

CENTRE FOR ANTIBIOTIC RESISTANCE RESEARCH IN GOTHENBURG

# CARe

#### ACTIVITY REPORT 2022-23



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"Our breadth puts us in a unique position to deliver new solutions to a growing health problem that causes more than a million deaths per year"

# Where we are TODAY

# WORDS FROM THE CENTRE DIRECTORS

Since the launch in 2016, CARe has become a well-recognized actor on both the national and international arenas. Our members have been highly successful in attracting grants, producing high quality science, and in several instances also in bringing research into global policy or clinical practice.

2022 was the last year that CARe was funded by the UGOTchallenges initiative. However, there is a shared ambition between the Sahlgrenska academy and the Faculty of Science at the University of Gothenburg, Chalmers University of Technology, the Västra Götaland Region, and the Sahlgrenska University Hospital to increase collaboration within the life science area. During 2022, the leadership of these organizations identified antibiotic resistance as an important, common challenge where options for increased collaborations should be pursued further. Scientists at CARe had, in parallel, started discussions on joining forces and expand CARe. This resulted in a re-start of CARe in 2023, supported financially by all of the above organizations. A slight name change from "...at University of Gothenburg" to "...in Gothenburg" was needed to reflect the new organization, while the old acronym was kept!

CARe is, as previously, hosted by the Institute of Biomedicine at the Sahlgrenska academy. The expanded centre hosts 155 active researchers from 18 departments. To our best knowledge, this makes CARe the broadest, most multi-disciplinary research centre on antibiotic resistance in the world. Given the highly complex nature of this global challenge, our breadth also puts us in a unique position to deliver new solutions to a growing health problem that currently causes more than a million deaths per year.

Recent activities, as laid out in this report, illustrate that CARe plays an important role in several arenas, not just producing scientific papers. As director and co-director, we are grateful for the confidence given to help developing CARe further.

Joakim Larsson and Michaela Wenzel





# ABOUT CARe

CARe represents a collaborative venture between the University of Gothenburg, Chalmers University of Technology, the Västra Götaland Region, and the Sahlgrenska University Hospital.

This interdisciplinary initiative bridges healthcare, academia, and regional stakeholders with a joint vision to limit mortality, morbidity and socioeconomic costs related to antibiotic resistance on a global scale through research.

CARe provides a regional network that facilitates cross-disciplinary interactions and collaborations

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Life Sciences Architecture and Civil Engineering Chemistry and Chemical Engineering Mathematical Sciences





# RESEARCH

CARe was originally structured to cover all priority research topics as identified by the The Joint Programming Initiative on Antimicrobial Resistance, JPIAMR; diagnostics, surveillance, transmission, environment, therapeutics and interventions, in order to enable a holistic approach to the global antibiotic resistance challenge. But what makes CARe truly unique is that we address this broad set of priority topics by integrating competence from an even broader panel of scientific disciplines. With the expansion from 2023, in particular the inclusion of many research groups from Chalmers University of Technology, the span of research questions, approaches and interdisciplinary collaborations has increased further.

Research results are primarily communicated by the members through peer-reviewed scientific publications and some are highlighted on the centres communication channels, including our website (<u>https://www.gu.se/en/care</u>).

A few selected research outputs are listed below:

- Per Daniel Sundvall, Ronny Gunnarsson, Ingmarie Skoglund and Egill Snaebjörnsson Arnljots have contributed to the development of a new decision tool than can reduce the use of antibiotics for urinary tract infections by half, while still ensuring patient safety.
- Research led by Fredrik Westerlund demonstrated feasibility of strain-level bacterial typing directly from patient samples using optical DNA mapping
- In 2022, Joakim Larsson and Carl-Fredrik Flach published a review article on Antibiotic Resistance in the Environment in Nature Reviews Microbiology. With more than 900 citations just two years after its publication, it has rapidly become the most frequently cited scientific review in the field.
- Research led by Erik Malmqvist has presented both moral and practical arguments why the praised "polluters pay principle" will be difficult to apply to effectively address environmental pollution with pharmaceuticals from human use.
- Advanced computational analyses of bacterial genetic material by the group of Erik Kristiansson have uncovered a plethora of new mobile antibiotic resistance genes, some of which are present in pathogens.
- Research from the Anne Farewell group showed surprising effects of copper, a common antibacterial agent, in that it can suppress the spread of antibiotic resistance under certain circumstances.

