subgroups of the CRG. Other intra-organisational collaborations at SUH includes the radiology department for MRI, CT and nuclear imaging, as well as academic collaborations in PhD theses. Finally, in managing extensive research datasets, collaboration with biostatisticians is crucial. External collaborations include national partners like the University of Oslo (UiO) for studies on inflammatory markers in cardiovascular disease and UiT The Arctic University of Norway for studies on skeletal muscle metabolism. International examples include Kings College UK and UiO for studies on contractile proteins, and The Cardiovascular Center of Salta and Universidad Catolica de Salta, Argentina, in conjunction with The Institute of Internal Medicine, UiB, for studying differences in biomarkers related to coronary artery disease between an inland and a coastal population.
Collaboration with other research sectors e.g. higher education, research institutes, health trusts and industry.	The group has had a long lasting relationship with the Dept. of Electrical Eng. and Comp. Science and the Department of Caring and Ethics, Faculty of Health Sciences, UiS. Moreover, the collaboration between the group and Nordsjørittet has been essential to the NEEDED study. Industrial cooperation, for example with MEDOX, has been fundamental in studies on the effect of anthocyanins in cardiovascular disease. In the NEEDED CV research program, new systems for non-invasive imaging determination of myocardial function have been developed using Echocardiography. Norway has, therefore, supported the program.
Transdisciplinary (including non academic stakeholders) *Transdisciplinary research involves the integration of knowledge from different science disciplines and (non-academic) stakeholder communities with the aim to help address complex societal challenges.*	Both the MRI in myocardial infarction and the coronary flow research programs have tight connections with UiS to develop mathematical models of myocardial texture for risk prediction and calculation of Myocardial Flow Velocity, which is essential in research on microvascular function. There has also been a close cooperation UiS on master and PhD theses for nurses focusing on quality of life and vulnerability. The collaboration between the NEEDED research group and the Nordsjørittet – "North Sea Bike Race" - has been essential to the early phase of the NEEDED CV research program. Identifying the increased risk of cardiac events is a major issue for physical exercise, also in workers on North Sea Oil platforms. Therefore, a cooperation with oil companies has been essential. Finally, Olympiatoppen and Rogaland Idrettskrets have been involved in the latest part of the program (NEEDED TopAthletic). Due to the potential impact on national health, LHL (Landsforeningen for Hjerte-Lungesyke) has been involved in the program.

2. Research quality

2.1 Research group's scientific quality

Describe the research profile of the research group and the activities that contribute to the research group´s scientific quality. Consider how the research group's work contributes to the wider research within the research group's field nationally and internationally.

The four sub-groups are: **(A to D)**

A. Heart failure research - Kenneth Dickstein (KD) – PhD – dr.med – 1991 UiB extended the work of Leik Woie, forming a subgroup of heart failure research fundamental to European studies on drug therapy. He led several large pharmacological studies like The OPTIMAAL trial: losartan or captopril after acute myocardial infarction. He extended his heart failure research into device research (pacemakers for heart failure) and was the founding power for the European CRT registries I and II Cardiac Resynchronisation Therapy Survey II. He was also president of the European Heart Failure Association administered under the European Heart Association. KD was central in the large BIOSTAT database BIOSTAT-CHF European Commission and is a coauthor of several central publications based on this database. Additionally, he was central in the development of the Heart Failure Information for Patients & Caregivers. KD (several times) and Stein Ørn (SØ 2012) have been coauthors of ESC Heart failure Guidelines. In addition, KD has been involved in the ESC guidelines. KD has been the main supervisor for 5 PhD candidates. He has been named among the most cited researchers in the world.

B. Myocardial Infarction - Dennis Nilsen (DN) retired in 2022 was responsible for parts of the new medical student program at UiB. He developed a research cooperation with Argentina in partnership with the former director of research at SUH Stein Tore Nilsen and Leik Woie. 3 PhDs were associated with this program. His focus has been inflammatory-, endothelial- and coagulation-markers, as well as the effect of fatty acids and antioxidants on outcome. He also established robust cooperations with international leading scientists including Mount Sinai - HORIZONS trial (Bivalirudin during Primary PCI in Acute Myocardial Infarction – and the TIMI group as national coordinator and member of the steering committee of TRA2P-TIMI 50. He has been main supervisor for in total 8 PhD candidates 2004 to 2022.

Stein Ørn is in the lead of a research program aiming to develop new tools for the assessment of myocardial injury using texture-based assessment MRI imaging and machine learning to predict future arrhythmic events. One candidate is basing his PhD on this work.

