Amsterdam UMC

IMPROVING HEALTH

CIRCLE OF LIFE

AMSTERDAM REPRODUCTION AND DEVELOPMENT

ANNUAL REPORT 2023

2023

REPRODUCTION

SOCIETAL IMPACT

DEVELOPMENT

RESEARCH

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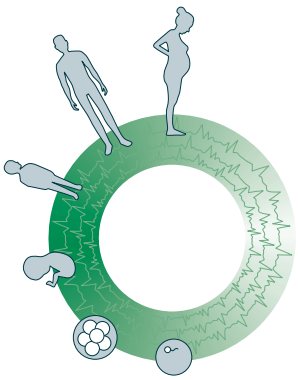

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A word from the directors

We are proud to present the 2023 Annual Report of the Amsterdam Reproduction and Development research institute. This report showcases the dedication and collective expertise of our researchers, clinicians, and support staff, who tirelessly pursue answers to some of the most pressing questions in reproductive health and development. Thanks to their perseverance, our institute continues to advance knowledge and unravel the mysteries of conception, embryonic and child development and beyond. We extend our gratitude to Tessa Roseboom, our former director, for her inspiration and dedication to AR&D!

In 2023, the annual AR&D retreat theme was “ALL ABOA&RD”, featuring an inspiring and fruitful program organized by our enthusiastic retreat committee of young researchers. Our institute values diversity, inclusion and connectedness, encouraging researchers to engage with colleagues from different disciplines, and to be open to and inspired by other perspectives and points of view. This report highlights our institute’s commitment to team science, supported by the grants awarded, which link various departments and disciplines to ensure coherent scientific progress.

We are excited to introduce some of our PhD researchers and their supervisors, share successes from the past year, and introduce three newly appointed AR&D professors. We hope you find the highlights of 2023 interesting!

Lidewij Henneman & Sebastiaan Mastenbroek
Directors of Amsterdam Reproduction & Development

Starting the Circle of life

The Amsterdam Reproduction and Development (AR&D) research institute is unique in its goals and ambition. Amsterdam UMC is the only academic medical center in the Netherlands with a research institute focusing on reproduction and development. Amsterdam Reproduction and Development is one of the eight research institutes of Amsterdam UMC, and as such associated with both the University of Amsterdam and Vrije Universiteit Amsterdam.

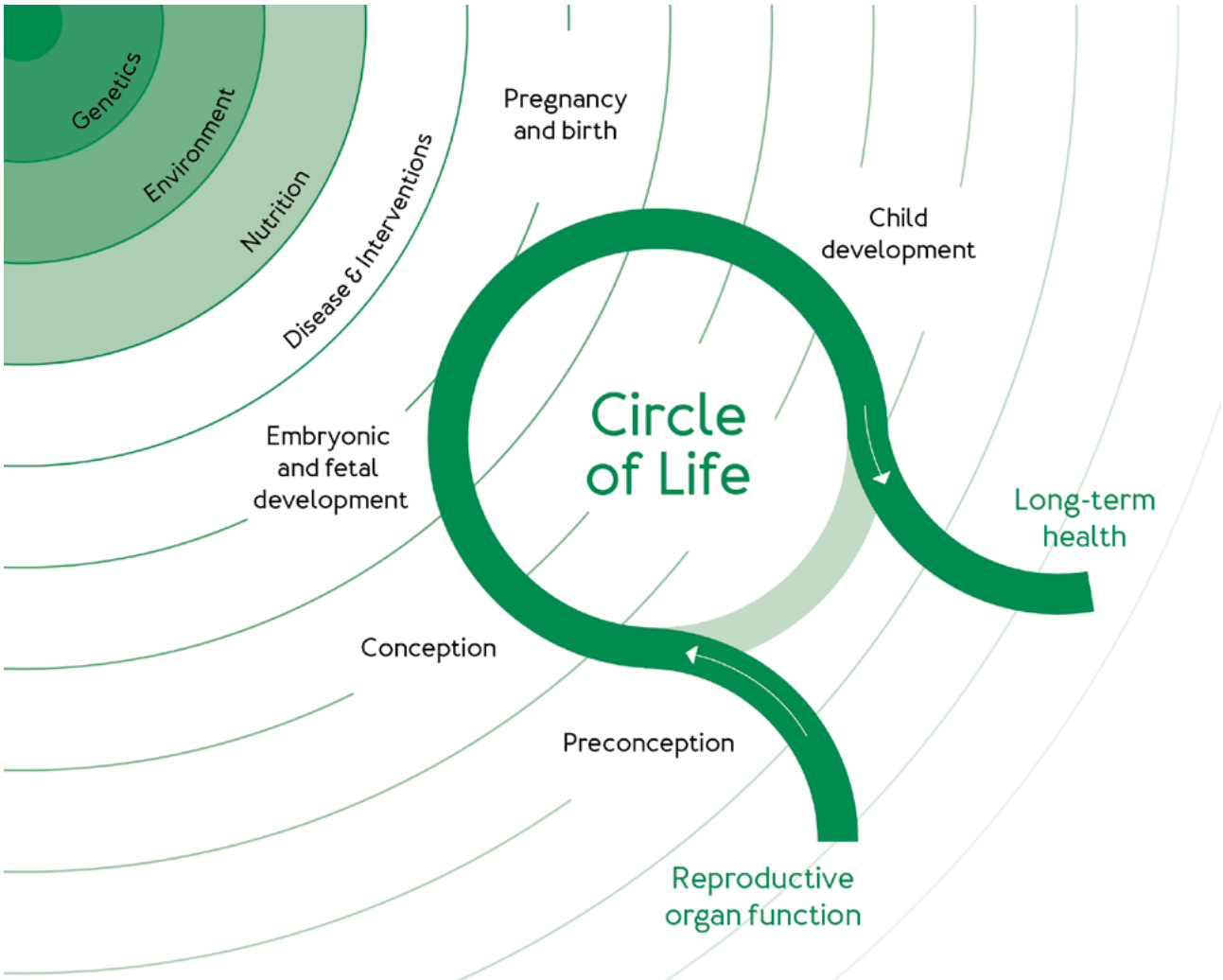
AR&D covers four research areas across the human life cycle: preconception and conception, embryonic and fetal development, pregnancy and birth, and child development. We host scientists from various backgrounds, including basic researchers, epidemiologists, psychologists, social and behavioral researchers, as well as clinicians and clinical laboratory specialists that are active in both clinical care and (pre)clinical research. Our research spans basic science, translational, clinical and epidemiological research, with a strong focus on scientific excellence and societal relevance.

For more information please visit the website of AR&D: www.amsterdamumc.org/ard.

MISSION AND VISION

Our mission is to advance knowledge in all aspects of human reproduction and development through interdisciplinary team science, aiming to improve health, from preconception to adulthood, for current and future generations.

We are inspired by a vision of continuous and sustainable improvement in health for all. We aspire to lead in fundamental, translational, and clinical science and public health research in human reproduction and development, creating a knowledge hub to guide science that serves society.



Research Areas

FROM PRECONCEPTION TO CHILD DEVELOPMENT

PRECONCEPTION AND CONCEPTION

Amsterdam Reproduction and Development supports optimal and evidence-based care for those wishing to conceive, now or in the future. We evaluate whether and how innovative genetic and reproductive techniques should be ethically weighed and implemented. We study the process of spermatogenesis, oogenesis, and the earliest stages of embryo development, from fertilization to implantation, to translate this knowledge into new diagnostics and therapies.

