

EXPERTISE

CIRCLE OF LIFE

AMSTERDAM REPRODUCTION AND DEVELOPMENT

ANNUAL REPORT

2019

REPRODUCTION

DEVELOPMENT

RESEARCH

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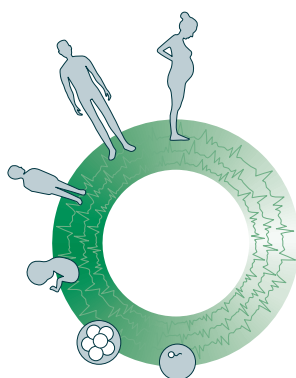
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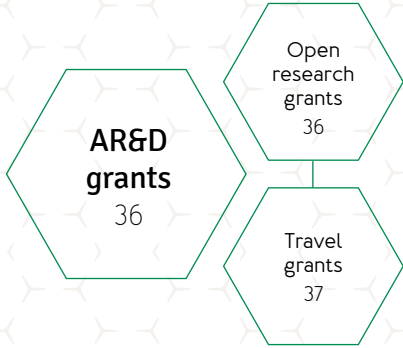
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A word from the directors



We are delighted to share the 2019 Amsterdam Reproduction & Development (AR&D) annual report. The stories of our researchers provide fascinating insights into just some of the ground-breaking work being conducted across our institute, contributing to a better understanding of many aspects within the field of reproduction and development.

In 2019, to stimulate societal debate, the Ministry of Health, Welfare and Sport facilitated several public dialogues including on germline genome editing and the use of embryo's for research. Members of our research institute actively participated by giving (inter)national radio interviews, attending café debates and writing for popular magazines. Participating in societal debate is something that we, in our research institute AR&D, greatly encourage. By doing so we present technological innovations into the Dutch society and contribute to the opinion about our research and (new) applications and developments.

AR&D scientific publications were also picked-up in the (inter)national media. Exemplary are the findings from the TRIDENT-2 study on implementation of non-invasive prenatal testing, the H2Oil study on tubal-flushing in case of infertility, and the INCIP network on safety of cancer treatment during pregnancy. Even more, two of our esteemed researchers were nominated for the Amsterdam UMC Societal Impact Award.

In the Autumn of 2019 we celebrated our first two-day Annual AR&D Retreat. It was a great success! An enthusiastic retreat committee of young researchers from the various themes within our institute organized a diverse and interesting program of events. Members of our institute had the opportunity to network, to attend workshops, and to present and discuss their work on the different aspects of the circle of life, from preconception through pregnancy to child development and long-term health.

AR&D focuses on innovation and excellence, and combines leading scientists of different disciplinary backgrounds, including clinicians active both in clinical care and research, but also fundamental researchers, epidemiologists,

psychologists, and social scientists.

With this report, we proudly present the highlights of 2019, introduce several AR&D PhD students and their mentors, as well as three new inaugurated AR&D professors. We are honored to share our institute with you.

We wish you an interesting reading and stay tuned!

Christianne de Groot & Lidewij Henneman
Directors Amsterdam Reproduction and Development