Alf Inge Larsen (AIL) has been involved in the ESC guidelines for myocardial infarction. Further the group has focused on research on treatment effects of high dose statins in ST elevation myocardial infarction (AIL) and effect of blocking the mitochondrial permeability transition pore in the MITOCARE study EU-FP7 grant, MITOCARE Study Group (AIL). In addition the group participated in the Large PROSPECT TRIAL originating from Colombia University NY and Lund SE which evaluated plaque morphology in patients admitted for myocardial infarction (AIL, LANCET): Percutaneous Coronary Intervention for Vulnerable Coronary Atherosclerotic Plaque. Finally, the group (AIL) is national leader for the large COMPLETE II myocardial infarction study originating from Canadian Institutes of Health Research/McMaster University/Hamilton Health Science (CANADA) COMPLETE-2. Nationally the group (AIL) has been active in the BETAMI study evaluating the use of beta blockers after myocardial infarction.

C. Exercise training in heart disease – Alf Inge Larsen (AIL) dr.med UiB 2004 established tight relationships during his fellowship in interventional cardiology at the University of Calgary (2001-2) with leading scientists in the field. This includes Merrill Knutson who was a fellow of the PCI founding father Andreas Gruentzig in Atlanta. Moreover, there has been a close relationship to Todd Anderson who is central in endothelial function research. The research group has had several research trips to

central research institutions like Kings College UK, University of Texas US and Aalborg University Hospital DK, establishing memorandum of understanding cooperations (MOU). These cooperations arranged by the research department at SUH have been very helpful for further research, publication of invited editorials, and for cooperation for applications for funding. Six PhDs have been the result of research on functional capacity and effect of exercise training. We have been very active in large exercise training RCTs like the SMARTEX trial [Norwegian] (Alf Inge Larsen) on exercise training in heart failure (Circulation 2017). This study also is the basis for 2 PhDs in the group and the ongoing NOREX study [Norwegian] evaluating exercise training after myocardial infarction (AIL). Based on this, the group is now focusing on effects of exercise training on microvascular disease using new invasive methods for assessing absolute flow developed by our research partners in Eindhoven (Prof Nico Pijls). Three PhDs on this issue are funded from the Western health regional authority in addition, 1 PhD is funded by the same organisation to assess alterations of serum levels of contractile proteins in heart failure after exercise training using samples from the SMARTEX biobank. (Please see 1.2). AIL has been a main supervisor for 8 PhD candidates and part supervisor for 5 PhD candidates. (Exercise training in Heart Failure, In Patients with an ICD, in patients with stable coronary heart disease and in Microvascular coronary artery disease)

D. The NEEDED cardiovascular research program (NEEDED CVRP) aims to develop markers that can provide more precise recommendations for exercise intensity and duration at an individual level to optimize benefits and reduce the risk of cardiac events to physical exercise. The NEEDED CVRP is led and designed by Stein Ørn (SØ) and involves cooperation with national and international experts. One PhD candidate has completed her thesis, and four PhD candidates and one post-Doc is currently working in this program.

In general, The group has increased number of publications from 24 in 2011 to 77 in 2021 (Pubmed). 12 PhD dissertations in the period from 2013 to 2022. Internationally, several MOUs with subsequent research cooperations have been signed the last few years, e.g. Texas Medical Centre, Stanford University, Kings College and University of Calgary. This results in cooperation in clinical trials and in the scientific publication process including editorials in cooperation with leaders in the field. The group has a broad cooperations with several other leading centres in the field resulting in large exploratory databases like the BioStat cooperation. The group was also involved in the large NORSTENT trial evaluating bare metal stents and drug eluting stents in coronary artery disease. Finally, research is increasingly integrated in clinical work and as a natural part of the daily activity in the department.

Please add a link to the research group`s website: Research Group of Cardiology - Helse Stavanger HF (helse-stavanger.no)

Table 4. List of projects

Instructions: Please select 5-10 projects you consider to be representative/the best of the work in the period 1 January 2012 – 31 December 2022. The list may include projects lead by other institutions nationally or internationally. Please delete tables that are not used.