EMBRYONIC AND FETAL DEVELOPMENT

Humans all originate from a single cell, the fertilized oocyte, and develop through a fascinating, highly orchestrated process to become the individuals that we currently are. We study how these processes are regulated, how perturbations lead to congenital abnormalities or (late-onset) disorders, and the effect of genetic and environmental factors on development.

PREGNANCY AND BIRTH

Amsterdam Reproduction and Development is dedicated to deliver the best possible care for prospective parents and their children. We conduct multicentre clinical trials to assess the benefits of targeted interventions in obstetrics, midwifery and neonatology. Our research includes cohort and registry studies, some spanning multiple generations. We examine the requirements for the responsible implementation of technical advancements in prenatal screening and diagnostics. Additionally, we focus on reducing the incidence of preterm birth, and the prevention of morbidity of mother and child in high-risk pregnancies. To ensure every child has the best possible start in life, we investigate how various environmental factors influence human development from a single cell to a fully formed individual and its long-term health outcomes.

CHILD DEVELOPMENT

Healthy child development is a crucial foundation for a lifetime of health and wellbeing. Our research includes long-term development of children conceived via assisted reproductive techniques and the prevention of infertility already at young age. We study the effects of disease and treatment on children's development, considering physical, psychosocial and behavioral aspects, including for those who have spent part of their early life in hospital. With technological advancement, we aim to optimize genetic diagnosis in children. We monitor development and track individuals, as they become the parents of the next generation, continuing the circle of life recommences.

“Improving
health across
the lifecycle”

RESEARCH AT AR&D

SARAH VAN DEN BERG AND BERBER KAPITEIN
Disparities influencing health

JANTINE VAN VOORDEN AND GIJS AFINK
New tools to investigate early placenta development

ANOUK GROENEWEGEN AND LOTTE HAVERMAN
The importance of PROMs in clinical practice

JESKE BIJ DE WEG AND MARJON DE BOER
Aspirin in pregnancy


“We need to work together with our patients and their caregivers. Meet them at their homes.”

SARAH VAN DEN BERG AND BERBER KAPITEIN

Disparities influencing health

NOT ONLY TREATING THE DISEASE BUT ALSO THE CIRCUMSTANCES AGGRAVATING THE DISEASE

The number of children growing up in poverty in the Netherlands is increasing, with an estimated 230.000 children living under the poverty line according to the CPB Netherlands Bureau for Economic Policy Analysis. Poverty has a large impact on a child's (respiratory) health, influencing all social determinants of health. For example, increased food prices contribute to poorer nutritional status. Furthermore, the energy crisis leads to cold houses, increasing risks of respiratory infections and subsequent asthma attacks.

Sarah van den Berg

Berber Kapitein

This is exacerbated by overcrowded housing, poor ventilation, formation of mold and house dust mite proliferation. There is also a higher likelihood of tobacco smoke exposure from parents experiencing financial strain. International studies have shown that children growing up in vulnerable circumstances, such as an extremely poor household, are more likely to have severe asthma, with a doubled risk of a PICU admission. The accessibility of a health care system also seems to be important. However, how all these factors collectively influence childhood asthma is unknown. Dr. Berber Kapitein and Sarah van den Berg are determined to shed more light on these matters and create awareness among policymakers to implement interventions not only for individual patients, but also for the entire community.

BREATHPRINT

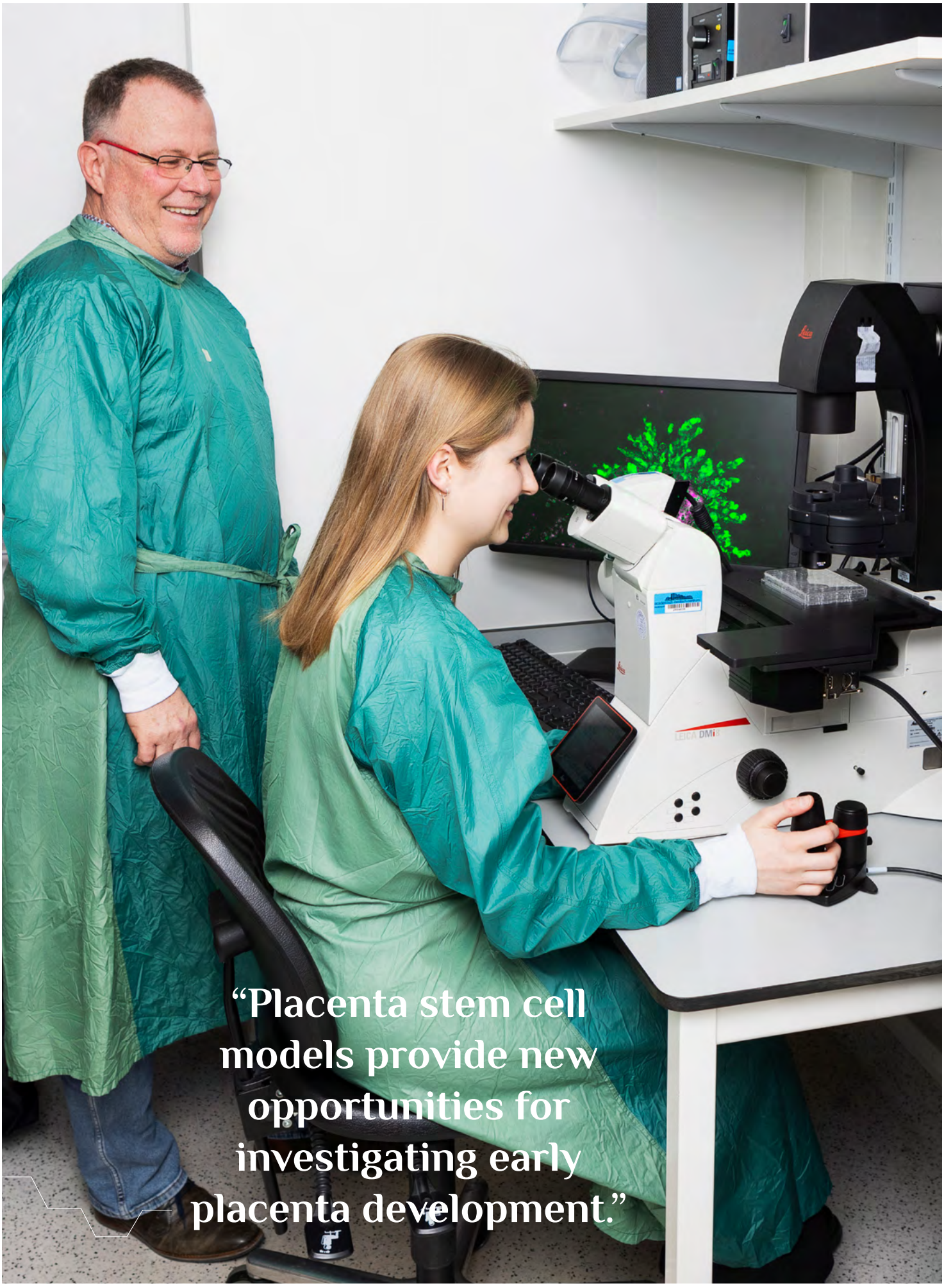
At the pediatric intensive care unit (PICU) the most severe exacerbations of asthma are seen, where admissions have been increasing since 2006 without a known cause. Berber and Sarah examine severe asthma at different levels. First, they have established a cohort of acute asthma cases at Emma Children's Hospital and are investigating different biomarkers to better understand what type of asthma is seen at the PICU. They do so in close collaboration with the research group Precision Medicine in Respiratory Diseases led by Prof. Anke-Hilse Maitland-van der Zee, working alongside respiratory researchers Dr. Susanne Vijverberg, Dr. Paul Brinkman and Dr. Simone Hashimoto. One such marker is a child's exhaled "breathprint", providing a non-invasive biomarker to facilitate disease phenotyping and in the future potentially even treatment. Furthermore, together with Tahira Hussain, pediatrician-in-training, they are analyzing socioeconomic and living circumstances in a large cohort using existing literature and publicly available data from the Central Bureau of Statistics and the Dutch site Atlas voor Leefomgeving.