Starting the circle of life



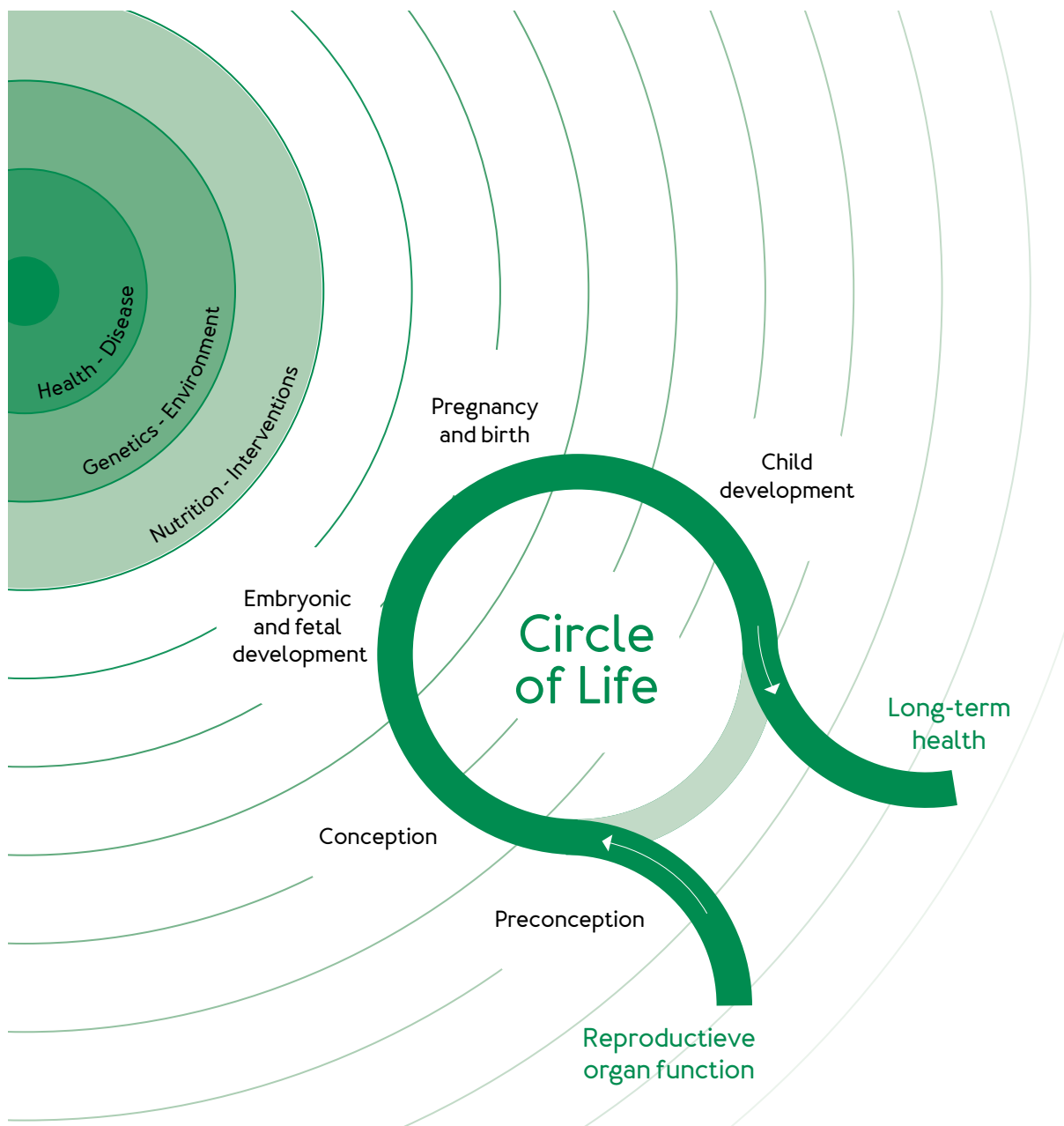
The Amsterdam Reproduction and Development (AR&D) research institute is unique in its goals and ambition. The institute covers themes that comprise the Circle of Life: from preconception through pregnancy and child development to long-term health. It encompasses research that focuses on long-term health effects on both mother and child, of disease and interventions during preconception, conception, embryonic and fetal development, pregnancy and birth, as well as child development and effects on reproductive organ function.

The ambition of AR&D is to enhance the field of reproduction and development nationwide and to sustainably improve health care for mother and children and as such for future generations. We strive for all people to have access to high

quality sexual and reproductive health information, and to support the foundation that enables children to make the best start in life.

AR&D integrates various disciplinary approaches within the Amsterdam UMC and their affiliated centers and has connections with virtually all other Amsterdam UMC research institutes. AR&D researchers study the effects of genetics, environment, nutrition, disease and interventions on the developmental process from gamete to adult. In the institute, basic, translational, psychosocial and clinical research scientists work together to maximally improve health care.

For more information and videos of AR&D, please visit www.amsterdamresearch.org.



Research Areas

○○○ FROM PRECONCEPTION TO CHILD DEVELOPMENT



PRECONCEPTION AND CONCEPTION

The desire to have children is a fundamental driving force for all species. We provide optimal care for people who have difficulty conceiving. Our prediction models provide accurate and reliable prognoses for medical help. Thus, we stand for optimal evidence-based shared decision-making. AR&D does not only offer novel medical treatments but we also evaluate whether they are truly of benefit for our patients. We investigate how to best counsel couples who are confronted with a high risk of serious genetic diseases in their future children, and to provide them with options for autonomous reproductive choice. We evaluate how medical professionals and other stakeholders view novel genetic and reproductive techniques and how innovative techniques should be ethically weighed and implemented. Within AR&D, we also study the process of spermatogenesis and oogenesis and the earliest stages of embryo development from fertilization to implantation and translate this knowledge to new therapies.



EMBRYONIC AND FETAL DEVELOPMENT

Humans all originate from a single cell, the fertilized oocyte, and developing through a fascinating highly orchestrated process to become the individuals that we currently are. AR&D studies how these processes are regulated, how perturbations can lead to congenital abnormalities or late onset diseases and how genetic and environmental factors affect development. We use experimental model systems to study and simulate human development and use our unique twin register to disentangle environmental and genetic contributions to health and disease. By focusing on embryonic development, we provide the basis for understanding a huge variety of human disease and disease susceptibility. We link these fundamental studies to clinical trials. We use highly sensitive ultrasound measurements and genetic tests to examine the developing fetus, and evaluate innovative implemented techniques. These are used for developing new tests to improve our clinical capacities.