Project 1: **SMARTEX Heart Failure Study** 2009-2014	**Project owner(s)** (project leaders organisation)	Norwegian University of Science and Technology (CERG NTNU)
	Total budget and share allocated to research group	Several PhD stipends including 2 at SUH. CRG. 900 000 x 3 + 500 000 x 4 In addition to 25 mNOK from RCN
	Objectives and outcomes (planned or actual) **and link to website**	Study of Myocardial Recovery After Exercise Training in Heart Failure. Small studies have suggested that high-intensity interval training (HIIT) is superior to moderate continuous training (MCT) in reversing cardiac remodelling and increasing aerobic capacity in patients with heart failure with reduced ejection fraction. The present multicentre trial compared 12 weeks of supervised interventions of HIIT, MCT, or a recommendation of regular exercise (RRE). An improvement of left ventricular geometry was found with both interventions. Main publication: Ellingsen Ø et al, Circulation. 2017 Feb 28;135(9):839-849 **Websites:** SMARTEX-HF (ntnu.no) [Norwegian] and The SMARTEX HF Study (clinicaltrials.gov)
Project 2: **PROSPECT II trial** *2014-2020*	**Project owner(s)** (project leaders organisation)	D Erlinge, Lund SW and Gregg Stone NY, US
	Total budget and share allocated to research group	Abbott Vascular, Infraredx, and The Medicines Company. SUH (CRG) share: 420 000 NOK
	Objectives and outcomes (planned or actual) **and link to website**	Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (PROSPECT II). Still publishing. Combined Near Infra-Red Spectroscopy (NIRS) and intravascular ultrasound detects angiographically non-obstructive lesions with a high lipid content and large plaque burden that are associated for increased risk for future adverse cardiac outcomes. Main publications: (1) Erlinge D et al, Lancet. 2021 Mar 13;397(10278):985-995;

		(2) Gyldenkerne C et al., Circulation. 2023 Feb 7;147(6):469-481; **Websites:** PROSPECT II Study (infraredx.com) and PROSPECT II & PROSPECT ABSORB (clinicaltrials.gov)
Project 3: **MITOCARE EU study** 2011-2013	**Project owner(s)** (project leaders organisation)	EU study with SUH (AI Larsen) as partner
	Total budget and share allocated to research group	The MITOCARE project is supported by the EU-FP7 for RTD – Project MITOCARE (Grant Agreement No. HEALTH-2010-261034). One of the beneficiaries of this grant is Trophos SA, Marseille, France. 30 mNOK
	Objectives and outcomes (planned or actual) **and link to website**	This study in STEMI patients treated with contemporary mechanical revascularization principles did not show any effect of TRO40303 in limiting reperfusion injury of the ischaemic myocardium. Main publications: (1) Eur Heart J. 2015 Jan 7;36(2):112-9. doi: 10.1093; (2) Eur Heart J Acute Cardiovasc Care Year: 2020 DOI: 10.1177/2048872620923641 **Website:** https://www.clinicaltrialsregister.eu/ctr-search/search?query=2010-024616-33
Project 4: **SYNDEX study** 2014-2018	**Project owner(s)** (project leaders organisation)	AI Larsen, SUH
	Total budget and share allocated to research group	Local grants and 1 PhD funded by Western Norway Regional Health. Charlotte Sæland MD. 3MNOK.
	Objectives and outcomes (planned or actual) **and link to website**	In site designed and funded study on effect of structured exercise training on myocardial microvascular function. Effect of exercise training on microvascular function I patients with angina and no obstructive coronary disease. 5 papers published. A 3-month program of monitored high intensity training program was feasible, with high adherence resulting in improved functional capacity in patients with ANOCA. CFVR improved and this improvement was associated with improved endothelial function and quality of life.

		Main publications: (1) Eur Heart J Open. 2023 Mar 22;3(2):oead030. doi: 10.1093/ehjopen/oead030; (2) Front Cardiovasc Med. 2019 Jan 22;6:1. doi: 10.3389/fcvm.2019.00001; (3) J Clin Nurs. 2017 Jul;26(13-14):2006-2015. doi: 10.1111/jocn.13609. Epub 2017 Mar 20 Website: The Syndrome X-ercise Study SYNDEX (clinicaltrials.gov)
Project 5: **TRA2P-TIMI 50** 2007-2011	**Project owner(s)** (project leaders organisation)	DWTN National coordinator and member of the steering committee of TRA2P-TIMI 50 in collaboration with the TIMI group
	Total budget and share allocated to research group	Total budget: 50 mNOK (international funding, USA) SUH (CRG) share: 6,5 mNOK
	Objectives and outcomes (planned or actual) **and link to website**	Study describing the effects of Vorapaxar, a novel antiplatelet therapy. The study was designed to determine whether vorapaxar, when added to the existing standard of care (SOC) for preventing heart attack and stroke (eg, aspirin, clopidogrel) in participants with a known history of atherosclerosis, would yield additional benefit over the existing standard of care without vorapaxar in preventing heart attack and stroke. The study was also designed to assess risk of bleeding with vorapaxar added to the standard of care versus the standard of care alone. Main publication: J Am Coll Cardiol 2014 Dec 9;64(22):2318-26. Website: TRA 2°P-TIMI 50 - STUDY GROUP and TRA 2°P - TIMI 50 (clinicaltrials.gov)
Project 6: **BETAMI study** *2018 - 2034*	**Project owner(s)** (project leaders organisation)	Oslo University Hospital, local PI SUH/member of steering committee: AI Larsen was local PI
	Total budget and share allocated to research group	15 MNOK from KLINBEFORSK and 12 MNOK from RCN Dan Atar - Institutt for klinisk medisin - Det medisinske fakultet Tildelt 12 mNOK from RCN
	Objectives and outcomes (planned or actual) **and link to website**	BETAMI is a national study conducted at major hospitals in Norway. This study the aim to verify an existing treatment and is important to future patients. The results from the trial have