The yearly, internal conferences arranged by CARe, spiced with a few prominent invited external speakers, have become imperative for enabling new research collaborations and to widen everyone's perspective on the AMR challenge. We foresee that this will continue to be a central part of our activities in the future as well.

In 2023, CARe arranged the largest international research meeting in the world on environmental dimensions of antibiotic resistance, attracting attendants from 41 countries. The conference was also co-funded and welcomed by the Västra Götaland Region/City of Gothenburg.

# IMPACT AND COMMUNICATION



United Nations' "High Level Ministerial Meeting on Antimicrobial Resistance", Oman, November 2022, with invited representation from CARe. The objective of the meeting was to prepare an agenda for the United Nations Global Assembly meeting in September 2024. The meeting was attended by over 50 governments. Photo: Anna Strömgren / Swedish Government

#### POLICY AND PRACTICE

With representation in the scientific advisory board of the Joint Programme Initiative on AMR, CARe has contributed to a Strategic Research and Innovation Agenda for the "European Partnership on One Health AMR". This document is anticipated to guide directed research calls and other activities in ca 30 countries in the coming decade.

Expertise from CARe was invited to the High-Level Meeting on AMR in Stockholm in 2023 under the Swedish Presidency to help capturing discussions and debates.

Our director has been appointed as an adviser to Lena Hallengren and subsequently, Jakob Forssmed, the Swedish Ministers of Social Affairs, in their capacity as members of the <u>"Global Leaders Group on AMR."</u> This advisory role is shared with two other Swedish researchers, Otto Cars and Susanna Sternberg-Lewerin.

CARe researchers also contributed to the comprehensive UNEP report "<u>Bracing for Superbugs: Strengthening environmental action in the One Health response to antimicrobial resistance</u>".



In 2023. Joakim Larsson was awarded the first national prize in effective research communication by Örebro University and the Hamrin Foundation

CARe has provided support to the Swedish Environment Agency on aspects related to expected mandatory sewage surveillance of AMR in the EU as well as the Swedish Medicines Agency in their ongoing work to revise the generic substitution system to also take into account pollution control during manufacturing in reimbursement decisions.

CARe has contributed to the <u>WHO Global Research Agenda for</u> Antimicrobial Resistance in Human Health published in 2023.

As a direct result of earlier research on antibiotic pollution from drug manufacturing by CARe members, the WHO is now developing an <u>international guidance on antibiotic emissions</u>. Joakim Larsson is supporting the WHO in the process.



#### WEBSITE



#### CARe's website has had over 14000 visitors from 113 countries during 2022-23

On the website we present a comprehensive overview of the centre's activities, goals, and contributions to the field of antibiotic resistance research. We also advertise career opportunities, news, events and webinars etc.





#### MEDIA - a selection

- Swedish Radio 2023-01-23 <u>Nya forskningsgruppens dröm: Hitta antibiotika mot resistenta bakterier</u>
- Wired, 2023-02-07 The antibiotic-resistance crisis has a troubling twist
- Dagens medisin, 2023-02-13 <u>Antibiotikaresistente bakterier truer både helsa og verdensøkonomien</u>
- Dagens medicin 2023-05-16 Oroande för sjukvårdssystemet med olika regeltolkningar
- Läkemedelsvärlden, 2023-02-15 Slående starkt stöd för nya miljökrav
- Ny Teknik, 2023-02-09 FN-rapport: Så kan resistenta bakterier stoppas
- Göteborg & co, 2022-12-15 Ambassadörerna som lyfter mötesstaden Göteborg
- Läkemedelsvärlden, 2022-06-14 Industrin sätter standard för utsläpp på egna villkor



#### PODCASTS

- <u>One Health Trust podcast Poops and Pathogens with Professor Joakim Larsson</u>
- <u>Microbiology Lab pod Environmental antibiotic resistance with Johan Bengts-</u> <u>son-Palme, Emil Burman, Anna Abramova, Marcus Wenne, Mirjam Dannborg and</u> <u>Agata Marchi</u>
- <u>AMR Studio podcast Carl-Fredrik Flach & sewage surveillance. Water chlorination</u> <u>& microbiome. C. difficile spread between humans & animals</u>
- <u>AMR Studio podcast Björn Rönnerstrand & political sciences. Non-prescribed antibiotic acquisition. Prescribing consensus. Contextual factors for prescribing</u>