PREGNANCY AND BIRTH

AR&D constantly strives to provide the best possible care for mother and child. Therefore, we routinely perform multi-center clinical trials. With these trials, we aim to establish the benefit of specific interventions in reproductive medicine, gynecology, obstetrics and neonatology. Results of these trials are integrated into clinical protocols so that we can provide the best possible treatment for our patients and to allow for truly informed decision-making. In addition, we are developing tailored made tools for the shared decision-making. Our trials are conducted in the context of national networks of collaborating hospitals, gynecologists, midwives, nurses, neonatologists, and health care providers coordinated from Amsterdam. These professionals focus on optimally treating pregnancy complications and preventing premature delivery, as well as optimizing care for prematurely born infants. We study the requirements for responsible implementation of advancements in prenatal screening. We also investigate effects of environmental exposures during pregnancy on women's and offspring's health. This in order to learn more about how to give each child the best possible start in life.



CHILD DEVELOPMENT

Healthy child development is essential for later health and wellbeing. AR&D follows children through their development after they have spent part of their early life in the hospital. For instance because they were born prematurely. We monitor their behavior, growth and development to better understand the long-term consequences of our treatments and to inform our patients more accurately. We develop online tools that help patients and their parents keep track of various aspects of child development. This covers the full range of psychosocial, mental as well as physical and behavioral aspects of life. We follow up children whose mothers participated in intervention trials. This provides insight into the underlying mechanisms of diseases before they become clinically overt. With the advancement of sequencing technologies, we strive to optimize the genetic diagnosis in children with developmental disorders. We monitor development and follow individuals as they become the parents of the next generation and the circle of life begins again.





“Participating in societal debate is something that we, in our research institute AR&D, greatly encourage. By doing so we present technological innovations into the Dutch society and contribute to the opinion about our research and (new) applications and developments.”



MARTIJN OUDIJK, JOB KLUMPER
AND CAROLIEN DIJKSTRA-ROOS
*Towards an evidence based treatment
strategy for women in threatened preterm
birth: the APOSTEL line of research*

JAAP OOSTERLAAN AND
NOOR SONNAVILLE
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RESEARCH AT AR&D

ARNE POPMA AND
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*No health without
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SEBASTIAAN MASTENBROEK
AND MIRIAM ZAGERS
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Towards an evidence based treatment strategy for
women in threatened preterm birth:

the APOSTEL line of research



For many years, members of the Dutch Consortium for Healthcare Evaluation and Research in Obstetrics and Gynecology (NVOG Consortium) have been working on the improvement of care for patients with threatened preterm birth. The APOSTEL research line systematically investigates the effectiveness of methods of diagnosis and treatment of women in preterm labor. APOSTEL stands for 'Assessment of Perinatal Outcome with [S....] Tocolysis in Early Labour' - in this acronym the 'S' had different meanings in the different APOSTEL trials. Tocolytics are medications used to suppress uterine contractions, possibly postponing delivery. We would like to highlight finished APOSTEL trials, provide an update on the current project, and give an insight into the future.



Carolien
Dijkstra-Roos



Job
Klumper



Martijn
Oudijk

OVERVIEW OF APOSTEL TRIALS

First, in the APOSTEL I study, a combination of clinical signs of preterm labor, the cervical length as measured by transvaginal ultrasound combined with the analysis of fetal fibronectin, was found to be most predictive of birth within 7 days of admittance. Secondly, the routine policy of maintenance tocolysis after an episode of acute treatment was proven ineffective in the APOSTEL II trial. In the APOSTEL III and IV trials, the effectiveness of a 48 hour course of tocolytic drugs was investigated. APOSTEL 5 and 7 were designed, but not pursued, as other research groups had recently published their results before funding had been obtained for our trials. APOSTEL VI investigated the effect of a pessary as an additive treatment after arrested preterm labor, however proven to be ineffective.

For decades, it was thought that tocolytics improved perinatal outcome, since tocolytics could prolong pregnancy. Especially in the fifties and sixties, when tocolytics were

first described in the literature, they seem to be very effective since the effect of corticosteroids on the neonatal outcome was not yet investigated and neonatal intensive care was less developed as in present time. In those situations, prolongation of pregnancy was the only method in an attempt to improve perinatal outcome. Since that time, over 24 randomized placebo controlled trials on different tocolytic drugs have been performed. In overview, it seems that tocolytics could postpone delivery a bit, but an improvement in neonatal outcome has never been shown in these trials.

The main goal of tocolytic therapy should be improvement of neonatal outcome, not prolongation of pregnancy in itself. Threatened preterm birth could be the result from a problem within the uterine environment, like infection or decreased placental function. In these cases, tocolytic therapy may not be beneficial and may even be harmful by exposing the fetus longer

to a suboptimal uterine environment. In several large hospitals in Scotland, Ireland and Canada, the administration of tocolytic therapy to women in threatened preterm birth is highly unusual.