		potential to change current clinical practice for treatment with betablockers following acute myocardial infarction in patients without reduced left ventricular ejection fraction. Main publication: Am Heart J. 2019 Feb;208:37-46. doi: 10.1016/j.ahj.2018.10.005. **Website:** BETAMI study (betami.org) and BETAMI study (clinicaltrials.gov)
Project 7: **SMASH II study**	**Project owner(s)** (project leaders organisation)	AHUS and SUS Local PI SUH/steering committee: AI Larsen
	Total budget and share allocated to research group	25 MNOK from NRC and KLINBEFORSK
	Objectives and outcomes (planned or actual) **and link to website**	Scandinavian Multicenter study to Advance risk Stratification in Heart disease (SMASH). Contribution: Assessment of biomarkers for ventricular arrhythmias to establish new methods for early detection of a serious heart rhythm disorder. The aim is to study patients with implanted defibrillators (ICDs) to better understand the mechanisms of serious cardiac arrhythmia and to better find the patients at highest risk for future heart rhythm disturbance. Main publication: Clin Cardiol. 2023 Aug;46(8):989-996. doi: 10.1002/clc.24074. Epub 2023 Jul 3. Website: Smash Study - Study Progress (smash-study.com)
Project 8: **NEEDED** 2012 -	**Project owner(s)** (project leaders organisation)	Project leader Stein Ørn. The NEEDED research program is owned in collaboration with the Cardiology Department and the Research Department at Stavanger University Hospital.
	Total budget and share allocated to research group	25 MNOK (Current). So far, the yearly budget is 2,5 million NOK (combined public and private funding) The aim is to increase the budget and thereby increase the project activity
	Objectives and outcomes (planned or actual) **and link to website**	The NEEDED CVRP assessed cardiac risk to physical exercise in healthy middle-aged individuals and identified severe coronary artery disease in several participants despite the absence of symptoms using biomarkers and CT scans (2013-14). Subsequent studies used assessment of biomarkers, sensors and imaging tools to identify new patterns of hidden cardiac disease (2018) and to assess reproducibility and differences between healthy individuals and patients with established coronary artery disease (NEEDED diagnostic; 2022). NEEDED TopAthletic 2024 aimed

		to relate the biomarkers to physical exercise and potential cardiac risk in top athletes. In parallel, there is an analysis of collected data and in 2024 10-year data will provide the world's largest dataset to assess long-term risk of cardiac events with by the biomarker used by the NEEDED program. **Website:** NEEDED Research Programme - Helse Stavanger HF (helse-stavanger.no)
Project 9: **NORSTENT study** 2008-2015	**Project owner(s)** (project leaders organisation)	National multi-centre project, coordinated by University of Tromsø
	Total budget and share allocated to research group	Funded by the Norwegian Research Council, The Royal Norwegian Ministry of Health and the Norwegian Council on Cardiovascular diseases
	Objectives and outcomes (planned or actual) **and link to website**	In patients undergoing PCI, there were no significant differences between those receiving drug-eluting stents and those receiving bare-metal stents in the composite outcome of death from any cause and nonfatal spontaneous myocardial infarction. Rates of repeat revascularization were lower in the group receiving drug-eluting stents. Main publication: N Engl J Med 2016 Sep 29;375(13):1242-52 Webpage: NORSTENT - Study Details (clinicaltrials.gov)
Project 10: **European CRT survey I and II**	**Project owner(s)** (project leaders organisation)	The two ESC CRT surveys were investigator initiated and managed by researchers at SUH (Dickstein) in cooperation with the European Society of Cardiology and the data management centre, IHF, in Germany.
	Total budget and share allocated to research group	The work was supported by the European Heart Rhythm Association; the Heart Failure Association; Biotronik; Boston Scientific; Medtronic; Sorin; St. Jude; Abbott; Bayer; Bristol-Myers Squibb and Servier. Two PhDs were based on these initiatives.
	Objectives and outcomes (planned or actual) **and link to website**	CRT Survey II provides a valuable source of information on contemporary clinical practice with respect to CRT implantation in a large sample of ESC member states. The survey permits assessment of guideline adherence and demonstrates variations in patient selection, management, implantation procedure and follow-up strategy. The 2 surveys represent major international cooperation and collected information from 2,438 patients in 13 countries (CRT Survey I) and 11,088 patients in 42 countries. (CRT Survey II). Main publication: Eur J Heart Fail. 2018 Jun;20(6):1039-1051 Website: Cardiac Resynchronisation Therapy Survey II (escardio.org)