“Why treat a child only to send it back to the circumstances which made it sick in the first place?”

OUTDOOR EXPOSURE

Additionally, they are researching the effects of outdoor exposures. In Europe, The Netherlands has the highest incidence of childhood asthma attributable to Nitrogen Dioxide (NO2) exposure. Research by Investico and the newspaper Trouw revealed that at least 100,000 children are exposed to air pollution when at school or daycare due to the proximity of a highway (Van de Beld et al. Platform Investico 2023). As these risks are higher in children with poorer socioeconomic circumstances, air pollution warrants serious consideration. Therefore, Berber and Sarah will examine air pollution at neighborhood level in collaboration with exposome expert Dr. George Downward from both Amsterdam UMC and the University Medical Center Utrecht.

At this moment Berber and Sarah are initiating a large consortium to study health disparities and co-create interventions alongside patients and their caregivers, bringing together not only clinical researchers, but also exposome experts and social scientists. “If we want to know what interventions are needed to decrease disparities in pediatric asthma, we need to work together with our patients and their caregivers. Meet them, not at a table in a consulting room, but at their homes, in their neighborhood. Only there will we see and hear what is really needed to make a difference”. And a difference is needed, because why treat a child only to send it back to the circumstances which made it sick in the first place?


“Placenta stem cell models provide new opportunities for investigating early placenta development.”

JANTINE VAN VOORDEN AND GIJS AFINK

New tools to investigate early placenta development

Many obstetrical complications have their origin in defective early placenta development. Research into this field has been complicated by both practical and ethical restraints. Within the Reproductive Biology Laboratory, the research group led by Dr. Gijs Afink, which includes PhD candidate Jantine van Voorden, has established placenta stem cell model systems that enable the identification of molecular mechanisms involved in both normal and defective placenta development.

“Our studies will provide new leads for improved predictive biomarkers and pharmacological interventions.”

RUBINSTEIN-TAYBI SYNDROME AS A MODEL FOR DEFECTIVE PLACENTA DEVELOPMENT

One way of identifying molecular mechanisms that regulate placentation is by looking at diseases or states that are at risk for pregnancy complications, for example Rubinstein-Taybi syndrome. This is a developmental disorder characterized by mutations in the CREBBP or EP300 gene. Pregnancies of Rubinstein-Taybi fetuses with an EP300 gene mutation are at high risk of developing preeclampsia and fetal growth restriction, suggesting that EP300 is important in normal placentation. Therefore, we investigated the function of EP300 in early placentation events, using human trophoblast (placenta) stem cells and trophoblast organoids. By manipulating the expression level of EP300 in these models we discovered that EP300 is required for stem cell differentiation into the two major functional cell types of the placenta, making EP300 a central regulator of trophoblast differentiation. Inaccurate trophoblast differentiation may negatively affect placenta function, thereby resulting in pregnancy complications. The results of this study were published last year. Currently we are continuing the study of EP300 by exploring its upstream regulators and downstream targets and investigating the differences and similarities between EP300 and its related protein CREBBP.

REPROGRAMMING CELLS FROM FETAL GROWTH-RESTRICTED PREGNANCIES

Another strategy to identify mechanisms involved in placentation is to compare healthy and diseased placentas. Since trophoblast stem cells can only be isolated from first-trimester placentas, the outcomes later in pregnancy and therefore the health status of these cells are unknown. To overcome this, we are reprogramming cells from term pregnancies – with known pregnancy outcomes – into induced pluripotent stem cells, and subsequently convert these into trophoblast stem cells, representing early placenta development. In collaboration with Dr. Wessel Ganzevoort and supported by an AR&D research grant, we are collecting umbilical cords from pregnancies affected by early-onset fetal growth restriction and healthy controls. By analyzing these induced trophoblast stem cells generated from normal and growth-restricted pregnancies, we are aiming to uncover mechanisms affected in fetal growth restriction.

Gijs Afink

Jantine van Voorden

PLACENTA STEM CELL MODELS TO DIRECTLY ANSWER CLINICAL QUESTIONS

Although our research is intended to generate new insights in placenta development that would finally result in better treatment of pregnancy complications, there is a large gap between laboratory and clinic. However, sometimes it is possible to directly respond to questions from the clinic and translate these into lab experiments. An example of this is our recent collaboration with Dr. Liesbeth van Leeuwen, Prof. Christianne de Groot and Dr. Carrie Ris-Stalpers, where we investigated the possible adverse effect of COVID-19 mRNA vaccination on the placenta, using serum samples collected in the PREGCOVAC-19 study and our trophoblast model system. The results of this study were also published recently (Van Voorden et al. Int J Infect Dis 2024).

The efforts within our research group are all centered on understanding the intricacies of early placenta development and their implications for pregnancy outcomes. This will provide new leads for improved predictive biomarkers and pharmacological interventions to treat pregnancy complications, ultimately enhancing maternal and fetal well-being.

“Application of PROMs in daily clinical practice has shown promising results”

ANOUK GROENEWEGEN AND LOTTE HAVERMAN

The importance of PROMs in clinical practice

Chronic illness in childhood can significantly impact a child's course of life, and long-term quality of life (QoL). It is paramount to measure patient outcomes along a life course; from childhood to adulthood. One way to do so is to focus on Patient Reported Outcomes (PROs), measured with Patient Reported Outcome Measures (PROMs), and integrated into clinical practice. By allowing patients to self-report on their physical, mental, and social functioning and symptoms, healthcare professionals get insights into the patient's experience beyond traditional measures.

> “It is important to study if and how PROMs can support Shared Decision-Making.”

KLIK PROM PORTAL

In 2008, AR&D researcher Lotte Haverman, Department of Child and Adolescent Psychiatry and Psychosocial Care, initiated the KLIK PROM portal (www.hetklikt.nu), which enables patients to complete PROMs before their clinic visits. The evidence-based portal generates individualized dashboards for clinicians, facilitating patient-clinician discussions and tailored interventions. The portal is implemented in 47 patient populations in the Emma Children’s Hospital and >40 hospitals in the Netherlands (Haverman et al. Clinical Practice in Pediatric Psychology 2014).

In 2019, Lotte’s team together with the Department of Care Support and Strategy and Innovation started the Amsterdam PROM Expertise Center (PEC); a multidisciplinary team implementing PROMs through Epic. PEC collaborates with various stakeholders (clinicians, implementation experts, PROM-researchers and most important; patients) to expand PROM usage, transitioning from solely focusing on pediatric patients to a broader population. With over 65 patient groups in Amsterdam UMC utilizing PROMs in Epic, PEC’s impact continues to grow, driving advancements in patient-centered care and population health outcomes.