In 2015, the World Health Organization (WHO) stated that no effectiveness of tocolytic therapy on perinatal outcome has been proven so far and that randomized placebo-controlled trials on this topic are urgently needed. Our project group completely agreed with this statement and believes that tocolytics should only be administered in routine care in case of proven effectiveness.

The currently recruiting APOSTEL 8 trial investigates the effectiveness of 48 hours of tocolytics with atosiban versus placebo in women with threatened preterm labor between 30 and 34 weeks. The standard treatment of corticosteroids is administered to all participants. They will be randomized to either 48 hours of atosiban or 48 hours of placebo.

CURRENT STATUS OF APOSTEL 8

We need to recruit 1514 participants in this study. All perinatal centers in the Netherlands participate, together with many large secondary hospitals. Our group from AR&D at Amsterdam UMC is also closely collaborating with enthusiastic research groups in the UK and Ireland, and will be the first large international multicenter trial performed within the obstetric branch of our NVOG consortium. As with many trials, the initial phase has been time and energy consuming and costly. Randomizing within a trial for a placebo has been difficult for many of our colleagues and also our patients. Luckily we have managed to change the standard tocolysis protocol in many regions in the Netherlands. We would only like to give those treatments to our patients that have proven to be effective, which is lacking in the case of tocolytics. We have seen a steep rise in inclusions the last 6 months, and many centers abroad will open in 2020. Hopefully, we will be able to settle the question of effectiveness of tocolytic drugs once and for all. ●

APOSTEL	Research topic	Conclusions
I	Effectiveness of nifedipine in low-risk women with cervical length of 10-30 mm and negative fetal fibronectin test	Nifedipine is not effective in prolonging pregnancy in low-risk women; surprisingly women in the nifedipine group had a significant lower gestational age than women in the placebo group
II	Effectiveness of maintenance tocolysis with nifedipine	Maintenance tocolysis with nifedipine does not improve adverse neonatal outcome or prolongation of pregnancy
III	Effectiveness and safety of nifedipine and atosiban	Nifedipine and atosiban are equally effective with respect to adverse neonatal outcome. A non-significant higher mortality rate was present in the nifedipine group
IV	Nifedipine in women with preterm prelabour rupture of membranes	No differences in perinatal outcome and prolongation of pregnancy between nifedipine and placebo groups
VI	Pessary versus no treatment in women with successful treatment of threatened preterm birth (not delivered after 48 hours tocolysis and corticosteroids)	Pessary treatment is not effective in reducing adverse perinatal outcome

“A wide range of disciplines participate in the Follow Me program in multidisciplinary teams aimed at improving future tertiary treatment care.”



Effects of disease and treatment on the developing child brain



Professor Jaap Oosterlaan acts as director of the Emma Children's Hospital Follow Me program at Amsterdam UMC, a structured follow-up program for all tertiary care pediatric patients that integrates care and research. He also leads the Emma Neuroscience Group, a research group focusing on the effects of disease and treatment on the developing brain in relation to daily life functioning.



Noor
Sonnaville

FOLLOW ME PROGRAM

The Follow Me program has three aims. First, to further advance clinical care by implementing empirically-based and structured multidisciplinary follow-up programs, providing clinical follow-up at fixed time points during child development. Follow-up is organized in a single visit to the outpatient clinic and closely tailored to children's and parents' needs. Second, to implement routine outcome monitoring and systematic evaluation of outcome, exposing targets to further improve quality of care and enhancing accountability for the care delivered. The third aim of the Follow Me program is to fuel clinical research by utilizing the rich database that is generated by comprehensive prospective registrations of clinical follow-up. These data will facilitate building of clinical prediction models and allow the study of risk and protective factors for long-term outcomes, thus further enhancing treatment and care.

Currently, Follow Me follow-up programs are offered to children admitted to the neonatal ICU, pediatric ICU (PICU) and to children that had early life surgery for congenital malformations. Novel follow-up programs are currently developed for children who underwent open-heart surgery in the first year of life and children with congenital anomalies of the kidney and urinary tract.

A wide range of disciplines participate in the Follow Me program, all collaborating not only

to provide the best possible multidisciplinary treatment and care, but also to closely work together in multidisciplinary research aimed at improving future tertiary treatment care. Oosterlaan's research group contributes from a neuroscience perspective.

