

Annual Report

University Research Clinic for Cancer Screening

2022



Annual Report 2022
University Research Clinic for Cancer Screening

Department of Public Health Programmes
Randers Regional Hospital
Central Denmark Region

Department of Clinical Medicine
Health
Aarhus University

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Editor: Louise Dybdahl Pedersen
Portrait photos: Helle Brandstrup Larsen
Co-author map: Louise Stenholt
Layout/tryk: Ecograf Gruppen ApS

The report can be downloaded from www.cancerscreeningresearch.rm.dk or by contacting Research Secretary Marianne Rævsbæk Pedersen, tel. +45 7842 0172, email: marape@rm.dk



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Preface

As 2022 came to an end, so did the second full year of the University Research Clinic for Cancer Screening and once again we summarize the year in an annual report.

Since its appointment, the University Research Clinic for Cancer Screening has gradually expanded as more and more grants have been won, more and more projects have been launched, and more and more students have joined us. As a result, we have moved to new premises with room to grow during the summer of 2022.



The growth of the University Research Clinic is first and foremost due to our many researchers' excellent work and their ability to attract significant external funding. However, it is also the result of a persistent strategic focus within the University Research Clinic. A strategic focus to link research and operations, prioritize visibility of our research activities, strengthen and establish excellent research collaborations, value and encourage multidisciplinary research, and, last but not least, stimulate a positive and rewarding daily research and learning environment.

As the University Research Clinic grows and evolves, our scientific goal remains the same: to optimise organised cancer screening. Our current research activities are organised within four research themes: 1) evaluation of outcomes in population-based cancer screening; 2) informed participation; 3) risk perception and screening behaviour; and 4) diagnostics and screening derived activities.

In this annual report, we briefly introduce all four themes and expand the fourth with a detailed overview of our current research in HPV diagnostics and screening derived activities within the cervical cancer screening programme. This has been one of our prioritised topics since 2016. The report also provides an overview of our staff, collaborators, funding and dissemination, and presents highlights such as distinctions, impact of research and new prestigious grants. As management, we are especially proud of our EU4Health grant won by Senior Researcher Pia Kirkegaard and our EU Horizon Europe grant won by Associated Professor Sisse Njor, who was also awarded an Ascending Data Science Investigator grant from the NOVO Nordic Foundation. Our ability to achieve external funding is key to expanding our research activities and a recognition of the quality of our research.

We would like to conclude by extending our warmest thanks to all our staff for their continuous endeavours. We would also like to thank all our collaborators - especially the Department of Clinical Medicine at Aarhus University, Randers Regional Hospital and Central Denmark Region for their extensive support.

Berit Andersen
Professor, Co-Head of Department

Gitte Jessing
Co-Head of Department

Staff

Management



Professor Berit Andersen

MD, PhD, specialist in community medicine

Co-Head of Department and Clinical Professor in Screening. Specialises in public health interventions. Head of the national steering committees for breast and cervical cancer screening (NSBS and NSLS). Member of the steering committees for all three national screening databases (DKLS, DKMS and DTS) and member of the professional committee of the Danish Comprehensive Cancer Center (DCCC), and Vice Chairman of the Danish Council on Ethics.



Co-Head of Department Gitte Jessing

BSc Nursing, MSc in Public Health, Master of Business Administration

Co-Head of Department. Working with both clinical and research management within the Department of Public Health Programmes.

Former Head of Clinical Research Unit in Oncology with experience in stakeholder management, research management, leadership, economics, private-public relations etc.

Senior Researchers



Senior Researcher Pia Kirkegaard

MA Anthropology, PhD

Specialises in screening and follow-up seen from the resident's perspective using exploratory qualitative research based on sociological theory and interviews, focus groups, and field work. Focuses on ensuring informed choice about screening participation among all residents in the target groups for cancer screening. Work-package leader in the EU Horizon 2020 project CBIG-SCREEN and Visiting Scientist in WHO.



Associate Professor Sisse Njor

MSc Statistics and Computer Science, PhD

Specialises in register-based research focusing on how to maximise the residents' benefits of screening while minimising the harms. Part-time biostatistician at the Danish Clinical Quality Program – National Clinical Registries. Member of the steering committee in the Danish Colorectal Cancer Group's Database. Collaborator in several major international collaboration projects and associated editor in BMC Cancer and BMC Public Health. NOVO Nordic Ascending Data Science Investigator.



Senior Researcher Mette Bach Larsen

MSc Public Health, PhD

Specialises in health services research within the field of early diagnosis of cancer using quantitative methods such as surveys, register-based epidemiological research, and intervention studies with focus on different aspects of participation in cancer screening including effectiveness of screening, reasons for (non)participation, and interventions to improve informed screening participation. Responsible for teaching the Department's bachelor course in screening.



Post Doc Mette Tranberg

MSc Health Science, PhD

Specialises in improving cervical cancer screening through self-sampling and use of molecular biomarkers combining diagnostic test accuracy studies and population-based intervention trials. Currently abroad at University of Antwerp on an DFF International Postdoctoral Fellowship.

Honorary Professor



Professor Adrian Edwards

MB BS (Medicine), PhD

Professor of General Practice at Cardiff University, Wales, UK. Director of the Wales COVID-19 Evidence Centre, Director of PRIME Centre Wales, and part-time General Practitioner in Cwmbran, South Wales. Specialises in shared decision-making, risk communication, health literacy, and support to patients with chronic diseases.



Clinical Associate Professor Pinar Bor

MD, PhD, specialist in gynaecology

Specialises in cervical dysplasia and surgery.

Affiliated Researcher

Staff

Postdoctoral Researchers



Rikke Buus Bøje

MSc Nursing, PhD

Specialises in co-constructive methods focusing on reducing inequality in cervical cancer screening among vulnerable women.



Line Winther Gustafson

MD, specialist in gynaecology, PhD

Specialises in diagnosis and clinical follow-up following a positive cervical cancer screening result.



Susanne Fogh Jørgensen

MSc Health Science, PhD

Specialises in register-based research focusing on the evaluation of follow-up after abnormal screening results.

Research Support



Louise Dybdahl Pedersen

Research Advisor/PA



Marianne Rævsbæk Pedersen

Research Secretary



Bo Søborg

Data Manager



Charlotte Riff

Project Assistant

Research Students



Vibe Munk Bertelsen

MD, PhD Student

Vibe is focusing on improving the diagnosis of precancerous cervical lesions among women aged ≥ 50 years.