DAILY CLINICAL PRACTICE

The application of PROMs in daily clinical practice has shown promising results in several studies, including reduced symptom severity, higher QoL, better patient-clinician communication, and even increased survival. Despite these positive effects, successful implementation of PROMs in daily clinical practice remains challenging (van Oers et al. Qual Life Res 2021). This highlights a crucial gap between research and practice. Research projects may not capture the complexities of real-world settings, leading to a “voltage drop” in effectiveness upon implementation. Lotte Haverman therefore focusses on a scientific approach to understand the mechanisms, barriers & facilitators (Teela et al. Qual Life Res 2021, Muilekom et al. J Patient Rep Outcomes 2022) and solutions of successful PROMs implementation.

Important barriers are at hospital, ICT, PROMs, clinician, and patient level. Using and studying (Luijten et al. Qual Life Res 2021)

Anouk Groenewegen

Lotte Haverman

standardized generic PROMs (more specifically; PROMIS CATs) has significantly mitigated barriers at different levels; it lowered patient burden, enabled comparison across patient populations, and reduced ICT costs to maintain and sustain electronic PROMs. In addition, it provided the opportunity to measure the same constructs over a life course. Ultimately, this will allow for monitoring, follow-up, and early detection of important functional decline of the child, adolescent, young adult, parent, grown-up or elderly person.

SHARED DECISION-MAKING

PhD researcher Anouk Groenewegen is studying if and how PROMs can support Shared Decision-Making (SDM). PROMs offer insight into outcomes important to patients, and SDM sets the scene for discussing these topics. However, clinicians and researchers have not yet widely recognized the integrated application of PROMs and SDM. Therefore, Anouk aims, with an expert group, to develop a conceptual framework demonstrating the collaborative utilization of PROMs and SDM. Other current and future research projects focus on inclusiveness of PROMs, psychometrics, PROM visualization preferences and PROM implementation evaluation studies to further lower the barriers of PROM use in daily clinical practice, with the ultimate goal to facilitate patient-centered care.


“Aspirin doesn’t work in patients who don’t take it.”
Amsterdam UMC

JESKE BIJ DE WEG AND MARJON DE BOER

Aspirin in pregnancy

Aspirin has been shown to be effective in the prevention of pregnancy complications, mainly preterm pre-eclampsia, and thereby reduces adverse outcomes for mother and child. AR&D researchers Jeske bij de Weg (PhD candidate, resident OBGYN) and Dr. Marjon de Boer (gynaecologist-perinatologist) investigated the current clinical dilemmas among aspirin in pregnancy: the uncertainty about which women will and will not benefit from aspirin, non-adherence and implementation in clinical practice.

Marjon de Boer

Jeske bij de Weg

RESISTANCE

Aspirin resistance, the phenomenon of no or reduced response to aspirin, might hinder the risk-reducing effect of aspirin during pregnancy, potentially leading to adverse obstetric outcomes. In a longitudinal cohort study, we revealed a pregnancy-induced effect on platelet function since aspirin resistance rates in the third trimester of pregnancy were higher in comparison to postpartum. One can wonder if higher aspirin dosing is needed in pregnancy. To gain more insight in the optimal dosing of aspirin in pregnancy, we assessed the effect of aspirin 80mg on platelet function compared to placebo. A clear inhibitory effect on platelet function of aspirin 80mg compared to placebo was shown, with thromboxane reduction to almost undetectable levels, suggesting that aspirin 80mg is sufficient for platelet inhibition. However, it is unknown if higher aspirin doses could be more effective, as the anti-inflammatory effect of aspirin might contribute to the preventive effect as well. A substantial part of “aspirin resistance” was shown to be caused by non-adherence..

ADHERENCE

Aspirin doesn’t work in patients who don’t take it (inspired on a statement by US Surgeon C. Everett Koop who once said: “Drugs don’t work in patients who don’t take them”). We performed a literature review on aspirin adherence in pregnancy, showing an association between non-adherence and adverse obstetric outcomes [Bij de Weg et al. PEC Innov 2024]. Convinced of the importance of aspirin adherence in pregnancy, we tested the effect of an educative application about aspirin in pregnancy, designed in collaboration with the Technical University Delft, on aspirin adherence. Unfortunately, no added effect of our educative application to standard counselling was found. The null-finding of our study could mainly be explained by the already high tablet intake in both groups, probably caused by the highly educated population and the tertiary setting. Moreover, future applications that include interactive features such as a reminder function or active registration of pill intake, might be more effective.

“Aspirin resistance rates in the third trimester of pregnancy are higher in comparison to postpartum.”

IMPLEMENTATION

After collecting scientific evidence, transition to clinical practice has to be made. We evaluated the implementation of aspirin among community midwives and gynecologists. Community midwives considerably contribute to the implementation of aspirin in pregnancy, however, practical issues with prescribing aspirin occur often. Integrated care might be the solution. Among Dutch gynecologists, we showed a substantial increase in prescribing aspirin for various indications in a five-year timeframe after introduction of the national guideline. Evaluation of the implementation of new guidelines should become standard practice to overcome the science-to-practice gap.

Organization

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SEBASTIAAN MASTENBROEK
Center for Reproductive Medicine
› Nov 2023

TESSA ROSEBOOM
Obstetrics & Gynecology
‹ Sept 2023

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AR&D OFFICE

WENDY DE LA RAMBELJÉ
Policy Officer
› June 2023

PEGGY VAN DEN BIGGELAAR
Impact Developer
› May 2023

AR&D events 2023

AR&D ANNUAL SYMPOSIUM

June 2nd, 2023

The AR&D Annual symposium was held on 2 June 2023. The theme of the symposium organized and chaired by Prof. Velja Mijatovic and Prof. Ank de Jonge was **Strong people in vulnerable situations**. More than fifty participants attended three interesting presentations on that topic.

The symposium started with international speaker **Helena Lindgren**, professor of Reproductive Health at Sopiahemmet University, Sweden. She spoke about her research on doulas; women who speak the native language of the mother and provide emotional support before, during and after birth. The second speaker, **Kitty Bloemenkamp**, professor of Obstetrics at UMC Utrecht, talked about maternal health inequities due to their ethnicity or race. Finally, Dr. **Norah van Mello**, gynaecologist, gender surgeon, endocrinologist and fertility counselor at Amsterdam UMC, spoke on reproductive rights, the wish for children and parenthood amongst transgender people. At the end of the afternoon, with the participation of the audience, there was a lively debate on **"the value of the p-value"** with Dr. **Rik van Eekelen**, methodologist, researcher and consultant at Epidemiology and Data Science, Amsterdam UMC, and Dr. **Michiel de Boer**, associate professor of Methodology and Applied Statistics at the VU University.

The **AR&D Grant award ceremony** was also part of the symposium. Twelve researchers received an AR&D Travel grant, and three researchers were awarded an AR&D Team Science grant.

AR&D RETREAT 2023 – ALL ABOAR&D

November 2nd and 3rd, 2023

On the 2nd and 3rd of November 2023, the annual AR&D Retreat took place! Following last year's successful Showtime-themed edition, this year's participants embarked on a 2-day journey themed 'All AboAR&D', focusing on inclusion & diversity.