RESEARCH ON BRAIN DEVELOPMENT

The human brain continues to develop during the first three decades of life, yet most rapid development takes place during the first few years of life. The young child's brain is therefore particularly sensitive to disruptions of normal development. There is a number of challenges to normal brain development that are often involved in disease and associated treatment, including for example exposure to trauma, inflammation, hypoxia, ischemia, metabolic dysfunction, pharmaceutical agents, repetitive pain, and stress. Together with his team, and close colleague dr. Marsh Königs, Oosterlaan's research is aimed at developing tools to assess the effects of disease and treatment on the brain, charting the very effects, elucidating the underlying pathophysiological mechanisms and, finally, to develop new treatment approaches to enhance brain function.

To study the effects of disease and treatment on the developing child brain, a wide range of methods is used. Advanced imaging techniques are used to assess structural brain networks (e.g. diffusion tensor imaging) and functional brain networks (e.g. functional MRI and high density EEG). The impact on

behavioral aspects of brain function are measured by neurocognitive functioning and is considered to be of great importance to fully capture the effects of disease and treatment on the brain. Neurocognitive functioning involves a wide range of functions that facilitate daily life functioning, such as information processing, attentional processes (the ability to focus, flexibly adapt and sustain attention), sensory and motor functioning, learning, memory and the so-called executive functions that enable top-down control over behavior. The research group has recently launched a fully computerized assessment battery to assess neurocognitive functioning: the Emma Toolbox. As neurocognitive testing is only feasible in children aged around six, eye-tracking has been implemented to assess neurocognitive functioning in newborns, infants, and toddlers. Eye-tracking uses looking behavior to infer attentional and memory abilities that have been found highly predictive of the child's later cognitive abilities.

The research group addresses a great diversity of research questions. For example, eye-tracking is used to study the neurocognitive development in children exposed to anesthetics in the first months of life and in preterm born children having received glucocorticoids to prevent bronchopulmonary dysplasia. Another study investigates the effects of an online motor training program in preterm born toddlers with impaired motor development. PhD candidate Noor de Sonnaville's research is embedded in the Follow Me follow-up program of the PICU led by pediatric intensivists professor Job van Woensel and dr. Hennie Knoester. Her work focuses on long-term outcomes of critically ill children who have been admitted to the PICU. One of her studies is on the long-term effects of sedatives used during mechanical ventilation on later neurocognitive development. Animal studies have indicated that exposure of the immature brain to these agents may cause neurodegeneration. Studies in children have thus far not been carried out. In her study, Noor de Sonnaville has selected a

“The research group has recently launched a fully computerized assessment battery to assess neurocognitive functioning: the Emma Toolbox.”

homogenous group of children requiring mechanical ventilation because of respiratory insufficiency due to severe viral lower respiratory tract infections. All these children received sedatives such as midazolam and morphine during their PICU admission. Compared to age, sex and socio-economic status matched healthy peers, children treated with sedatives have significantly lower IQs and memory functions. These results contributed to the decision to replace the use of midazolam as sedative during mechanical ventilation by other agents. ●



Jaap
Oosterlaan

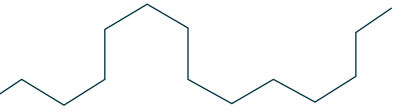
“To improve effectiveness of psychiatric care for the kids, I believe we have to dare to change some fundamental underpinnings of the youth care and psychiatric services we have built.”



No health without psychological health



Redesigning our services and treatments by involving young people and families, taking their needs serious, is warranted to create a trusting relationship that is a precondition for effective treatment in any psychological or psychiatric intervention.



ARNE POPMA

Personally, my research interests have always been motivated by clinical experience with children and adolescents displaying [self] harmful behavior [ranging from aggression, oppositional behavior, delinquency to self-harm and suicidality] who often don't come asking for help or even reject the help we offer. To improve effectiveness of psychiatric care for these kids, I believe we have to dare to change some fundamental underpinnings of the youth care and psychiatric services we have built. Redesigning our services and treatments by involving young people and families, taking their needs serious, is warranted to create a trusting relationship that is a precondition for effective treatment in any psychological or psychiatric intervention.

In addition to these services-related research- and policy endeavors, there is still a lot of knowledge needed to improve the effectiveness of specific treatments. Studying

“There is still a lot of knowledge needed to improve the effectiveness of specific treatments.”

underlying neural mechanisms of aggressive and antisocial behavior in children and youngsters, for example through functional MRI scanning, is one of the ways in which we try to find specific targets for treatment. One can imagine it's not easy to recruit youngsters with serious antisocial behavior problems for such a study. In one of our previous projects there was one particular student that stood out in motivating delinquent youngsters to participate in our studies. When all the other research assistants gave up on a potential participant, we asked Koen to try one more time and he surprised us more than once by finding a way to win the trust and interest of these kids. Off course it was clear to us that Koen was the guy for us to conduct our next PhD project on the effect of methylphenidate on neural correlates of fear conditioning and reward sensitivity in conduct disordered adolescents, both neural processes previous found to be aberrant in conduct disordered adolescents. He now had to not only motivate these kids and parents to participate in a rather long MRI protocol but they now also had to agree on participating in a double blinded RCT with a methylphenidate challenge. We are currently finalizing the analyses and the results show a normalizing effect of methylphenidate on



Arne
Popma



Koen
van Lith

both fear learning and reward sensitivity. By showing the possibility to normalize these processes, we hope the work improves effectiveness of intervention in these youngsters, either by adding methylphenidate to psychosocial interventions and/or directly through pharmacological effects. Meanwhile, Koen is finishing his training as a child and adolescent psychiatrist this year and off course we hope to keep him in our team as one of our talented and committed scientist-practitioners.