Table 5. Research group's contribution to publications

Instructions: Please select 5-15 publications from the last 5 years (2018-2022) with emphasis on recent publications where group members have a significant role. **If the publication is not openly available, it should be submitted as a pdf file attached to the self-assessment.**

Publication 1: Title: Fractional Flow Reserve-Guided PCI as Compared with Coronary Bypass Surgery Journal: N Engl J Med. Year: 2022 DOI: https://doi.org/10.1056/nejmoa2112299 URL: https://www.nejm.org/doi/full/10.1056/NEJMoa2112299	**Authors** (Please highlight group members)	Fearon WF, Zimmermann FM, De Bruyne B, Piroth Z, van Straten AHM, Szekely L, Davidavičius G, Kalinauskas G, Mansour S, Kharbanda R, Östlund-Papadogeorgos N, Aminian A, Oldroyd KG, Al-Attar N, Jagic N, Dambrink JE, Kala P, Angerås O, MacCarthy P, Wendler O, Casselman F, Witt N, Mavromatis K, Miner SES, Sarma J, Engstrøm T, Christiansen EH, Tonino PAL, Reardon MJ, Lu D, Ding VY, Kobayashi Y, Hlatky MA, Mahaffey KW, Desai M, Woo YJ, Yeung AC, Pijls NHJ; FAME 3 Investigators **AI LARSEN** national PI).
	Short description	Evaluating physiology guided PCI with angiography guided CABG in patients with multi vessel disease.
	Research group's contribution	AIL national PI with Haukeland as surgical centre. No other centre In Norway participated.
Publication 2: Title: Guideline-Recommended Time Less Than 90 Minutes from ECG to Primary Percutaneous Coronary Intervention for ST-Segment-Elevation Myocardial Infarction Is Associated with Major Survival Benefits, Especially in Octogenarians: A Contemporary Report in 11 226 Patients from NORIC. Journal: J Am Heart Assoc. Year: 2022 DOI: https://doi.org/10.1161/jaha.122.024849 URL:	**Authors** (Please highlight group members)	**Larsen AI**, Løland KH, Hovland S, Bleie Ø, Eek C, Fossum E, Trovik T, Juliebø V, Hegbom K, Moer R, Larsen T, Uchto M, Rotevatn S.
	Short description	Time from ECG-diagnosis to sheath insertion is strongly correlated with mortality. Using contemporary data from NORIC (Norwegian Registry of Invasive Cardiology) we investigated the predictive value of patient age and time from ECG diagnosis to sheath insertion (ECG-2-sheath) in primary percutaneous coronary intervention for ST-segment-elevation myocardial infarction (STEMI). Time from ECG-diagnosis to sheath insertion is strongly correlated with mortality. This applies especially to octogenarians who derive the most in terms of absolute mortality reduction.
	Research group's contribution	AIL first author and SUH representative in the Norwegian Registry of Invasive Cardiology (NORIC). *First publication published on pure registry data from NORIC*. *URL: https://helsedata.no/en/forvaltere/norwegian-institute-of-public-health/norwegian-registry-of-invasive-cardiology/.*

https://www.ahajournals.org/doi/10.1161/JAHA.122.024849		
Publication 3: Title: Effects of n-3 Fatty Acid Supplements in Elderly Patients After Myocardial Infarction: A Randomized, Controlled Trial Journal: Circulation Year: 2021 DOI: https://doi.org/10.1161/CIRCULATIONAHA.120.052209 URL: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.052209	**Authors** (Please highlight group members)	Kalstad AA, Myhre PL, Laake K, Tveit SH, Schmidt EB, Smith P, **Nilsen DWT**, Tveit A, Fagerland MW, Solheim S, Seljeflot I, Arnesen H;
	Short description	High intake of marine n-3 polyunsaturated fatty acids (PUFA) has been associated with reduced risk of cardiovascular events; however, this has not been confirmed in patients with a recent acute myocardial infarction (AMI). A reduction in clinical events in 1027 elderly patients with recent AMI who were treated with 1.8 g n-3 PUFAs daily for 2 years could not be confirmed.
	Research group's contribution	The Cardiology Research Group took part in all process including design, recruiting and publication of results.
Publication 4: Title: Occult obstructive coronary artery disease is associated with prolonged cardiac troponin elevation following strenuous exercise. Journal: Eur J Prev Cardiol. Year: 2020 DOI: 10.1177/2047487319852808	**Authors** (Please highlight group members)	**Kleiven Ø**, Omland T, Skadberg Ø, **Melberg TH**, Bjørkavoll-Bergseth MF, Auestad B, Bergseth R, Greve OJ, Aakre KM, **Ørn S**.
	Short description	The study demonstrated that troponin release patterns can be used to identify individuals with severe coronary artery disease despite complete absences of symptoms and ECG findings.