It was a stormy journey, considering the code yellow weather, but the ambiance could not have been better at the venue in Soesterberg. The first day kicked off with three inspiring keynotes by Dr. **Bahar Goodarzi**, midwife and post-doc researcher, who discussed 'Using Race and Ethnicity in Research: From Discrimination to Inclusion,' Dr. **Bernadette de Bakker**, who spoke about her work as an assistant professor of Human Embryology and Fetal Anatomy, and Dr. **Dries Budding**, founder of inBiome, whose talk was titled 'Essential Passengers: Microbes Matter'.

In the afternoon it was time for the PhD candidates to present pitches about their research they prepared. Distributed over multiple rooms, the students were judged by pairs of principle investigators, who selected the best pitch per room. In a subsequent plenary session, three finalists competed together to win a final prize of €250 for **Krista van Rest** for the best pitch! Congratulations! The first day was closed by a networking opportunity with drinks and snacks.

The second day, attendees could choose to keep themselves on board by doing workshops like **Law of Attraction** by FirmaVitaliteit and **Managing stress** by Saskia Beijer on personal skills and development. Alternatively, there was the option to keep your research on board through workshops like **Cultural communication** by Pharos and **Valorization & research** impact by Peggy van den Biggelaar.

At the end of the second day a final plenary session was hosted involving a panel discussion on **Diversity & Inclusion** with moderator Ilja Swets, Amsterdam UMC Diversity & Inclusion advisor, Dr. Wessel Ganzevoort, Obstetrician-gynecologist/ perinatologist at Amsterdam UMC, Sarai Keestra, MD/PhD student Epidemiology & Data science, Dr. Jordi Cabanas-Danés, PhD advisor at Doctoral school Amsterdam UMC, and Rashmi Kusurkar, professor on Inclusion & Motivation in Health Professions. An intriguing exchange of viewpoints and opinions took place. Statements varied from "I communicate identically to my international and Dutch colleagues" to "A project can be too multidisciplinary" and a conclusive statement "More diversity in my working environment is a necessity".

We were pleased to observe the social interaction both PhD and principal investigators and other attendees displayed, as well as the insightful keynotes, workshops and shared panel discussion opinions on diversity and inclusion. These discussions raised awareness and conscience on topics sometimes overlooked.

The AR&D Retreat was a huge success, thanks to the organization by the Retreat committee consisting of Arda Arduç, Wieke Beumer, Annelotte van Haaps, Hannah Juncker, Danah Kamphuis, Kavish Kohabir, Jacqueline Muts and Eva Vermeer.

AR&D grants 2023

The AR&D research grant round 2023 enabled researchers from Amsterdam UMC to perform research in the field of reproduction and development (the circle of life).
All research projects, including fundamental (biological) research, clinical or epidemiological research, paramedic as well as translational research aimed to improve health care within the field of AR&D, were eligible. Trans-disciplinary research projects were especially encouraged to be submitted. Three grants of €50.000 were awarded.

This year's grant focused on the development of novel ideas or projects, funding for salary and material costs or to spark novel ideas for small to middle sized research projects. The goal was to support **Team Science** across different (sub) departments and preferably working across different disciplines within AR&D.

Nikki Hubers
The Epigenetic signature of monozygotic twinning in pre- and perinatal tissues: a new collaboration between the department of Human Genetics, the Dutch Fetal Biobank, the PANDA obstetrics biobank, and the Netherlands Twin Register

My name is Nikki Hubers and I am a third year PhD student at the department of Biological Psychology at the Vrije Universiteit Amsterdam. My research focusses on the etiology of twinning and I work together with Dr. Jenny van Dongen and Prof. Dorret Boomsma. We received the Team Science grant together with collaborators from two departments of Amsterdam UMC; Dr. Peter Henneman and Prof. Marcel Mannens from Human Genetics and Dr. Bernadette de Bakker and Dr. Carrie Ris-Stalpers from Obstetrics and Gynecology.

Our aim is to investigate whether the epigenetic signature of monozygotic twins, identified by Jenny van Dongen and Dorret Boomsma with international colleagues from the Twining Genetics Consortium in 2021 (Van Dongen et al. Nature 2021), is present in pre- and perinatal tissue. The grant allows us to perform genotyping and epityping of samples of the Dutch Fetal Biobank and the PANDA obstetrics biobank. Since receiving the grant, we have started the selection of the samples and tissues and the DNA isolations. We expect our first results near the fall of 2024.
I remember reading the email about receiving the AR&D grand over an after-work drink and basically running back to my department to tell Jenny and Dorret the good news. I have since been grateful, that I can include this project in my PhD work and that we as a team are given the opportunity to work with such unique samples and form a strong collaboration between the Netherlands Twin register, the two biobanks and the Human Genetics department.

Nikki Hubers

Daniël Docter

Daniël Docter
Studying surgical anatomy and embryology of the anorectal region

My name is Daniël Docter and I'm a PhD student working between Pediatric Surgery, Embryology and high resolution imaging. I study, together with Ramon Gorter (Pediatric Surgeon) and Bernadette de Bakker (Embryologist), the microscale morphology of congenital anomalies through micro-CT imaging. Our aim is to use this fundamental research to improve treatment strategies. My PhD trajectory was started last year through the AR&D Team Science grant and I'm still amazed and grateful that it has given me the chance to perform this research by AR&D. Now, six months later, the research has led to a stream of promising results and new research lines.
The Team Science grant has enabled us to image fistulae resected during reconstruction of anorectal malformations. The discussion we had on the first results awed everyone involved and this instance even made it into the Eureka moment! in the New Scientist magazine. The scans were not only amazing to look at but also provided new insights in this fistula that has set us on a course to rethink the current surgical approach. The 3D and high resolution nature of the scans were so enlightening that new pilot studies have started into other congenital anomalies such as esophageal atresia and Hirschsprung disease.
We are now in the process of analyzing our results on the anorectal malformations and building on our pilot studies of other congenital diseases. Moreover, we have started international collaborations to utilize even more advanced imaging techniques at the European Synchrotron Radiation Facility. The future looks bright!

Gerben Vader

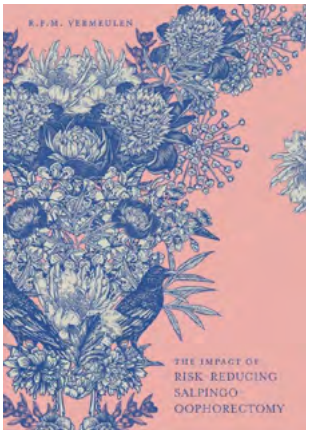
Gerben Vader
Finding the missing link in partner choice during germ cell-specific DNA repair

My name is Gerben Vader, Principal Investigator within the department of Human Genetics (until April 2024). In a collaboration with the group of Dr. Geert Hamer (Reproductive Biology Laboratory), we are interested in revealing the control of a key step during sexual reproduction: the coordinated reshuffling of the genetic material during gametogenesis.
Inspired by earlier work done in budding yeast, we are searching for a key enzymatic regulator of this process in human cells. We aim to use a hybrid approach of non-germ cell systems and primordial germ cell cultures, coupled to affinity purification and mass spectrometry. The AR&D Team Science grant has allowed us to initiate this exciting research endeavor, aimed at identifying the putative protein kinase that is responsible for idiosyncratic DNA repair behavior in germ cells. Revealing this kinase that controls an essential step in successful reproduction will fill a key gap in our knowledge and understanding of human reproductive biology.
In the future, this knowledge might also impact clinical practices: other factors that influence DNA repair in germ cells have been identified as causative factors of infertility. Therefore, we believe that knowing the identity of this kinase might aid the diagnosis and stratification of currently undefined infertility syndromes. We are excited to be able to embark on this scientific journey, entirely made possible by the generous support of the AR&D Team Science initiative.