Karen Omann Binderup

Medicine Research Year Student

Karen is evaluating biomarkers for risk-stratifying women with an abnormal cervical cancer screening result.



Anne Dorte Lerche Helgestad

MD, PhD Student

Anne Dorte is exploring cross-programme synergies in the national cancer screening programmes.



Pernille Thordal Larsen

MSc Health Science, PhD Student

Pernille is evaluating the recommendations for follow-up in the colorectal cancer screening programme.



Bayan Sardini

MSc Appl. Mathematics, PhD Student

Bayan is developing methods for estimating the effect of and risk stratifying breast cancer screening.



Rikke Stokholm

MSc Public Health, Research Assistant

Rikke is focusing her research on how to measure knowledge about cancer screening.



Camilla Rahr Tatari

MSc Public Health, PhD Student

Camilla is exploring attitudes and identifying barriers towards cancer screening among vulnerable residents.



Signe Bülow Therkildsen

MSc Health Science, Research Ass.

Signe is examining the participation in the Danish colon cancer screening programme using registry data.

Highlights

New staff and distinctions

New Co-Head of Department

In October, **Gitte Jessing** joined the department as our new Co-Head of Department. Gitte joins us from a position as Head of the Clinical Research Unit within the Department of Oncology at Aarhus University Hospital. Gitte has more than 20 years of experience in management and research facilitation in a large organisation and holds two Master Degrees - MPH and MBA. Gitte is also appointed as Head of the Research Unit at Randers Regional Hospital.



WHO appointment

Pia Kirkegaard has been appointed visiting scientist at the International Agency for Research on Cancer (IARC). IARC is the specialized cancer agency of the World Health Organization (WHO). As visiting scientist, Pia Kirkegaard will help WHO develop 'best practice' for health authorities on how to communicate screening programmes for cervical cancer screening.



Vice Chair of the Danish Council on Ethics

Our Professor **Berit Andersen** has been extended as Clinical Professor in Screening Behaviour and Organisation of Screening Programmes at the Department of Clinical Medicine, Aarhus University, for another 5-year period.

Berit Andersen has furthermore been elected Vice Chair of the Danish Council on Ethics. She has been a member of the council since January 2020.



New researchers

During 2022, the University Research Clinic welcomed two new PhD students: MSc in Applied Mathematics **Bayan Sardini** who is working on the project 'DEVELOP: Do breast cancer survivors and chronic ill women benefit more or less from mammography screening?'. MSc in Public Health **Rikke Stokholm** who's project is entitled 'Defining and measuring knowledge in cancer screening – is there a need for new information materials?'. We have also welcomed **Line Winther Gustafson** as a post doc in a 20% shared position alongside a position as a Senior Registrar in the gynaecological oncology team at the Department of Obstetrics and Gynaecology at Aarhus University Hospital. Line will be continuing the research from her PhD project on diagnostics and screening derived activities related to HPV and dysplasia in cervical cancer screening.

Highlights

New staff and distinctions

Exceptional Young Scientist

Post doc **Susanne Fogh Jørgensen** won the „Exceptional Young Scientist Abstract“ award at the Danish Cancer Research Days. The award was one of seven awards given for the best abstracts submitted to the conference out of a total of 167 abstracts. Along with the award, Susanne had the honour of presenting her research on the main stage.

At this year's conference, twelve researchers were also selected to present their abstract in a flash talk. Among those were **PhD Student Bayan Sardini**.



PhD defence

Line Winther Gustafson successfully defended her PhD thesis „Cervical cancer prevention in post-menopausal women – aspects of clinical management, risk stratification, and patient aspects“ on June 14. Line evaluated the clinical management of women aged ≥ 45 years referred to colposcopy following an abnormal cervical cancer screening result and investigated the potential of risk stratification using a new biomarker.



Students, guests, and interns

During 2022, we have had the pleasure of hosting Public Health Student **Mie Lykkeberg** and Health Science Student **Signe Bulow Therkildsen** during their master projects, Medicine Student **Karen Omann Binderup** during her research year, and PhD student and MD **Alexander Laschke** from University of Southern Denmark during his change of research environment.

During the year, we also hosted a number of interns as we welcomed MSc in Public Health **Sofie Meyer Andersen** as a company intern as well as medicine students **Anna Emilie Krarup**, **Ellen Cunningham Ogilby**, **Ida Birkbak Højen**, **Marie-Louise Dirchsen Thomassen** and **Mathilde Sidsel Nielsen** during their 8-week research internship.

Best poster

PhD Student **Anne Dorte Lerche Helgestad** won the prize for the best poster presentation presented by an experienced researcher at the annual Research Symposium at Randers Regional Hospital. Along with the honour, Anne Dorte received a travel scholarship.



Highlights

External funding

EU grants

From the EU Horizon Europe programme, the DIOPTRA consortium was awarded approx. DKK 102 million out of which the University Research Clinic receives DKK 3.6 million. The consortium consists of 28 European partners from 15 countries who will join forces to develop early dynamic screening for colorectal cancer via novel protein biomarkers reflecting biological initiation mechanisms. The project starts January 2023 and Sisse Njor will be the principal investigator from the University Research Clinic.

From the EU4 Health Programme, the PRAISE-U consortium was awarded approx. DKK 73 million. The University Research Clinic's share is DKK 3.7 million. The project starts April 2023, and has the vision that EU member states should be able to offer high quality clinical standards including state-of-the-art individualised approaches to achieve timely prostate cancer detection in men who can benefit from early treatment. Pia Kirkegaard will be the principal investigator from the University Research Clinic.



novo nordisk foundation

National grants

Sisse Njor won an Ascending Data Science Investigator grant from the NOVO Nordic Foundation in the amount of DKK 8.9 million. The project 'DEVELOP: Using data science to estimate overdiagnosis and mortality reduction in cancer screening programs' started in November and will run for five years.

The University Research Clinic was awarded three grants from the Danish Cancer Society's 'Knæk Cancer' funds. The funded projects include 'Urinary HPV and DNA methylation testing as a novel cervical cancer screening method – a diagnostic accuracy study' (Mette Tranberg), 'An educational intervention to increase cancer screening participation and awareness of cancer symptoms among non-Western ethnic minorities in Denmark' (Berit Andersen), and 'Social inequity in follow-up after cancer screening in Denmark' (Sisse Njor and Susanne Fogh Jørgensen).