In January 2020, we will start a new department in the Amsterdam UMC, integrating child and adolescent psychiatry, pediatric psychology and psychosocial care for children and families. Right in between the Gynecology & Obstetrics and the Pediatric departments we aim to further develop the traditionally strong philosophy in the Amsterdam UMC of family centered care in which psyche and soma are equally important in restoring healthy development in children. It's exciting to think about the potential synergy within the variety of care and research activities. With respect to our research ambitions we have now outlined four themes that each relate to AR&D in various ways: pediatric psychology

[for example quality of life and patient reported outcomes], gender dysphoria (within the multidisciplinary gender center), neurodevelopmental disorders (ranging from precision psychiatry to genetic studies) and youth at risk for antisocial development. ●

“We aim to further develop the traditionally strong philosophy in the Amsterdam UMC of family centered care in which psyche and soma are equally important.”

“The reversibility of epigenetic modification leads to opportunities regarding treatment of diseases and prevention in case environmental factors play a role in the disorder.”



MARCEL MANNENS AND IZABELA KRZYZEWSKA

Clinical implications of epigenetic changes



Within the AR&D research institute, the research led by professor Marcel Mannens focusses on epigenetic changes that lead to disease and/or aberrant development.



Izabela
Krzyzewska



Marcel
Mannens

EPIGENETICS

The activity of genes is regulated by numerous epigenetic modifications to our DNA or RNA. Multiple chemical modifications lead to “open” or “closed” conformations of chromatin, making genes accessible or not to transcription factors and other proteins of the transcription machinery. Well studied modifications are DNA methylation [making genes in general less accessible to transcription] or acetylation of histone tails [making genes in general more accessible to transcription].

A hallmark of such an epigenetic modification is that such modification does NOT change the genetic code, that the change can be reversible and that this change is time and tissue dependent. This reversibility leads to opportunities regarding treatment of diseases and prevention in case environmental factors play a role in the disorder. It provides new opportunities for clinical genetics.

IMPRINTING DISORDERS

The laboratory of professor Mannens has a long standing interest in clinical epigenetics both in research as in diagnostics starting with research on the Beckwith Wiedemann syndrome (BWS) in 1984. This syndrome is

characterized by gigantism at birth and/or overgrowth of various parts of the body. A 1000 fold increased risk for the development of childhood tumors of the abdomen is associated with this syndrome. Resolving the etiology of this syndrome and finding the complex epi[genetic] changes associated with this syndrome has not only led to diagnostic tests but also predictive tests that enabled us to determine which of the BWS children were at risk for the development of tumors. BWS is an imprinting disorder that is caused by genes that do not follow mendelian inheritance. Around 150/23.000 genes are imprinted which means that only one of the two parental alleles is active [transcribed]. These imprinted genes are crucial to normal development of the fetus and placenta.

CHROMATINE ASSOCIATED PROTEINS CODED BY EPIGENES

The more recent development of genome-wide methylation analyses tools, has enabled us to look for methylation markers in the genome that are associated with diseases. These can be associated to a single gene or can be complex [several to many sites] but in all cases they must be specific for these

disorders. There are several hundreds of proteins that are involved in the correct establishment of all epigenetic modifications to the chromatin. These epi-enzymes are referred to as epi-writers, epi-readers, epi-erasers and epi (chromatin)-remodelers. Together they maintain the correct epigenome in all our different cell types throughout life. Mutations in genes coding for these epi-enzymes cause a large variety of disorders particularly those associated with intellectual disability. Currently it is possible to apply array technology to establish the methylation status of 850.000 specific sites in the epigenome in a single experiment. With this technology it has become possible to diagnose a growing number of disorders based on specific epi-signatures in a single experiment. The number of disorders that can be diagnosed this way grows exponentially. This type of research (epi-sign diagnostics) was nominated as within the top ten most influential studies in Clinical Genomics 2019 (www.cell.com).