AR&D PHD THESES

In 2023, 74 researchers obtained their PhD in the area of reproduction and development.

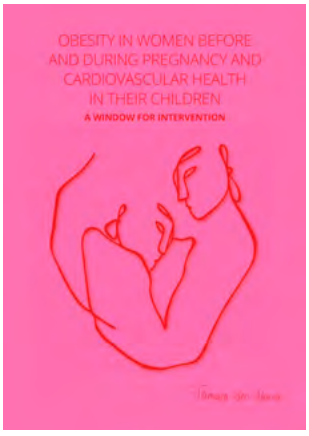
Below a cross section of the PhD theses.



The impact of risk-reducing salpingo-oophorectomy

Ravi Vermeulen

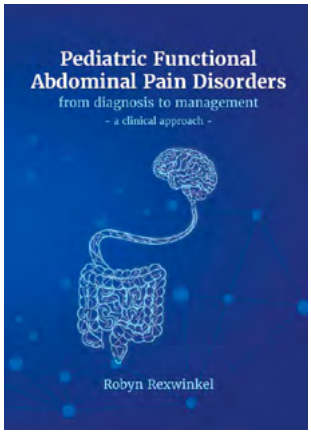
Women who have a high (hereditary) risk of ovarian cancer are offered the option of having their ovaries and fallopian tubes removed preventively. Many women who have this done have not yet gone through menopause and are entering menopause because of this surgery. This dissertation describes the effects of this surgery on women who have already been menopausal and those who have not.



Obesity in women before and during pregnancy and cardiovascular health in their children. A window for intervention

Tamara den Harink

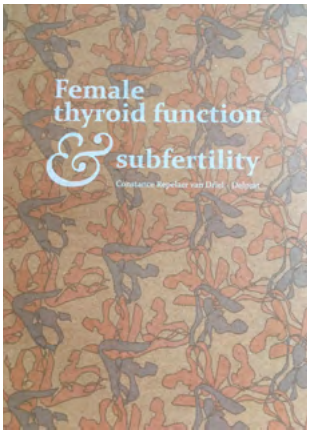
Children born to women with obesity before or during pregnancy have an increased cardiovascular disease (CVD) risk. Research indicates that children born to women with obesity have alterations in cardiac function and structure associated with an increased CVD risk. We found that a lifestyle intervention for women with obesity before pregnancy has the potential to improve the lifestyle of obese women before they become pregnant and has a positive effect on the (heart) health of their children.



Pediatric Functional Abdominal Pain Disorders from diagnosis to management – a clinical approach

Robyn Rexwinkel

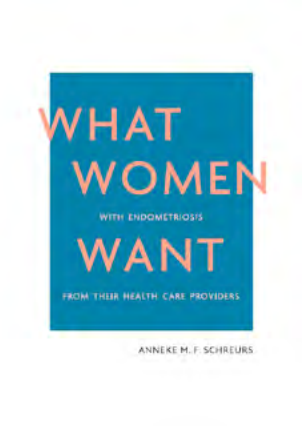
Functional abdominal pain is common in pediatrics and characterized by chronic abdominal pain (≥2 months) and alterations in stool pattern. It is associated with decreased quality of life and school attendance, but the pathophysiology is not completely understood and diagnosis is generally symptom-based. This thesis describes novel insights regarding diagnostic and management strategies, shared decision making and clinical outcome measures for research, with the aim to enhance patient care, improve quality of care, and allow better evidence-based decision making.

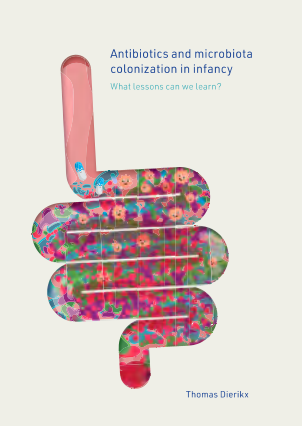


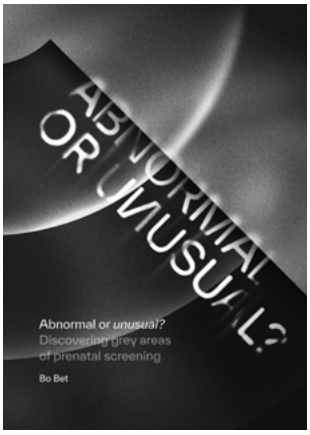
Female thyroid function and subfertility

Coes Delprat

Subtle thyroid problems seem to matter for certain women of reproductive age, especially for women who were not pregnant before and with unexplained subfertility. In these women higher TSH levels within normal range are associated with less live born children after IVF, and with more live born children after ICSI. This resulted in the hypothesis that higher TSH, associated with thyroid autoimmunity, might interfere with fertilization and early embryo development, to be investigated soon.







What women with endometriosis want from their health care providers

Anneke Schreurs

This thesis presents an overview of patient-centeredness of women with endometriosis. It presents the most important aspects for improving care, identified which women were more at risk for being dissatisfied with care and presented a plan for improvement of patient-centeredness. Furthermore patient satisfaction with fertility treatments was investigated as well as patient preferences and wishes concerning fertility treatment. Finally cases of abdominal bleeding in pregnancy were presented along with patient experiences and tools for diagnosing and treatment.

Preterm birth: Risk factors and treatment

Job Klumper

Preterm birth, defined as a delivery before 37 completed weeks of gestation, is a major cause of neonatal mortality and morbidity worldwide. The first part of this thesis studies population trends in the Netherlands and studies risk factors for preterm birth. The second part of this thesis focuses on improving neonatal and long-term outcomes in threatened preterm birth, specifically the effectiveness of tocolysis (inhibiting labor).

Antibiotics and microbiota colonization in infancy: What lessons can we learn?

Thomas Dierikx

In the thesis titled “Antibiotics and microbiota colonization in infancy: What lessons can we learn?” the effect of antibiotic use during childbirth on the microbiome of the child is described. Blood tests are also being investigated to reduce antibiotic use in newborn babies. In addition, the protective role of probiotics during antibiotic use is being investigated.