Highlights

Research impact and network



Self-sampling in the cervical cancer screening programme

Research carried out in the University Research Clinic for Cancer Screening has demonstrated that offering the possibility of vaginal self-sampling to non-attendees in the cervical cancer screening programme can improve the participation of under-screened women. Based on these results, among others, the Danish Health Authority has endorsed the Danish regions to offer under-screened women the possibility of vaginal self-sampling as part of routine screening. This was initiated in the Central Denmark Region in August 2022 and, now, women invited for cervical cancer screening receives an additional offer in the form of an HPV self-sampling test kit. The offer is extended with the second reminder which is sent 6 months after the invitation.



Effective colorectal cancer screening

A study carried out in the University Research Clinic for Cancer Screening and published in Journal of Medical Screening shows that FIT-based colorectal cancer screening has reduced mortality due to colorectal cancer among older men. This is mainly due to the fact that the cancer is detected at an earlier stage thereby improving the prognosis.

Furthermore, the National Steering Committee for Colorectal Cancer Screening has recently decided to change the invitation reminder process in the national programme based on research from the University Research Clinic.

Contribution to report on equity in health and national guidelines

The Danish Health Authority has published a report suggesting that equity in health can be increased by tailoring the health care system's meeting with the patients based on each patient's individual level of health literacy. The University Research Clinic contributed with a case on health literacy and cancer screening based on research results from the LEAD and the SWIM projects, respectively.

Moreover, Line Winther Gustafson has contributed to the Danish Society of Obstetrics and Gynecology (DSOG) guideline:

Prevention, diagnostic work-up, and treatment of cervical cancer and precancer, which is currently under review.



Highlights

Research impact and network

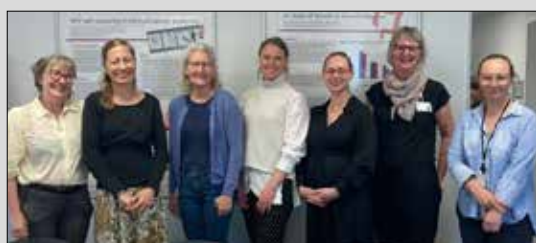
Enabling impact of our research

The University Research Clinic takes active part in the public screening agenda through national, interregional, and regional forums addressing operation, administration, quality assurance, and guidelines in cancer screening programmes. This includes, among others, the national steering groups for breast and cervical cancer screening, the steering committee of the Danish quality database for cervical cancer screening, the Danish colorectal cancer screening database, and the Danish Health Authority's advisory committee on screening programmes. These fora are an excellent channel for bringing research results forward to relevant national stakeholder, thereby ensuring optimal conditions for our research leading to identifiable changes.

An approach to ensure that our research findings are generalizable and implementable, is by testing our findings in implementation studies. An example of such an implementation study is a new project granted by the Danish Cancer Society. In this project, we will test a tailored educational intervention to increase cancer screening participation and awareness of cancer symptoms among non-Western ethnic minorities in Denmark. This project is based on the findings in our former SWIM project in which we evaluated non-Western ethnic women's perceptions of cancer in qualitative studies, their barriers for participating in the Danish cancer screening programs, and their preferences and ideas for interventions aiming at increasing their participation in cancer screening.

New Nordic network

In 2022, researchers at the University Research Clinic for Cancer Screening took the initiative to establish Nordic Network on Colorectal Cancer Screening. The network consists of researchers from Finland, Iceland, Sweden, Norway, the Faroe Islands, and Denmark, and had its first meeting in Copenhagen in November.



National stakeholders

We have had the pleasure of hosting visits by two national stakeholders in 2022.

In May, the Cancer Prevention and Information Unit from the Danish Cancer Society came to exchange knowledge and discuss research results related to (informed) participation in cancer screening.

In June, the Department of Evidence-based Medicine from the Danish Health Authority visited. The Department is, among other things, in charge of the national clinical guidelines and screening programmes. The visit was an excellent opportunity to present and discuss research in the national cancer screening programmes.



Current research themes

The scientific focus of the University Research Clinic for Cancer Screening is population-based screening and the research is centred on optimising cancer screening programmes on a regional, national, and international level while utilising our unique possibility to address cross-programme synergies within the Department of Public Health Programmes. We employ different scientific disciplines and seek to promote synergies between Health Sciences, Social Studies, and Humanities.

Our current research activities are clustered in four research themes:

1. Evaluation of outcomes in population-based cancer screening;
2. Informed participation;
3. Risk perception and screening behaviour; and
4. Diagnostics and screening derived activities.

Within each theme, the University Research Clinic has affiliated several researchers and is involved in several projects - internal as well as external.

In this annual report, we have chosen to give a brief introduction to the four research themes followed by a detailed overview of our activities within diagnostics and screening derived activities related to HPV and dysplasia in cervical cancer screening including three examples of projects.

Evaluation of population-based cancer screening

Introducing and maintaining cancer screening programmes is a delicate balance between benefits and harms. Earlier diagnosis with better prognosis and possibly less treatment, changes in resources in the health care system, false test-results, overdiagnosis, over-treatment, and residents' desires all have to be taken into consideration. The balance may change over time, as treatment and diagnostic procedures change or improve and the prevalence of relevant risk-factors change within the community.

In this research theme, new methods to evaluate benefits and harms of organised cancer are developed and tested. Register-based evaluation of effectiveness and use of health care resources are combined with resident's perspectives on the subject. The overall aim is to secure relevant and continuous focus on the benefit-harm ratio of cancer screening for residents as well as for the health care system.

Informed participation

Participation is a key factor in securing the effectiveness of a cancer screening programme, still, most organised screening programmes have suboptimal participation rates. Increasing participation has to be combined with allowing residents to make an informed choice about participation. Benefits and harms need to be communicated allowing the resident to make an informed decision of whether or not to participate.

This research theme is focused on developing methods for allowing resident to make an informed choice and to study initiatives aimed at reducing barriers to participation. This includes use of e.g. appropriate information and decision aids, refined reminder systems, self-sampling procedures, and tailored interventions to vulnerable groups. Register-based evaluation of participation and PROM data are some of the methods used. The overall aim is to increase (informed) participation in all cancer screening programmes and among all groups of residents with a special focus on reducing social inequity.

Risk perception and screening behaviour

The choice of whether or not to participate in organised cancer screening is based on health seeking behaviour in general as well as psychological, social, and cultural perceptions about the risk of positive screening results, and the risk of having a cancer detected. Participation in screening can furthermore be associated with trust and feasibility.