URL: https://academic.oup.com/eurjpc/article/27/11/1212/5950974?login=true	**Research group's contribution**	The research group was the sole contributor to the study's design, conduction, collection, analysis and writing and publication.
Publication 5: Title: PROSPECT II Investigators. Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (PROSPECT II): a prospective natural history study. Journal: Lancet. 2021 Year: 2021 DOI: 10.1016/S0140-6736(21)00249-X URL: Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (PROSPECT II): a prospective natural history study - ClinicalKey	**Authors** (Please highlight group members)	Erlinge D, Maehara A, Ben-Yehuda O, Bøtker HE, Maeng M, Kjøller-Hansen L, Engstrøm T, Matsumura M, Crowley A, Dressler O, Mintz GS, Fröbert O, Persson J, Wiseth R, **Larsen AI**, Okkels Jensen L, Nordrehaug JE, Bleie Ø, Omerovic E, Held C, James SK, Ali ZA, Muller JE, Stone GW
	Short description	Near-infrared spectroscopy (NIRS) and intravascular ultrasound are promising imaging modalities to identify non-obstructive plaques likely to cause coronary-related events. Combined NIRS and intravascular ultrasound detected angiographically non-obstructive lesions with a high lipid content and large plaque burden that were at increased risk for future adverse cardiac outcomes.
	Research group's contribution	Recruitment of patients. Measurements of actual coronary lesions in a substantial part of patients. Writing and publication process.
Publication 6: Title: Beyond pharmacological treatment: an insight into therapies that target specific aspects of heart failure pathophysiology. Journal: Lancet. Year: 2019 DOI: 10.1016/S0140-6736(18)32216-5 URL: Beyond pharmacological treatment: an insight into therapies that target specific aspects of heart failure pathophysiology - ClinicalKey	**Authors** (Please highlight group members)	**Normand C**, Kaye DM, Povsic TJ, **Dickstein K.**
	Short description	Review paper in Lancet on the complex pathophysiology of heart failure with focus on electromechanical dyssynchrony and dysrhythmia and the treatment of this by cardiac resynchronisation and implantable cardioverter-defibrillators; neurohumoral modification by baroreflex and vagal stimulation; prevention of adverse cardiac remodelling by interatrial shunts; and finally targeting the myocardium directly by cell therapy in an attempt to regenerate new myocardial cells.
	Research group's contribution	First and last author.

Publication 7: Title: Effects of sildenafil on symptoms and exercise capacity for heart failure with reduced ejection fraction and pulmonary hypertension (the SilHF study): a randomized placebo-controlled multicentre trial. Journal: Eur J Heart Fail Year: 2022 DOI: https://doi.org/10.1002/ejhf.2527 URL: https://onlinelibrary.wiley.com/doi/10.1002/ejhf.2527	**Authors** (Please highlight group members)	**Cooper TJ**, Cleland JGF, Guazzi M, Pellicori P, Ben Gal T, Amir O, Al-Mohammad A, Clark AL, McConnachie A, Steine K, **Dickstein K.**
	Short description	Pulmonary hypertension (PHT) may complicate heart failure with reduced ejection fraction (HFrEF) and is associated with a substantial symptom burden and poor prognosis. Sildenafil, a phosphodiesterase-5 (PDE-5) inhibitor, might have beneficial effects on pulmonary haemodynamics, cardiac function and exercise capacity in HFrEF and PHT. Compared to placebo, sildenafil did not improve symptoms, quality of life or exercise capacity in patients with HFrEF and PHT.
	Research group's contribution	Design, recruiting and publication of results.
Publication 8: Title: Increased functional capacity after 12 weeks of exercise training does not transform into improved skeletal muscle metabolism or ultrastructure in heart failure patients on modern optimal medical therapy. Journal: Eur J Prev Cardiol. Year: 2021 DOI: 10.1177/2047487320919863 URL: https://academic.oup.com/eurjpc/article/28/9/e32/6145650?login=true	**Authors** (Please highlight group members)	**Valborgland T,** Isaksen K, Yndestad A, Lindal S, Myreng K, Scott Munk P, **Larsen AI.**
	Short description	Despite an increase in functional capacity after 3 months of structured exercise training there were no significant changes in improved skeletal muscle metabolism or ultrastructure in heart failure patients on modern optimal medical therapy. This was in contrast to the findings from the group in a similar population 20 years ago when none of the modern pharmacological treatments were available.
	Research group's 'contribution	Design, recruiting, statistical analyses, writing and publication of results was performed solely be the Cardiology Research Group. Skeletal muscle biopsy analyses in cooperation with department of Pathology at UiT. Professor Lindal 5 Department of Pathology UiT The Arctic University of Norway, University Hospital of North Norway,
Publication 9: Title: Texture-based probability mapping for automatic scar assessment in late gadolinium-	**Authors** (Please highlight	**Frøysa V**, Berg GJ, Eftestøl T, **Woie L, Ørn S.**