### PUBLIC DEBATE

- Pharmaceutical Pollution from Human Use and the Polluter Pays Principle
- Djurhållning och antibiotika: en gyllene triangel! Albatross
- Låt skiten löpa! Albatross
- <u>I ett friskare samhälle är vi sjukare</u> Albatross
- Sverige har en chans att påverka antibiotikans framtid Dagens Medicin
- Oroande för sjukvårdssystemet med olika regeltolkningar Dagens Medicin

# EXAMPLES OF OTHER STAKEHOLDER INTERACTIONS

- Lecture and guided lab experiments for high school students prompted by Antibiotikasmart Sverige and RISE Research Institutes of Sweden (M Wenzel)
- Learning from nature's design From antimicrobial siderophore-drug conjugates, novel griselimycin derivatives and artificial glucosinolates talk at AstraZeneca (P Klahn)
- Seminar at the infectious disease clinic at the Östra Hospital (VGR): "Predicting antibiotic resistance using AI (A Johnning)
- Antibiotikapolitik idag och imorgon, panel discussion at the Festival of Science (E Malmqvist, B Rönnerstrand and D Carelli)
- Presentation of CARe's research on wastewater surveillance to the Surveillance Technical Working Group, which reports to South Africa's Ministry of Health's Advisory Committee on AMR (Ministerial Advisory Committee on AMR) (C-F Flach)
- Supporting the Swedish Environment Agency on aspects related to expected mandatory sewage surveillance of AMR in the EU (J Larsson)
- Presentation of CARe at seminar arranged by Axfoundation (J Larsson)



- Panelist at UN-led webinar on One Water One Health (J Larsson)
- Speaker at UN-led webinar on Antimicrobial Resistance in the Environment (J Larsson)

• Speaker at Antibiotikaforum 2023 arranged by the Public Health Agency of Sweden and the Swedish Board of Agriculture (J Larsson)

• Training of the leadership of the German Federal Environment Agency (UBA) on issues related to environmental and antibiotic resistance (J Larsson)

# SCIENTIFIC MEETINGS ARRANGED BY CARe

#### EDAR6, 2022

The 6th International Conference on the Environmental Dimension of Antibiotic Resistance, EDAR6 welcomed 325 participants from 41 countries to Gothenburg. The meeting lasted six days, and was given in hybrid-format (onsite and online). Keynote speakers were Andrea Hinwood, chief scientist at UNEP, and Kim Lewis, the developer of the iChip and discoverer of teixobactin







Aslan Akbas, Mayor of Gothenburg expresses his gratitude to centre director Joakim Larsson for contributing to making the city an attractive place for meetings

#### CARe ANNUAL MEETING 2022

Over 90 CARe scientists from GU and Chalmers participated in during the theme-based sessions over two days in May 2022s. The keynote speakers, Professor Thomas Van Boeckel, Dep. of Environmental Systems Science, ETH Zürich, and Associate Professor, Pamela Yeh, Dept. of Ecology and Evolutionary Biology, UCLA, gave much-appreciated talks about their work.



Pär-Daniel Sundvall gives a talk at CARe's annual meeting 2022

#### CARe ANNUAL MEETING 2023

This meeting took place in May and gathered 95 researchers who listened to 18 speakers on the main topics of:

- Politics, initiatives and interventions
- Therapeutics and materials
- AMR and microbiology
- Environmental surveillance and diagnostics

The keynote speakers were Malin Grape (Sweden's Ambassador on Antimicrobial Resistance and Gunnar Kahlmeter.

#### CARe WORKSHOP 2023

Mitigating Emerging Threats from Resistant Bacterial Infections in Association with Medical Devices



Margarita Trobos and Martin Andersson, hosts of the workshop Mitigating Emerging Threats from Resistant Bacterial Infections in Association with Medical Devices

This CARe workshop, held in December 2023, attracted 66 participants and aimed to foster dialogue, share insights, and spur innovations in combatting bacterial infections, particularly those associated with medical devices.

Topics: The utilization of medical devices and challenges in combatting infections and Identification of strategies and material-related challenges in combatting infections

Presentations were given by numerous companies and organizations active in the Västra Götaland Region, including Oticon Medical, Mölnlycke Healthcare, ESSITY, Neoss, Amferia, Promimic and RISE.