This research theme studies the psychosocial and cultural mechanisms in population-based cancer screening using social science and health services research. Perceptions of and barriers for participating in cancer screening are explored and co-creation of tailored interventions are pursued with a special interest in vulnerable groups. The overall aim is to understand the

underlying mechanisms behind risk perception and behaviour related to cancer screening. Ideally, the knowledge can be transferred into the organisation of the screening programmes to promote informed participation.

Diagnostics and screening derived activities

A positive cancer screening result requires subsequent diagnostics and clinical procedures of the highest possible standards. Special attention may be needed when new age-groups are targeted or when background risk factors change in the community.

This research theme spans widely from the development of new clinical diagnostic methods for cervical cancer across studies of the quality of colonoscopies to register-based studies of follow-up after positive screening results. The overall aim is to contribute to, develop, and evaluate diagnostics and screening derived clinical procedures in order to continuously secure the highest possible outcome of cancer screening programmes.

Since 2016, a prioritised area within this theme is diagnostics and screening derived activities related to HPV and dysplasia in cervical cancer screening.



Selected research theme

HPV and dysplasia in cervical cancer screening

The University Research Clinic for Cancer Screening has a wide range of research activities within diagnostics and screening derived activities related to HPV and dysplasia in cervical cancer screening.

Our activities include the development of non-invasive and accurate cervical cancer screening tools based on self-sampling. Intervention studies of vaginal self-sampling for HPV screening have been performed and test accuracy studies of new self-sampling procedures using e.g. urine are currently in progress. Qualitative studies are used to test the acceptability of new methods and co-create new and acceptable screening methods. Examples of current studies are described in detail in the Annual Report from 2021 which can be found on our webpage:

www.cancerscreeningresearch.rm.dk

The current move of cervical cancer screening from cytology to HPV based testing brings new challenges as HPV testing has a very high sensitivity for pre-cancerous lesions but a poor specificity. An ongoing research effort is therefore focused on methods to improve risk-stratification following a positive HPV screening result. This will provide a more precise answer

to the women and at the same time avoid overtreatment and unnecessary follow-up.

Timely and appropriate follow-up is crucial for the effectiveness of cancer screening programmes. To evaluate follow-up after positive screening, register-based studies are used. In a recent study presented in the Annual Report from 2021, we have shown that following an abnormal cervical cancer screening, less than half of the women had follow-up in accordance with the national recommendations. Follow-up was excessively long in many cases and the use of diagnostic tests and procedures was higher than expected. A patient group which often experiences long follow-up and, possibly, overtreatment is older women as they are difficult to diagnose accurately. Methods are thus developed to improve diagnostics following colposcopy referral in older women.

On the following pages are three examples of projects aiming to improve diagnosis of women referred to colposcopy.

Researchers working within this theme:

- **Mette Tranberg**, MHS, PhD, Post Doc
- **Line Winther Gustafson**, MD, PhD, Gynaecologist, PhD Student/Post Doc
- **Pinar Bor**, MD, PhD, Gynaecologist, Clinical Ass. Prof.
- **Berit Andersen**, MD, Clinical Professor
- **Susanne Fogh Jørgensen**, MSc, PhD, Post Doc
- **Sisse Njor**, MSc, Statistician and Epidemiologist, PhD, Ass. Prof.
- **Pia Kirkegaard**, MA, Anthropologist, PhD, Senior Researcher
- **Rikke Buus Bøje**, MSc, PhD, Post Doc
- **Vibe Munk Berthelsen**, MD, PhD Student
- **Karen Omann Binderup**, stud. med., Research Year Student
- **Sofie Meyer Andersen**, MHS, intern
- **Ellen Cunningham Ogilby**, stud. med.
- **Anna Emilie Atterdag Krarup**, stud. med.
- **Ida Birkbak Højen**, stud. med.
- **Marie-Louise Dirksen Thomassen**, stud. med.

Cervical cancer prevention in postmenopausal women

– aspects of clinical management, risk stratification, and patient aspects



PhD project by Line Winther Gustafson

Today, women are routinely referred for colposcopy following an abnormal cervical cancer screening test. Colposcopy is the most important diagnostic tools to detect cervical precancerous lesions and thereby prevention of cervical cancer.

At colposcopy, biopsies are collected for histopathologic diagnosis according to the Danish national guidelines. However, in older women, results based on biopsies may lead to underdiagnosis due to an incomplete visibility of the area within the cervix where precancerous lesions and cancer develops – the transformation zone in the cervical canal – and thereby an increased risk of overlooking the disease.

The aim of Line's PhD project was to improve the clinical management of women ≥ 45 years referred to colposcopy following an abnormal cervical cancer screening result. Line investigated if the clinical examination of women with an incomplete visualization of the transformation zone at colposcopy could be improved by offering a diagnostic cervical excision.

To ensure that the offer of diagnostic cervical excision was an acceptable alternative to biopsies, Line evaluated the anxiety levels in women undergoing diagnostic cervical excision at their first visit to the colposcopy clinic. The study showed that women referred for diagnostic cervical excision generally had low anxiety levels but that there was an elevated risk of anxiety among women with poor physical and, in particular, poor mental health.

The results of the project showed that the precancerous lesion detection rate was significantly higher

in the cervical excision specimens than in biopsies, and more than half of the precancerous lesions were missed in biopsies. However, the procedure also led to a substantial risk of overtreatment as 68% of the women were overtreated.

To avoid overtreatment, Line investigated if the biomarker p16/Ki67 dual-stain cytology could help risk stratify women into those who do and do not need excisional treatment, thereby allowing women with a low cancer risk to undergo follow-up instead.

The results showed that dual-stain cytology had a higher sensitivity and negative predictive value than cytology for precancerous lesion detection. The superior negative predictive value of dual-stain cytology supports that a diagnostic cervical excision may safely be avoided in dual-stain-negative women. The results therefore suggest that the biomarker can be used for risk-stratifying women with an abnormal screening result and thereby avoid excessive diagnostic cervical excisions while minimizing underdiagnosis.

Line defended her PhD thesis on June 14, 2022.

Publications from the project can be found on:

www.cancerscreeningresearch.rm.dk

Improving diagnostics in cervical dysplasia

- testing new technology, pre-diagnostic treatment and present procedures



PhD project by Vibe Munk Bertelsen

The aim of Vibe's PhD project is to improve the diagnosis of precancerous cervical lesions in women of all ages through optimisation of present procedures and new interventions.