enhanced cardiovascular magnetic resonance images. Journal: Eur J Radiol Open. Year: 2021 DOI: 10.1016/j.ejro.2021.100387 URL: Texture-based probability mapping for automatic scar assessment in late gadolinium-enhanced cardiovascular magnetic resonance images - ClinicalKey	group members)	
	Short description	To evaluate a novel texture-based probability mapping (TPM) method for scar size estimation in LGE-CMRI. The TPM method is comparable with current SI-based methods, both for the scar size assessment and the relationship with left ventricular remodelling when applied on LGE-CMRI.
	Research group's contribution	Design, wiring and publication Cardiology Research Group in cooperation with University of Stavanger.
Publication 10: Title: Angiopoietin-2 and angiopoietin-like 4 protein provide prognostic information in patients with SUHpected acute coronary syndrome. Journal: J Intern Med. Year: 2021 DOI: 10.1111/joim.13339 URL: https://onlinelibrary.wiley.com/doi/10.1111/joim.13339	**Authors** (Please highlight group members)	**Aarsetøy R,** Ueland T, Aukrust P, Michelsen AE, de la Fuente RL, Pönitz V, Brügger-Andersen T, Grundt H, Staines H, **Nilsen DWT.**
	Short description	Plasma levels of angiopoietin-2 (ANGPT2) and angiopoietin-like 4 protein (ANGPTL4) reflect different pathophysiological aspects of cardiovascular disease. Their association with outcome in a hospitalized Norwegian patient cohort (n = 871) with suspected acute coronary syndrome (ACS) and in a similar Argentinean cohort (n = 982) was evaluated. Both ANGPT2 and ANGPTL4 were significantly associated with outcome in similar ACS patient cohorts recruited on two continents.
	Research group's contribution	Design, recruiting and publication of results. Based on the local RACS biobank.

Table 6. Please add a list with the research group´s monographs/scientific books.
Please delete lines which are not used.
Not relevant for our group.

2.2 Research group´s societal contribution

Describe the societal impact of the research group's research. Consider contribution to education, economic, societal and cultural development in Norway and internationally.

Education: Our group makes extensive contributions to the education of researchers and health care professionals. These include organization of congresses like the annual spring meetings of the Norwegian Society of Cardiology. The group is also active in the publication of treatment guidelines and articles in the national journal of the Norwegian Society of Cardiology. In addition, we regularly educate patients and the public through organized courses for patients with implanted cardioverter defibrillators and patients with coronary artery disease. A collaboration with the department of paediatrics is aimed at grownups with congenital cardiac disease.
Economic: The past cardiologist Leik Woie founded the Hjertelaget Research Foundation 1988. A research-and-rehabilitation centre was established. Experienced physiotherapists developed large programmes for patients who had suffered from myocardial infarction and for patients undergoing heart surgery. Later this was extended to include all types of cardiac patients with thousands of individuals passing through for the last 30 years. The physiotherapists also took part in trials on exercise training which have been a cornerstone for the investigator-initiated trials at SUH. This early approach to exercise training rehabilitation and focus on a healthy life has been fundamental to the decrease of heart disease.
Societal: As mentioned above CRG has been central (KD) in the development of the Heart Failure Information for Patients & Caregivers - Heart Failure Matters, which is a central educational tool for patients with heart failure and their next to kind. In addition, the group actively communicates the beneficial effect of exercise training. There is a close relationship to the press to convey information about how to react when somebody experience acute chest pain and the importance of ASAP action to medical contact, ECG and subsequent reperfusion. Moreover, the NEEDED program is shedding light on cardiovascular effects of taking part in endurance sports, with inclusions of more than 1000 participants in the 2014 Nort Sea Endurance Race.

Table 7. The research group's societal contribution, including user-oriented publications, products (including patents, software or process innovations
Instructions: Please select 5–10 of your most important user-oriented publications or other products from the last 5–10 years with emphasis on recent publications/products. For each item, please use the following formatting. Please delete lines which are not used.