#### WEBINARS

#### EDAR6 Countdown webinars, 2022

- Profesor Ed Topp, EDAR1 to EDAR6, what progress has been made?
- Professor Yong-Guan Zhu, AMR in soil-plant systems
- Professor Kornelia Smalla, <u>Plasmid-mediated adaptation of soil and plant bacteria to</u> <u>antibiotics introduced via organic fertilizers into plant production systems</u>
- Professor James Tiedje, Drilling down on environmental ARG risk
- Professor Tong Zhang, <u>Assess the risk of antimicrobial resistance genes using meta</u> <u>genomics methods</u>
- Professor Joakim Larsson, <u>An overview of the environment's role in evolution, trans-</u> mission and surveillance of antibiotic resistance

#### **EMBARK Topics 2022**

- On the environment's role in evolution, transmission and surveillance of antibiotic resistance
- Host and vehicles of antibiotic resistance genes in urban sewage
- Genomic surveillance of human-invasive Salmonella in Nigeria
- Understanding and predicting resistance in Bacteroides fragilis group bacteria using clinical and modern genomics tools
- Antimicrobial resistance in a UK dairy farm
- Invasion dynamics of AMR bacteria into microbiomes under stress
- Towards the development of CRISPR-Cas based tools to remove AMR from microbial communities
- CRISPR-Cas antimicrobials: Resistance mechanisms
- Global database of ARGs in the environment
- Meta-analysis reveals the global picture of antibiotic resistance gene prevalence across environments
- Implementing citizen-based projects on Antimicrobial Resistance Awareness in Southern Europe: the experience from MicroMundo
- From AMR surveillance to research in the French veterinary sector
- AMR in aquaculture- Averting the crisis and the way forward



Johan Bengtsson-Palme, host of the EMBARK webinars, photo: Chalmers University of Technology



#### EMBARK WebinarTopics 2023

- AMR Surveillance in aquatic environments
- ARG annotation
- Strategies for AMR surveillance with a One Health approach
- Molecular and culture based methods for AMR surveillance in aquatic environments and animals
- AMR: a link between clinical settings and other environments
- Ecology and evolution of ARGs: From surveillance to intervention strategies

# ORGANIZATION

#### MANAGEMENT

Professor Joakim Larsson Centre director, Institute of Biomedicine, University of Gothenburg

Associate professor Michaela Wenzel Deputy centre director of CARe, Department for Life Sciences, Chalmers University of Technology

Coordinator Lovisa Aijmer Institute of Biomedicine, University of Gothenburg

#### STEERING COMMITTEE

Professor Erik Kristiansson Chair of CARe steering committee, Department of Mathematics, Chalmers University of Technology

Professor Joakim Larsson Centre director of CARe Institute of Biomedicine, University of Gothenburg

Associate professor Michaela Wenzel Deputy centre director of CARe, Department for Life Sciences, Chalmers University of Technology

Associate professor Anne Farewell Department of Chemistry and Molecular Biology, University of Gothenburg

Professor Martin Andersson Department of Chemistry and Chemical Engineering, Chalmers University of Technology

Assistant professor Alesia Tietze Department of Chemistry and Molecular Biology, University of Gothenburg

Birgitta Vallhagen Head of administration, Institute of Biomedicine, University of Gothenburg

Researcher Björn Rönnerstrand The SOM Institute, University of Gothenburg



Associate professor Carl-Fredrik Flach Institute of Biomedicine, University of Gothenburg

Professor Christian Munthe Department of Philosophy and Logics, University of Gothenburg

Professor, Christina Åhrén Strama network, Västra Götaland Region and the University of Gothenburg

Associate professor Elina Lampi Department of Economics, University of Gothenburg

Professor Fredrik Westerlund Department of Life Sciences, Chalmers University of Technology

Assistant professor Johan Bengtsson Palme Department of Life Sciences, Chalmers university of Technology

Associate professor Margarita Trobos Department of Biomaterials, University of Gothenburg

#### **REFERENCE GROUP**

Dr Gunnar Kahlmeter Former President of European Society of Clinical Microbiology, former director of EUCAST and much more

Dr Camilla Björn Leader of the focus area Infection Management at RISE, and co-leader of Antibiotikasmart Sverige

Dr Leif Dotevall Deputy Infection Control Physician, Västra Götaland Region

Susanne Tumlin Head of Development, Gryaab

Dr Martin Johansson Senior Director, Oticon Medical

# NEW EXTERNAL GRANTS

#### - A SELECTION

Johan Bengtsson Palme has received more than 50 million SEK in new external grants in 2022-23. This includes a tenure-track position package from DDLS (Data-Driven Life Science) worth 17 million SEK, and another 15 million SEK from Vinnova for research on predicting pathogenicity and antibiotic resistance. Additionally, with his project SEARCHER, Bengtsson-Palme secured 21.4 million SEK from JPIAMR for studying emerging antimicrobial resistance in the environment.