As part of her PhD project, Vibe has initiated a multi-centre study, where she is including patients in a clinical trial. Vibe will investigate if the new digital colposcopy technology, DYSIS, can increase the detection of cervical precancerous lesions, in women aged ≥ 18 years referred for colposcopy with a positive HPV test and/or low-grade cervical dysplasia. The hypothesis is, that digital colposcopy will improve the sensitivity of cervical biopsies compared to conventional colposcopy, which can be subject to very low sensitivity for detecting precancerous lesions.

The PhD project will also include a randomized controlled blinded multi-centre study to investigate if

the diagnosis of cervical precancerous lesions can be improved in women aged ≥ 50 years by providing pre-treatment with vaginal oestrogen prior to the colposcopic examination. The hypothesis is that pre-treatment with oestrogen will improve visibility of the transformation zone in the cervical canal and thereby minimize unnecessary and repeated colposcopies and reduce the risk of missing disease. The project will include 150 women and is expected to start inclusion in May 2023.

The PhD project was initiated in September 2021 and, following a maternity leave, Vibe is expected to conclude the project in August 2025.

Utility of DNA methylation for risk-stratification of women aged ≥ 45 referred for colposcopy



Research year project by Karen Omann Binderup

The aim of Karen's Research Year project is to examine if DNA methylation can be used for risk-stratifying women aged ≥ 45 referred for colposcopy following an abnormal cervical screening result.

Colposcopy are challenging in older women due to an incomplete visualization of the transformation zone in the cervical canal. This may lead to an increased risk of overlooking the disease or potential over-treatment. The hypothesis is that DNA methylation may help risk-stratifying these women into high risk

groups that are in need of excisional treatment while allowing low-risk women to undergo follow-up.

Karen's research year project was initiated in February 2022 and will be concluded in January 2023.

Active projects related to HPV and dysplasia in cervical cancer screening:

	Project title	Type and participants
Project /WP lead	Working collaboratively with vulnerable women to identify the best implementation gains by screening cervical cancer more effectively in European countries (CBIG-SCREEN)	EU Horizon 2020 project involving 14 partners. Berit Andersen and Pia Kirkegaard WP leads, Mette Tranberg and Rikke Buus Bøje participates
	Urinary HPV and DNA methylation testing as a novel cervical cancer screening tool: A diagnostic test accuracy study	DFF International post doc project by Mette Tranberg
	Expanding the upper screening age in cervical cancer screening: a population-based intervention study	Post doc project by Mette Tranberg
	Value of a catch-up HPV test in women aged 65 and above: A population-based intervention study	Post doc project by Mette Tranberg
	Cervical cancer prevention in postmenopausal women - aspects of clinical management, risk stratification, and patient aspects	PhD project by Line Winther Gustafson
	Improving diagnostics in cervical dysplasia. Testing new technology, evaluating pre-diagnostic treatment and evaluating present procedures	PhD project by Vibe Munk Berthelsen
	Utility of DNA methylation for risk-stratification of women aged ≥45 referred for colposcopy	Research year student project by Karen Omann Binderup
	The use of first-void urine as a cervical cancer screening tool - pre-analytical parameters that could affect urine HPV testing	Student project by Ellen Cunningham Ogilby
	An evaluation of the viral load of high-risk human papillomavirus (HPV) reflected by the cycle threshold value (CT-value) in cervical samples as a triage test in HPV-screen positive women	Student project by Anna Emilie Krarup
Project participant	Acceptance and preference of self-collected urine and vaginal samples for HPV testing in a referral population: A cross-sectional study	Student project by Sofie Meyer Andersen
	iMproving thE Diagnostics And Treatment Of ceRvical precancer - the MEDIATOR study	PhD project by Ane-Kersti S. Knudsen, co-supervisor: Line Winther Gustafson
	Widening the offer of human papillomavirus self-sampling to all women eligible for cervical screening	Research project, participant: Sisse Njor
	Self-collected cervical cancer screening samples for detection of human papillomavirus in HIV-positive women in Africa	Research year student project by Kia Lærke Madsen, co-supervisor: Mette Tranberg
	Vaginal self-sampling for human papillomavirus among HIV-infected women – improving screening for cervical cancer	Pilot research project by Siri Halling, co-supervisor: Mette Tranberg
	Outcomes of cervical cancer screening among cohorts of women HPV vaccinated as girls (TRIAL 23)	Multi-centre study, Berit Andersen member of project group

Research funding

Record high external funding

During the past three years, the University Research Clinic for Cancer Screening has worked strategically to increase its external funding with emphasis on attracting prestigious national and international grants in free competition. The work has paid off, and in 2022 a new record was reached as the Clinic won grants for more than 20 million DKK. We look forward to initiating projects based on grants from the NOVO Nordic Foundation, Horizon Europe, EU4Health, and Knæk Cancer in 2023.

Grants won in 2022 in alphabetical order, amounts shown in DKK:

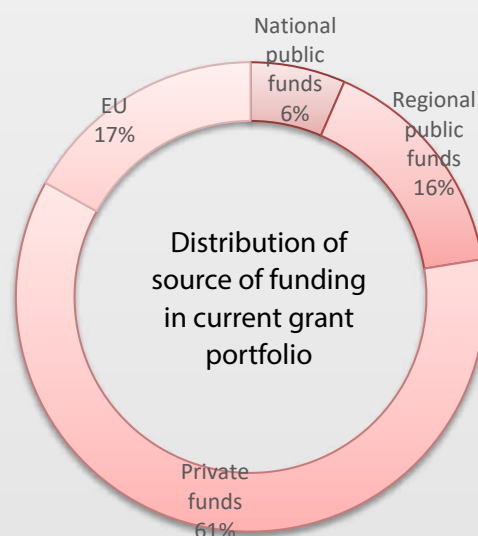
• Dagmar Marshalls Fond	70,000	
• Dagmar Marshalls Fond	40,000	
• EU – Horizon Europe	3,617,700	(total grant 101,622,271)
• EU – EU4Health	3,738,519	(total grant 73,343,376)
• Health Research Foundation of Central Denmark Region	99,754	
• Linds legat	13,000	
• NOVO Nordic Foundation	8,889,233	
• The Danish Cancer Society – Knæk Cancer	1,350,000	
• The Danish Cancer Society – Knæk Cancer	2,145,000	
• The Danish Cancer Society – Knæk Cancer	585,000	
• The Danish Cancer Society	11,875	
• The Danish Cancer Society	19,623	

Current grant portfolio

The grant portfolio that funded active projects in 2022 was DKK 20.7 million and the distribution of the type of funding source is shown in the diagram.