NATURE VERSUS NURTURE

Our daily uptake of food is an important factor for the correct assembly of the epigenome. It is known for years that a lack of folium acid uptake can cause birth defects such as spina bifida. Folium acid is an important component amongst others for the correct assembly of our epigenome. From epidemiological studies we know that famine can cause a variety of health problems later in life and more recently these health problems could be associated with changes in the epigenome. The same holds for environmental factors such as alcohol exposure of the foetus during pregnancy, and smoking. In parallel, we know since 1970 that continued stress during childhood such as child abuse, or other major traumatic experiences, also leads to health problems later in life. Again, stress has been linked to changes of our epigenome. There seems to be an interaction between genetic predisposition for these health problems

or protection against (resilience), and epigenetic changes due to the environment that lead to these health problems.

PHD PROJECT

One of our PhD students, Izabela Krzyzewska, has been utilizing methylation array technology to study the above mentioned epigenetic phenomena. She has been working on the further elucidation of the BWS syndrome and found patients that had hitherto undiscovered changes in the epigenome, some of them with numerous aberrations throughout the epigenome, raising further questions about the exact etiology of this syndrome. She has studied patient populations with post-traumatic stress disorders and found several epigenetic markers involved in this disorder, some of which were associated with specific clinical features. She studied patients with foetal alcohol syndrome (FASD) and demonstrated that alcohol use during pregnancy leads to numerous changes in the epigenome, some of which were very frequently seen in FASD and could account for the specific clinical features. Finally, Izabela has found a new epi-signature for patients with mutations in the SETD1B related syndrome, a newly discovered syndrome associated with this gene. The latter study was financed by a 2019 “start small, think big” grant from the Amsterdam Reproduction & Development Research Institute and published in *Clinical Epigenetics*. A follow up study in association with international collaborators has led to an impressive number of 40 different disorders that can be diagnosed in a single test for epi-signatures (to be published in the *Am. J. Hum. Genet* in 2020). We hope to increase that number rapidly. Despite the current Corona crisis, Izabela hopes to finish her PhD in 2020.

All in all, studying the epigenome has provided us with many new insights and has enabled many collaborations, many of which within AR&D. ●

“For the first time by means of a large randomized trial, it was proven that different culture conditions in the IVF lab can have an effect on child outcomes.”



SEBASTIAAN MASTENBROEK AND MIRIAM ZAGERS

Improving human embryo culture



Within AR&D, the research led by Dr. Sebastiaan Mastebroek focusses on early human development, assisted reproductive technology, and evidence based laboratory practice. One of his projects aims to translate earlier research findings into improved culture of human embryos and with that increase the safety and success rates of in vitro fertilisation (IVF) treatments.

IVF TREATMENT SUCCESS

Since the first successful treatment in 1978, IVF has revolutionized the field of reproductive medicine. Although controversial in the very beginning, IVF has now become well accepted and widely used in modern day societies. An estimated eight million IVF babies have been born, and currently more than a million treatments are performed worldwide each year. In the Netherlands one out of every 30 babies born is born after IVF.

Unfortunately, only about 30% of IVF treatments is successful and will result in a live birth. A central part of IVF is the laboratory phase where embryos are cultured for three to six days. One of the research lines led by Sebastiaan Mastenbroek aims to improve human embryo culture, as this will result in better quality embryos, and it is well established that good quality embryos lead to higher chances of a successful pregnancy.

“Different culture media result in different pregnancy rates.”

IVF embryos are cultured in embryo culture medium and currently more than twenty embryo culture media are commercially available for an embryologist to choose from. A Cochrane review from his group made clear that these different culture media result in different pregnancy rates. More recently he conducted a large RCT in collaboration with five IVF centers in the Netherlands comparing

two embryo culture media, and found not only a difference in pregnancy rates, but also a difference in birth weight between groups. This confirmed earlier indications, but now for the first time by means of a large randomized trial, it was proven that different culture conditions in the IVF lab can have an effect on child outcomes. Despite its clear relevance for IVF, it is strangely enough not exactly known what the contents of the embryo culture media are, as industry considers this proprietary information. Therefore his group obtained all commercially available embryo media and, in collaboration with the Laboratory Genetic Metabolic Diseases and Department of Clinical Chemistry of the Amsterdam UMC, analyzed the composition of these media and published the results. No two culture media were the same, and it became clear that there is no consensus on what the composition should be.

Although IVF labs mimic the in vivo conditions in the uterus as good as possible, actual measurements in the uterus, especially at the time of the menstrual cycle an embryo would normally implant, are very limited, even after forty years of routine clinical IVF. Realizing this, a study was performed together with Iranian PhD candidate Majid Tarahomi, who will defend his thesis at the University of Amsterdam in 2020, in a group of healthy volunteers in Tehran. Analysis of uterine fluid composition and the physiological conditions in the uterus of these healthy women resulted in clear clues on how to improve the culture conditions currently used in IVF centers worldwide.