No.	Name of publication/product	Date of publication/ product	Link to the document
1	Heart Failure Matters		Heart Failure Information for Patients & Caregivers (heartfailurematters.org)
2	Web site the NEEDED trial program		Nordsjørittet - NEEDED (nordsjorittet.no) [Norwegian]
3	The Norwegian Broadcasting Company	2015	Hjerteforskningsprisen (nasjonalforeningen.no) [Norwegian]
4	Cardiology Research Group website	2024	Research Group of Cardiology - Helse Stavanger HF (helse-stavanger.no)
5	Research societal journal. "Supplements with cod liver oil"		Mosjonister som tok tran jevnlig, var mindre støle etter langt

			sykkelritt (forskning.no) [Norwegian]
6	The Norwegian Broadcasting Company "Using Viagra for Heart Failure"		Han har tatt 13.000 Viagra (nrk.no) [Norwegian]
7	Stavanger AftenbladNewspaper Circulation 65000 issues. "Exercise training in heart failure"	2012	Hjertet trenger trening (aftenbladet.no) [Norwegian]
8	Stavanger Aftenblad Newspaper Circulation 65000 issues. "Treatment of acute myocardial infarction and sudden cardiac arrest. Focus on registries for our of hospital cardiac arrest (NorCAR)"	2014	Anita var død i én time (aftenbladet.no) [Norwegian]
9	Stavanger Aftenblad Newspaper Circulation 65000 issues. "A step up in the medical student education at SUH"	2020	SUS er klar for medisinutdanning (aftenbladet.no) [Norwegian]
10	The Norwegian Broadcasting Company. «Cooperation with oil companies in the Pumps and Pipes cooperation."		Vil bruke oljeteknologi – på hjertepasienter (nrk.no) [Norwegian]

3. Challenges and opportunities

Information about the strengths and weaknesses of the research group is obtained through the questions above. In this chapter, please reflect on what might be the challenges and opportunities for developing and strengthening the research and the position of the research group.

Economic Challenges:

- Securing funding for permanent research positions in the group remains uncertain. There is no in department support of study nurses or administrative staff.
- A significant proportion of our research funding is project-based in large national trials supported from the NRC and large investigator initiated RCTs in which SUH has the national leadership. To achieve our group's ambitions for growth, we must further augment the share of project-based funding.
- Despite our strong national and international standing, the evolving landscape of Norwegian research environments is intensifying competition for funding mainly due to the development of large study groups at the "original" university hospitals which have a better basic funding.
- There is no financial support for research in the Emergency and Medical Clinic or in the department of Cardiology. There is no expectation of research in the clinical part of the activity.
- Most research and funding originate from the professors' initiatives, which indicates less sustainable future research. Fortunately, new doctors funded externally might provide a milieu for research in the future. Research is partly integrated into the clinical working day, making it possible to do advanced technical procedures during daytime. The funding is solely external from research performed for external sponsors except for the PhD funding, which mostly is from the Regional Western Health Authority in sharp competition with other centres. On the other hand, 3 of the professors are emeritus and the other 2 are in their mid-fifties and sixties. Additionally, SUH has a lower budget compared to the original University Hospital Haukeland in Bergen. The 2 centres have regional responsibility for invasive cardiology and primary PCI with

24/7 on call service for approximately the same size population 650 000 HS and 500 000 SUH. External funded research is thus increasingly hard at SUH despite the university hospital status. However, the centre is involved in several large investigator-initiated studies funded by external sources like NRC (NOREX study 500 patients included) and over sea research institutions like Stanford (FAMEIII study) or Hamilton (COMPLETE 2 study) which both have national PI at SUH. In the clinical daily life, there is an urgent need for further support of administrative staff/study nurses at the department level. This is still a challenge.

The Research Group and Resources Challenges:

- Our field is very large, requiring access to highly skilled personnel. Recruiting and retaining qualified and promising clinical and basic researchers present challenges due to increasing clinical work.
- There is a large gap between the demand for administrative support and actual administrative and financial support.

Operational Challenges:

- A fragmentation of the clinical environment with 2 localizations after the acute cardiology units move to the new hospital will be a challenge for expanding our research.
- Due to increasingly limited resources and challenges related to clinical work, research will not be prioritized.

Economic Opportunities:

- Increased research activity has clearly strengthened our position both scientifically and to obtain funding from external sources including NFR and EU.
- This is also associated with an increase in externally funded PhDs.

The Research Group and Resources Opportunities:

- We will further strengthen our collaborations with UiB and their research groups in the field. This might provide new opportunities for cooperation and possibilities for funding.
- We have well-established international collaborations and will strengthen established MOUs.