We are very grateful to the funders of our current projects:

- Aage og Johanne Louis-Hansens Fond
- Central Denmark Region
- Dagmar Marshalls Fond
- Danish Comprehensive Cancer Center
- Fabrikant Einar Willumsens Mindelegat
- Harboefonden
- Health Research Foundation of Central Denmark Region
- Helsefonden
- EU Horizon 2020 Framework Programme
- Independent Research Fund Denmark
- Linds legat
- NOVO Nordic Foundation
- Public Health in Central Denmark Region
- Slagtermester Max Wørzner og Hustru Inger Wørzners Mindelegat
- The Danish Cancer Society



Scientific dissemination

Publications in international peer-reviewed journals

1. Andersen K, Holm K, Tranberg M, et al. Targeted next generation sequencing for human papillomavirus genotyping in cervical liquid-based cytology samples. *Cancers* 14(3): 652.
2. Bonde J, Schroll JB, Kristensen BK, et al. Phased implementation of HPV-based cervical cancer screening in Denmark (in Danish). *Ugeskrift for Læger* 184(9): V04210327.
3. Eriksen ARR, Fogh K, Hasselbalch RB, et al. SARS-CoV-2 antibody prevalence among homeless people and shelter workers in Denmark: a nationwide cross-sectional study. *BMC Public Health* 22: 1261.
4. Flander L, Dekker E, Andersen B, et al. What can we learn from high-performing screening programs to increase bowel cancer screening participation in Australia? *Cancer Control* 29 early online.
5. Fogh K, Eriksen ARR, Hasselbalch RB, et al. Seroprevalence of SARS-CoV-2 antibodies in social housing areas in Denmark. *BMC Infectious Diseases* 22, 143.
6. Fogh K, Eriksen ARR, Larsen TG, et al. A cross-sectional study of SARS-cov-2 antibodies and risk factors for seropositivity in staff in day care facilities and preschools in Denmark. *Microbiology Spectrum* early online.
7. Gustafson LW, Hammer A, Bennetsen MH, et al. Cervical intraepithelial neoplasia in women with transformation zone type 3: cervical biopsy versus large loop excision. *BJOG* 129(13): 2132– 2140.
8. Gustafson LW, Tranberg M, Christensen PN, et al. Clinical utility of p16/Ki67 dual-stain cytology for detection of cervical intraepithelial neoplasia grade two or worse in women with a transformation zone type 3: A cross-sectional study. *BJOG* early online.
9. Gustafson LW, Larsen MB, Hammer A, et al. Levels of anxiety in women aged ≥ 45 years undergoing diagnostic large loop excision of the transformation zone: A longitudinal study. *BJOG* early online.
10. Hansen J, Kirkegaard P, Folmann B, et al. "I feel reassured, but there is no guarantee." How do women with a future childbearing desire respond to active surveillance of cervical intraepithelial neoplasia grade 2? A qualitative study. *Acta Obstetrica et Gynecologica Scandinavica* 101: 616– 623.
11. Helgestad ADL, Larsen MB, Njor S, et al. Three birds with one stone: a protocol for a randomised intervention study to increase participation in cervical and colorectal cancer screening among women attending breast cancer screening. *BMJ Open* 12: e062824.
12. Ivarsson L, de la Campa MAS, Elfving K, et al. Changes in testing and incidence of Chlamydia trachomatis and Neisseria gonorrhoeae the possible impact of the COVID-19 pandemic in the three Scandinavian countries. *Infectious Diseases* 54: 623-631.
13. Jørgensen SF, Andersen B, Petersen LK, et al. Adherence to follow-up after the exit cervical cancer screening test at age 60–64: A nationwide register-based study. *Cancer Medicine* 11: 224-237.
14. Kirkegaard P, Larsen MB, Andersen B. „It’s cancer screening after all“. Barriers to cervical and colorectal cancer screening and attitudes to promotion of self-sampling kits upon attendance for breast cancer screening. *Journal of Medical Screening* early online.
15. Kleif J, Jørgensen LN, Hendel JW, et al. Early detection of colorectal neoplasia: application of a blood-based serological protein test on subjects undergoing population-based screening. *British Journal of Cancer* 126: 1387-1393.
16. Larsen MB, Hedelund M, Flander L, Andersen B. The impact of pre-notifications and reminders on participation in colorectal cancer screening – A randomised controlled trial. *Preventive Medicine* 164, 107229.

17. Larsen MB, Stokholm R, Kirkegaard P, et al. Making decisions on your own: Self-administered decision aids about colorectal cancer screening – A systematic review and meta-analyses. *Patient Education and Counseling* 105(3): 534-546.
18. Larsen MB, Søborg B, Njor SH, et al. The relative effectiveness of fecal immunochemical test-based colorectal cancer screening to detect adenomas and cancer in different demographic and socioeconomic groups. A nationwide cohort study. *European Journal of Cancer Prevention* 31: 489-496.
19. Larsen PT, Rasmussen M, Njor SH. Data from the Nielsen et al. study does not support their suggestion. *Colorectal Disease* 24(1): 133-134.
20. Larsen PT, Jørgensen SF, Njor SH. Colorectal cancer screening participation among citizens not recommended to be screened: a cohort study. *BMC Gastroenterology* 22 (256).
21. Njor SH, Larsen MB, Søborg B, Andersen B. Colorectal cancer mortality after randomized implementation of FIT-based screening - a nationwide cohort study. *Journal of Medical Screening* early online.
22. Njor SH, Rasmussen M, Friis-Hansen L, Andersen B. Varying fecal immunochemical test screening cut-offs by age and gender: a way to increase detection rates and reduce number of colonoscopies. *Gastrointestinal Endoscopy* 95(3): 540-549.
23. Njor SH, Søborg B, Tranberg M, Rebolj M. Concurrent participation in breast, cervical, and colorectal cancer screening programmes in Denmark: A nationwide registry-based study. *Preventive Medicine* early online.
24. Olesen TB, Jensen H, Møller H, et al. Participation in the nation-wide cervical cancer screening programme in Denmark during the COVID-19 pandemic: An observational study. *eLife* 12: e81522.
25. Rebolj M, Sargent A, Njor SH, Cuschieri K. Widening the offer of human papillomavirus self-sampling to all women eligible for cervical screening: Make haste slowly. *International Journal of Cancer*: 1-12
26. van Wifferen F, de Jonge L, Worthington J, et al. Prioritisation of colonoscopy services in colorectal cancer screening programmes to minimise impact of COVID-19 pandemic on predicted cancer burden: A comparative modelling study. *Journal of Medical Screening* early online.
27. van Wijhe M, Fogh K, Ethelberg S, et al. Persistent symptoms and sequelae after severe acute respiratory syndrome coronavirus 2 infection not requiring hospitalization: Results from Testing Denmark, a Danish cross-sectional survey. *Open Forum Infectious Diseases* early online.