Erik Kristiansson was awarded two grants, one of 3.5 million SEK from JPIAMR for developing new biosensors and AI techniques for diagnosing infections caused by antibiotic-resistant bacteria, and another of 4 million SEK from the Swedish Research Council for exploration of new resistance genes against antibiotics.

Anna Johnning received 3.5 million SEK from JPIAMR for a project to define E. coli diversity in complex samples, and another 9 million SEK from Erling Persson Foundation as a co-applicant for developing next-generation diagnostics of bacterial infections.

Anne Farewell's research on genomic surveillance of resistance genes against new antibiotics was funded with 3.5 million SEK from JPIAMR while Åsa Sjöling obtained 4 million SEK from the Swedish Research Council for her work on new virulence factors in E. coli.

Margarita Trobos was granted 3 million SEK from the Swedish Research Council for strategies against antibiotic-resistant biofilms in orthopaedic device-related infection.

Joakim Larsson received 3 million SEK from FORMAS and 4.5 million from Regional ALF funds for research on selection of multi-resistant bacteria in hospital wastewater.



Johan Bengtsson-Palme, Erik Kristiansson and Anna Johnning received grants from JPIAMR. Photo: Susanne Nilsson Lindh

# DOCTORAL THESES

- Karin Rystedt 2023, <u>Respiratory tract infections in primary care aspects of diagnosis</u> <u>and treatment</u>
- Matilda Emgård 2023, <u>Antibiotic use and respiratory pathogens with focus on Streptococcus pneumoniae in Tanzanian children</u>
- Juan Inda Diaz 2023, New AI-based methods for studying antibiotic-resistant bacteria
- Jon Edman Wallér 2023, Clostridioides difficile infections: Preventive strategies
- Erik Gerner 2022, <u>The role of sodium salicylate as a virulence inhibitor for soft tissue</u> <u>infections</u>

# EDUCATION



Pedagogical prize-winner Anne Farewell has successfully coordinated the development of CARe-courses Photo: Johan Wingborg

Although CARe's has a strong research focus, our members are highly active in teaching about antibiotic resistance at many undergraduate and graduate programmes. Some teaching is cross-disciplinary, for example education on ethical aspects connected to antibiotic usage at several courses and programs at the Sahlgrenska academy, and also antibiotic resistance challenges from a medical and environmental perspective taught to students at School of Business, Economics and Law.

CARe has developed a 3-credit bachelor course which addresses basic biology, approaches to limit the development of antibiotic resistance, environmental dimensions and new antibiotic drug development.

CARe also offers a very popular free online course called "The Problem of Antibiotic Resistance". The course cover the scientific basics behind the antibiotic crisis and gives insights into new research and possible solutions. In 2023, 320 students registered for the course. More than 2300 students have taken the course since the start.

CARe contributes to the National Doctoral Programme in Infection and Antibiotics, (ND-PIA). Carl-Fredrik Flach from CARe was one of the co-organizer for a well-attended course held just outside Gothenburg, attracted both local, national and international students and teachers.

# FINANCIAL STATEMENT

The following is a summary of income and expenditures in 2023, i.e. since the expansion of CARe. Note that the summary only covers administration, communication (internal and external), stakeholder interactions and related activities. The members are responsible for their own research budgets.

Total income 2023 (SEK)	1 533 830
- from Sahlgrenska University Hospital	240 000
- from Institute of Biomedicine, University of Gothenburg	374 300
- from Faculty of Science, University of Gothenburg	240 000
- from Chalmers University of Technology	300 000
- from Region Västra Götaland	379 530
Total expenditures 2023 (SEK)	-1 261 321
- personnel	-693 113
- running costs	-362 685
- out of which are travel costs	-50 924
- indirect costs (overhead)	-205 523
Result 2023 (SEK)	272 509

# PUBLICATIONS

#### 2023

Ahmed M. Kamal El-sagheir, Ireny Abdelmesseh Nekhala, Mohammed K. Abd El-Gaber, Ahmed S. Aboraia, Persson J, Schäfer AB, Wenzel M, and Farghaly A. Omar (2023). N4-Substituted Piperazinyl Norfloxacin Derivatives with Broad-Spectrum Activity and Multiple Mechanisms on Gyrase, Topoisomerase IV, and Bacterial Cell Wall Synthesis doi.org/10.1021/acsbiomedchemau.3c00038

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