Abnormal or unusual? Discovering grey areas of prenatal screening

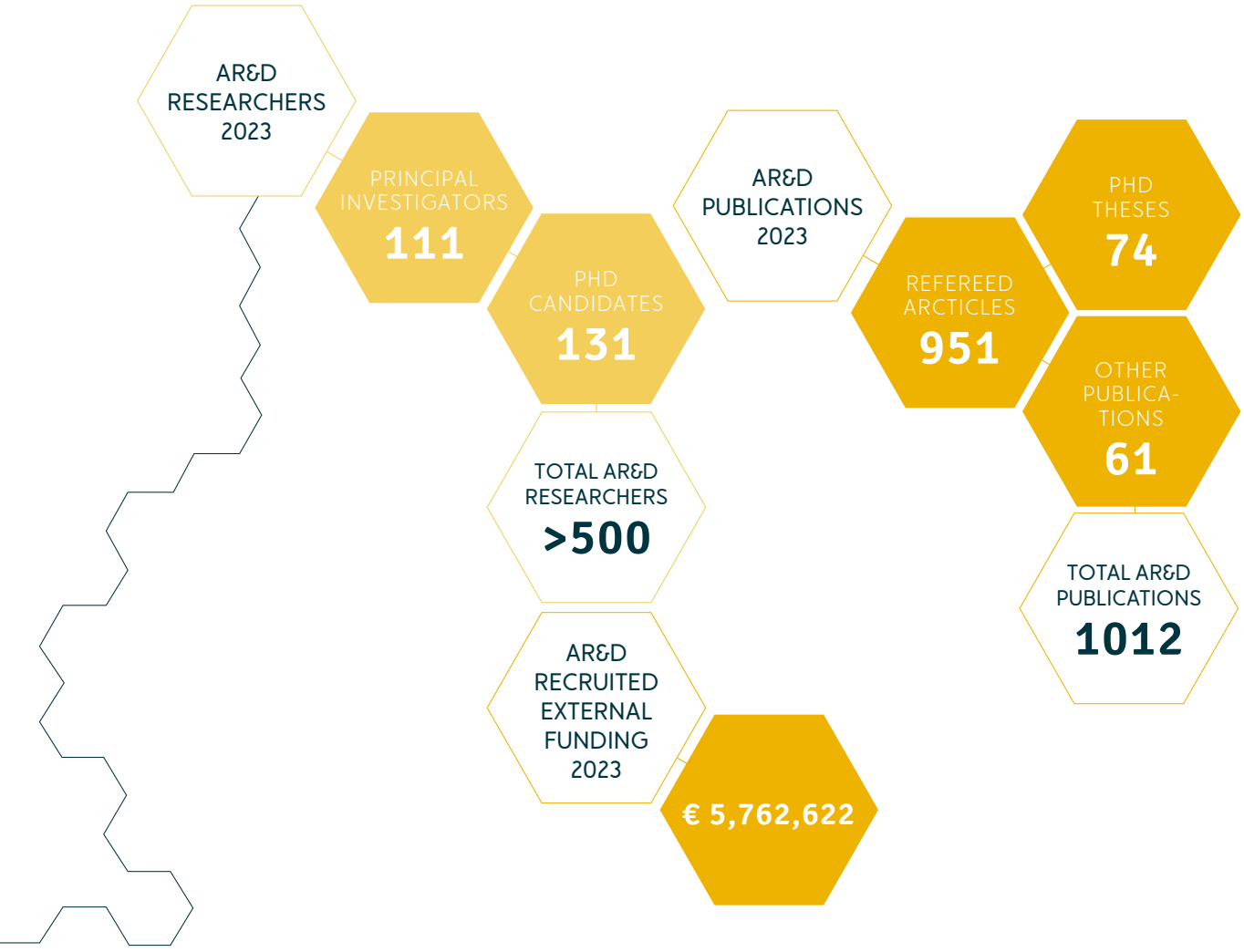
Bo Bet

Approximately 2% of all newborns worldwide are affected by congenital anomalies, contributing to perinatal mortality and long-term disabilities. Detection during pregnancy allows for informed decision-making and improves neonatal outcomes. The Netherlands’ national prenatal screening program encompass the non-invasive prenatal test (NIPT) and ultrasound examinations conducted in the first and/or second trimester. This thesis studied several grey areas of prenatal screening and tried to clarify some unusual findings, with emphasis on cardiac anomalies and first-trimester screening.

“Central to AR&D research is the integration of different interdisciplinary approaches and research methodologies within Amsterdam UMC and the universities VU and UvA.”

Numbers and highlights

AR&D IN NUMBERS



DISCLAIMER RESEARCH INFORMATION RESEARCHERS

Information about the number of researchers affiliated with AR&D was collected using the Research Information Systems Pure VUmc and Pure AMC on February 7th, 2024. Registration of research institute affiliation was done by the researchers themselves, by personnel from the Medical Library AMC, by secretary of corresponding AMC/VUmc department or by the policy officers of the AR&D research institute.

PUBLICATIONS

The reported data include all published research output as registered in the Research Information Systems Pure VUmc and Pure AMC on February 7th, 2024. Publications are ascribed to AR&D based on the affiliations of the authors and the content of the publication. A publication can be ascribed to one or more research institutes depending on the affiliations of the authors. Publications registered in the VUmc and AMC Pure instances have been combined and deduplicated. PhD-theses are ascribed to AR&D based on the affiliations of the (co-)supervisors. A thesis can be ascribed to one or more research institutes depending on the affiliations of the (co-) supervisors.

RECRUITED FUNDING

Information about funded research projects has been provided by the separate project administrations from location AMC and location VUmc.

EXTERNAL GRANTS AND PRIZES

In 2023, AR&D researchers were very active in obtaining grants and prizes. Below some of the external grants and prizes awarded to AR&D researchers are highlighted.

EUROPEAN RESEARCH COUNCIL – CONSOLIDATOR GRANT
€2,000,000
FGR PODS
Wessel Ganzevoort

EUROPEAN RESEARCH COUNCIL – CONSOLIDATOR GRAN
€1,934,500
NEOGRAFT
Elena Levtchenko, together with KU Leuven

NWO
€634,019
Triggering non-invasive ventilation
Jeroen Hutten, Ruud van Leuteren and others

FOUNDATION 'ALLE AMSTERDAMSE KINDEREN GELIJKE KANSEN'
€436,674
SugarDip
Improve care and reduce preterm birth rates for women in Amsterdam Zuid-Oost, Martijn Oudijk

ZONMW
€424,552
HERNIIA-2 trial
Sanne Maat and Joep Derikx

ZONMW
€171,059
Substitutie van zorg binnen de benigne gynaecologie gedurende de COVID-19 pandemie in Nederland
Wouter Hehenkamp

GUERBET NEDERLAND BV
€141,761
FOil study
Velja Mijatovic

STICHTING KIKA
€123,889
Fluorescence Imaging of the Parathyroid Glands of Children
Daniël van de Berg and Joep Derikx, together with UMC Utrecht and UMCG

STICHTING STEUN EMMA KINDERZIEKENHUIS
€122,000
Health Intelligence Program for Daan Theewes Centrum
Marsh Königs

AWARDS

ZonMw Pearl for Nationwide TRIDENT-2 study
NIPT Consortium with, among others, Erik Sistermans, Lidewij Henneman and Caroline Bax

New Scientist Wetenschapstalent 2023
Bernadette de Bakker (and Karuna van der Meij was nominated)

Anne Anderson Award
Madelon van Wely

Amsterdam Science Innovation Award for Novel wound-healing implant
Zeliha Guler

KEY PUBLICATIONS

2023 was a very productive year. Here is a selection of peer-reviewed publications that were highlights for our researchers.