Additional publications

1. Danish Health Authority. Sundhedskompetence i det danske sundhedsvæsen [in Danish]. ISBN: 978-87-7014-466-7 (contributed Case 8).
2. Petersen LK, Gustafson LW, Hammer A, et al. Danish Society of Obstetrics and Gynecology (DSOG) Guideline: Forebyggelse, udredning og behandling af dysplasi på cervix [In Danish]. Under review, DSOG 2022
3. Rasmussen M, Andersen B, de Haas N, et al. Dansk Tarmkræftscreenings Database (DTS) – Resumé af Årsrapport 2020. *Ugeskrift for Læger*, 21. februar 2022.
4. Serizawa R, Waldstrøm M, Andersen B, et al. Dansk Kvalitetsdatabase for Livmoderhalskræftscreening (DKLS) - Resumé af Årsrapport 2021. *Ugeskrift for Læger*, 26. september 2022

Presentations (as presenting author) at national and international conferences and meetings

- **ANCR**

Association of Nordic Cancer Registries, Torshavn, September 14-16:

- The diagnostic work-up performed after a false-positive mammography screening reduces breast cancer risk sufficiently: A population register-based study. Oral presentation by Bayan Sardini.
- Colorectal cancer mortality after randomized implementation of FIT-based screening - a nationwide cohort study. Oral presentation by Mette Bach Larsen
- Effect of individualized cut-off values in colorectal cancer screening. Oral presentation by Sisse Njor
- Adherence to recommended follow-up after colorectal cancer screening. Oral presentation by Susanne Fogh Jørgensen
- Subsequent participation in organized FIT based screening after screen-derived colonoscopy – National register-based cohort study. Poster presented by Signe Bülow Therkildsen

- **Annual Research Meeting**

Department of Clinical Medicine, Aarhus, November 24:

- Acceptability of an intervention to increase participation in cervical and colorectal cancer screening among women attending breast cancer screening. Flash talk & poster presentation by Anne Dorte Lerche Helgestad
- Utility of DNA methylation for risk-stratification of women aged ≥ 45 referred for colposcopy. Poster presentation by Karen Oman Binderup

- **Danish Cancer Research Days**

Arranged by DCCC and DMCG, Kolding, August 26-27:

- Får kvinder over 60 år de anbefalede undersøgelser efter screening for livmoderhalskræft? Exceptional young scientist award winner and oral presentation by Susanne Fogh Jørgensen
- The diagnostic follow-up procedures after a false-positive mammography screening reduces breast cancer risk sufficiently: a register-based study. Selected flash talk by Bayan Sardini
- The SWIM study: Ethnic minority women's ideas and preferences for a tailored intervention to promote national cancer screening programmes. A qualitative interview study. Poster presentation by Camilla Rahr Tatari
- Utility of host-cell DNA methylation for risk-stratification of women aged ≥ 45 referred for colposcopy. Poster presentation by Karen Omann Binderup
- The impact of pre-notifications and reminders on participation in colorectal cancer screening – a randomised controlled trial. Poster presentation by Mette Bach Larsen
- Working collaboratively with vulnerable women to identify the best implementation gains by screening cervical cancer more effectively in European countries: CBIG-SCREEN, EC Horizon 2020. Poster presentation by Pia Kirkegaard
- Balancing risks: Qualitative study of attitudes, motivations and intentions about attending for mammography during the COVID-19 pandemic. Poster presentation by Pia Kirkegaard
- Perspectives on barriers and solutions to cervical cancer screening for vulnerable women across European countries, professions and social boundaries. Poster presentation by Rikke Buus Bøje

- **EUROGIN**

EUropean Research Organisation on Genital Infection and Neoplasia, Düsseldorf, May 10-13:

- Value of a catch-up HPV cervical cancer screening test to women aged 65 and above: a population-based non-randomized intervention study. Oral presentation by Mette Tranberg

- **ISDM**

International Shared Decision Making Conference, Kolding, June 19-22 June:

- Defining and measuring knowledge in cancer screening – is there a need for new information materials? Oral presentation by Rikke Nicoline Stokholm

- **PhD Day**

Arranged by the PhD Association and Graduate School of Health, Aarhus University, June 24:

- Research protocol: Can we kill three birds with one stone? A randomised controlled trial to increase participation in cervical and colorectal cancer screening. Oral poster presentation by Anne Dorte Lerche Helgestad
- Incidence of colorectal cancer and advanced adenomas at surveillance colonoscopy in the Danish FIT-based screening program: A nationwide register-based cohort study. Oral poster presentation by Pernille Thordal Larsen
- How much does mammography screening reduce breast cancer mortality among breast cancer survivors? Flash talk by Bayan Sardini

- **Research Symposium**

Randers Regional Hospital's Annual Research Symposium, Randers, November 28:

- Acceptability of an intervention to increase participation in cervical and colorectal cancer screening among women attending breast cancer screening. Oral and poster presentation by best poster award winner Anne Dorte Lerche Helgestad
- An evaluation of the viral load of high-risk human papillomavirus (HPV) reflected by the cycle threshold value (CT-value) in cervical samples as a triage test in HPV-screen positive women. Flash talk and poster presentation by Anna Emilie Atterdag Krarup
- The use of first-void urine as a cervical cancer screening tool. Flash talk and poster presentation by Ellen Cunningham Ogilby
- Utility of DNA methylation for risk-stratification of women aged ≥ 45 referred for colposcopy. Flash talk and poster presentation by Karen Oman Binderup
- Subsequent participation in organized FIT based screening after screen-derived colonoscopy – a national register-based cohort study. Flash talk and poster presentation by Pernille Thordal Larsen
- The development of a stakeholder engagement tool for vulnerable groups of women in cervical cancer screening. Flash talk and poster presentation by Rikke Buus Bøje
- The psychometric properties of instruments to measure knowledge in population-based cancer screening targeting individuals at average risk: a systematic review. Flash talk and poster presentation by Rikke Nicoline Stokholm
- Acceptance and preference of self-collected urine and vaginal samples for HPV testing in a referral population: A cross-sectional study. Flash talk and poster presentation by Sofie Meyer Andersen
- Adherence to recommended follow-up after colorectal cancer screening. Flash talk and poster presentation by Susanne Fogh Jørgensen

Public communication

Press releases and social media

In University Research Clinic for Cancer Screening, we strive to communicate our research to the general public and to contribute constructively to the public debate.

We communicate our research – in particular new projects and results – to research and health care professionals through regular press releases, our personal LinkedIn profiles as well as Randers Regional Hospital's LinkedIn profile. We also update the public of relevant research news through the Hospital's Facebook profile.

Examples of press coverage in national media this year

1. „Faldende deltagelse i livmoderhalskræftscreening“. Participation in segment on the 19:30 News TV2 Østjylland January 19.
2. „Flere og flere kvinder bestiller ikke tid til undersøgelse for livmoderhalskræft: Nu gør regioner klar til hjemmeprøver“. Seneste Nyt DR January 19.
3. „Dansk seniorforsker får særlig opgave for WHO“. Sundhedsmonitor March 17.
4. „Seniorforsker Pia Kirkegaard, Universitetsklinik for Kræftscreening, Afdeling for Folkeundersøgelser, Regionshospitalet Randers, er ansat af WHO til en særlig opgave...“. Medicinske Tidsskrifter May 3.
5. „Det er meget markant: Kræft-program har reddet særligt mange indenfor denne gruppe“. Lokalavisen.dk August 1.
6. „En afføringsprøve reddede Ib fra at dø af tarmkræft“. DR August 1.
7. „Undgå besøg hos lægen: Nu kan kvinder teste sig selv for kræft“. TV MIDTVEST August 30.
8. „Hvert år dør 100 danske kvinder af livmoderhalskræft – det tal kan sænkes: Nu er der godt nyt for dig der frygter en tur på briksen til celledækning“. JP Viborg August 30.
9. „Hospital får 9 mio. kroner til forskning på kræftområdet“. JP Randers September 20.



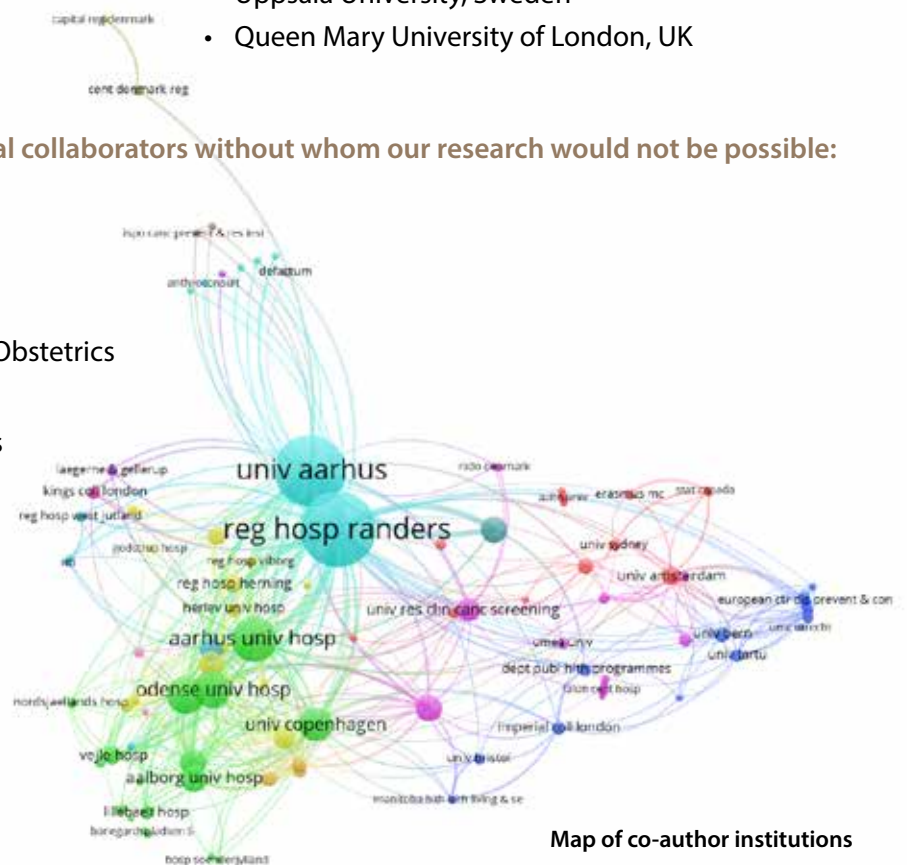
Collaboration

A huge thanks to all our collaborators – longstanding as well as new!

- Aarhus University
- Aarhus University Hospital
- American Cancer Society, USA
- Association of European Cancer Leagues, Belgium
- Azienda Unita Sanitaria Locale Di Reggio Emilia, Italy
- Bispebjerg University Hospital
- Copenhagen Business School
- European Institute of Women's Health, Ireland
- Finnish Cancer Registry
- Gødstrup Regional Hospital
- Health Psychology Research Centre, Bulgaria
- Horsens Regional Hospital
- Hvidovre Hospital
- INSERM, France
- ISPUP, Portugal
- IARC, France
- Karolinska University, Sweden
- King's College London, UK
- London School of Hygiene and Tropical Medicine, UK
- McGill University, Canada
- Medical Practice Brogaard & Skibsted
- National Cancer Institute, USA
- Norwegian Cancer Registry
- Nykøbing Falster Hospital
- Odense University Hospital
- Paris School of Economics (PSE), France
- Randers Regional Hospital
- Reference Centre for Epidemiology and Cancer Prevention, Italy
- Research Unit for General Practice, Aarhus
- Rigshospitalet
- Statens Serum Institut
- The Oncology Institute „Prof. Dr. Ion Chiricuță“, Romania
- Trinity College Dublin, Ireland
- Universitatea Babes Bolyai, Romania
- University of Copenhagen
- University of Antwerp, Belgium
- University of Heidelberg, Germany
- University of Melbourne, Australia
- University of Tartu, Estonia
- Uppsala University, Sweden
- Queen Mary University of London, UK

And a special thanks to our close clinical collaborators without whom our research would not be possible:

- Randers Regional Hospital
 - Laboratory Unit
 - Department of Surgery
 - Department of Gynaecology and Obstetrics
- Aarhus University Hospital,
 - Department of Infectious Diseases
- All Regional Gynaecological, Surgical and Radiology Departments



Map of co-author institutions