Environmental Impact Assessment of Reusable and Disposable Surgical Head Covers
Cohen et al.
JAMA Surg.
2023;158(11):1216-1217

[Non-]disclosure of lifetime sexual violence in maternity care: Disclosure rate, associated characteristics and reasons for non-disclosure
De Klerk et al.
PLoS One.
2023;18(10):e0285776

Growing Evidence and Remaining Questions in Adolescent Transgender Care
De Vries et al.
N Engl J Med.
2023;388(3):275-277

Left ventricular diastolic function in the fifth decade of life in women with a history of spontaneous preterm birth
Janssen et al.
Eur J Obstet Gynecol Reprod Biol.
2023;286:40-46

Clinical outcomes of uninterrupted embryo culture with or without time-lapse-based embryo selection versus interrupted standard culture (SelecTIMO): a three-armed, multicentre, double-blind, randomised controlled trial
Kieslinger et al.
Lancet.
2023;401(10386):1438-1446

Trends in preterm birth in the Netherlands in 2011-2019: A population-based study among singletons and multiples
Klumper et al.
Acta Obstet Gynecol Scand.
2023;103(3):449-458

Diversity of Parent Emotions and Physician Responses During End-of-Life Conversations
Prins et al.
Pediatrics.
2023;152(3):e2022061050

Sperm DNA methylation is predominantly stable in mice offspring born after transplantation of long-term cultured spermatogonial stem cells
Serrano et al.
Clin Epigenetics.
2023;15(1):58

Cancer risk in children, adolescents, and young adults conceived by ART in 1983-2011
Spaan et al.
Hum Reprod Open.
2023;2023(3):hoad027

Differences in analysis and treatment of upper airway obstruction in Robin sequence across different countries in Europe
Sullivan et al.
Eur J Pediatr.
2023;182(3):1271-1280

Functional Insight into and Refinement of the Genomic Boundaries of the JARID2-Neurodevelopmental Disorder Episignature
Van der Laan et al.
Int J Mol Sci.
2023;24(18):14240

Home-based monitoring of ovulation to time frozen embryo transfers in the Netherlands (Antarctica-2): an open-label, nationwide, randomised, non-inferiority trial
Zaat et al.
Lancet.
2023;402(10410):1347-1355

SOCIETAL IMPACT

In 2023, AR&D researchers have been contributing to the Societal Impact of research. A selection of societal impact events is presented.

Opening Amsterdam Pediatric Abdominal Center
AR&D Researchers at RTLnieuws and in newspaper Parool

De pil en het condoom zijn uit, 'natuurlijke' anticonceptie is in, zien UvA-onderzoekers op Lowlands
Wieke Beumer in Folia

Iets lagere Cito-scores na een ingeleide bevalling
Renée Burger in newspaper NRC

"Baarmoeder van 400 vrouwen per jaar onnodig verwijderd"
Wouter Hehenkamp at Nieuwsuur

Erkenning voor vrouwen die na keizersnede klachten houden stapje dichterbij
Saskia Klein Meuleman at NU.nl

Een dna-test voor iedereen met een kinderwens
Phillis Lakeman in newspaper NRC and at AVROTROS EenVandaag

Gratis en gezond, maar HPV-vaccin is nog weinig bekend onder jongeren
Luc van Lonkhuijzen on AT5

Embryo-onderzoek | Uitgelegd
Sebastiaan Mastenbroek on X @amsterdamumc and YouTube

“AR&D strategically focuses on translating scientific findings into policy and practice through valorization.”

Newly appointed professors

In 2023, three professors were appointed at Amsterdam UMC in the field of AR&D.

PROF. ELENA LEVTCHENKO

Elena Levtchenko has been appointed as professor of Translational Nephrology at the University of Amsterdam since June 2023. She works as a head of Pediatric Nephrology in Emma Children's Hospital and is a principal investigator in the laboratory of Pediatric Nephrology, Amsterdam UMC.

Elena Levtchenko

Her research focuses on unraveling disease mechanisms and finding curative therapies for children with congenital nephropathies, using drug retargeting, gene and cell therapy. Being part of Emma Centre of Personalized Medicine, together with UD Fanny Arcolino, Levchenko aims to find cure for the metabolic disease cystinosis. She is a Medical Advisor for the Dutch and Flemish Cystinosis Patients Group and of the Cystinosis Network Europe. By bridging the gap between fundamental science and clinical needs of the patients, Levtchenko's lab discovered a new type of kidney stem cells in urine of preterm neonates. These cells can be isolated non-invasively and represent a unique tool for kidney-targeted cell therapy and personalized medicine.

Levtchenko has an extensive international network; she leads a Working group on Metabolic and Stone-forming disorders of the European Reference Kidney Network and is a chair of the Educational Committee of the European Society for Pediatric Nephrology (ESPN). She is a council member of the International Pediatric Nephrology Association (IPNA) and is an Associate Editor of Pediatric Nephrology Journal. She is a holder of the European Research Council (ERC) Consolidator Grant.

“Improving the outcomes of psychiatric symptoms in children and their parents by providing targeted treatments.”

PROF. CHRISTEL MIDDELDORP

Christel Middeldorp has been professor in Family Mental Health since July 2023. She leads the academic collaborative center for family mental health “GEZIeN”. This is a collaboration between Amsterdam UMC, Arkin and Levvel. She works as a child and youth psychiatrist at “Project aan Huis”, Arkin youth and family. She also has an honorary professor position with the Child Health Research Centre (CHRC), UQ, and Child and Youth Mental Health Service (CYMHS), Children’s Health Queensland Hospital and Health Service (CHQ HHS) in Brisbane, Australia where she worked for six years before coming back to Amsterdam.

The aim of her research is to improve the outcomes of psychiatric symptoms in children and their parents by providing targeted treatments. This focuses partly on prevention, with, for example, one ongoing project aiming to implement an already available program in mental health services for children of parents with mental illness. Other projects investigate integrated treatment for families with both a child and parent affected by psychiatric symptoms.

Finally, she is involved in multiple projects aiming to improve prediction of outcomes of psychiatric symptoms in children and adolescents with a particular focus on genetics. She is the co-PI of the Behavior&Cognition working group of the EAGLE consortium (EArly Genetics and Lifecourse Epidemiology), a large collaborative of population based longitudinal child and adolescent cohorts from over the world.

Christel Middeldorp

Joep Derikx

PROF. JOEP DERIKX

Joep Derikx has been appointed professor in Compromised gut in neonates and children since October 2023. He is a pediatric surgeon and Amsterdam UMC Principal Investigator with a special interest in translational research that is in line with his clinical expertise. This comprises the care for neonates and children with a complex intestinal disease including necrotizing enterocolitis and Hirschsprung disease.

The focus of his research is understanding the pathophysiology and early detection of aforementioned diseases. Furthermore he studies how intestinal anastomoses heal and why leakage occurs.

Joep participates in several national and European consortia for patient care, research and development of guidelines. He generated a program for one-stop-shop pediatric inguinal hernia surgery in Amsterdam UMC and created a website for children and parents/caretakers on this topic (www.kinderliesbreuk.nl).

“Understanding the pathophysiology and early detection of complex intestinal diseases including necrotizing enterocolitis and Hirschsprung disease.”

“Unique about the research institute Amsterdam Reproduction & Development is that we investigate human reproduction and development in its totality: from the formation of oocyte and sperm, conception, embryonic and fetal development, pregnancy, birth, and postnatal development as the child grows up, and the circle of life eventually starts again.”

“The ambition of AR&D is the advancement of knowledge in all aspects of human reproduction and development through interdisciplinary team science aimed at improving health from preconception to adulthood of current and future generations.”

"Unique about the research institute Amsterdam Reproduction & Development is that we pay attention to reproduction and development in its totality: the stage before pregnancy, conception, pregnancy, childbirth, the child as it's growing up, and the resulting health of the adult stages of life"