PHD PROJECT

PhD candidate Miriam Zagers was then asked to help to translate these results into a new embryo culture medium and evaluate its safety and effectiveness. She obtained an AR&D research grant to repeat the uterine measurements performed in Tehran, but now in a Dutch population of healthy women. She also aims to study



Miriam
Zagers



Sebastiaan
Mastenbroek

possible genetic background or diet induced differences in uterine conditions. In the meantime she performed a pilot study where donated surplus IVF embryos were cultured in conditions better mimicking the in vivo uterine conditions as found in the Iranian study. First results were promising. An extensive literature review conducted by Miriam highlighted the differences between the in vivo and in vitro environment of human embryos. This also resulted in an interesting hypothesis. Has the extensive use of mouse embryos in the development of IVF, as human embryos are only limited available for these purposes, resulted in in vitro IVF conditions that mimic the mouse in vivo environment perhaps better than the human in vivo uterine environment?

One of the largest culture media companies was contacted to make a culture medium based on these research findings. In 2019, a ZonMw research grant of €742.150 was obtained to do pre-clinical tests on this new medium and then take it into the clinic. More than 500 human preimplantation embryos donated for research will be cultured in the new and currently used embryo culture media. Several outcome parameters used in

IVF laboratories, such as the morphological development of embryos, will be evaluated. More basic research on the effects on embryo metabolism, gene-expression, and methylation patterns should provide explanations for the clinical outcomes. Miriam has now obtained ethical approval of the Central Committee on Research Involving Human Subjects and is ready to start. If the pre-clinical research is successful, a pilot study that will involve 200 couples undergoing IVF has already been planned for. This should in the end be followed by a large RCT.

Whether the new embryo culture medium will indeed result in more live births still needs to be seen. In any case, a deal was made with the culture medium company that is involved in the project. At the end of the project all research findings, including the full ingredient list and all concentrations, will be published and available for all. "By making our new culture medium 'open-sourced' at the end of the project, we hope to break the current reluctance of culture medium companies to disclose the concentrations of components in their embryo culture media, and we certainly hope to kick-start innovation in this field of research again". ●

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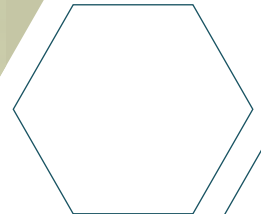
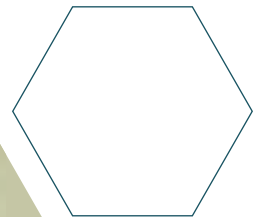
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AR&D events 2019



AR&D SYMPOSIUM: MAY 8, 2019

The AR&D symposium again took place in the Volkshotel Amsterdam, this time on May 8th. After enjoying a lunch the audience enjoyed inspiring talks on Open Science and Communication by Prof. dr. Frank Miedema and Prof. dr. Ysbrand van der Werf.

AR&D researcher Mandy Spaan, who received a AR&D Postdoc grant in 2017, presented her project “Studying the long-term health of IVF-children; facing challenges after the introduction of the GDPR [General Data Protection Regulation]”, followed by Thijs van Mens, who received a AR&D Out-of-the-box grant in 2017 and discussed his project about the role of the gut microbiome in obstetric antiphospholipid syndrome.

During the AR&D grant 2019 award ceremony, all 17 AR&D grant 2019 winners were presented and awarded their grant and flowers. After the award ceremony, Prof. dr. Anton van Kaam ended the very successful day by presenting new insights on preventing bronchopulmonary dysplasia after preterm birth.



AR&D TRAVEL GRANT AWARD CEREMONY: SEPTEMBER 13TH, 2019

On Friday September 13th, AR&D organized a mini symposium and the AR&D travel grant 2019 award ceremony. Dr. Geert Hamer and Prof. dr. Tessa Roseboom inspired the audience with their research experiences abroad.

Also, nine Travel Grants were awarded to young and talented AR&D researchers Ruud van Leuteren, Marinde van Lennep, Tamara den Harink, Tjitske Zaat, Ivy van Dijke, Britt van Keulen, Nienke van Welie, Sanne Stegwee and Maud van Muilekom!



AR&D RETREAT: OCTOBER 31ST AND NOVEMBER 1ST, 2019

Hakuna Matata, what a wonderful Retreat! On October 31st and November 1st the first Amsterdam Reproduction and Development (AR&D) Retreat was held in the Heerlijkheid in Ermelo. 65 participants travelled to the deep forest to find a hidden jungle full of scientific knowledge. The majority of participants representing the Circle of Life were PhD students, but also post-docs and PI's joined the Retreat.

The keynote lectures of Thursday were given by Wessel Ganzevoort and Pim Teunissen. Wessel Ganzevoort presented the STRIDER study and the story behind the media attention. It was very inspirational to hear how well thought out the study was set up, and how despite thorough considerations serious adverse events could still occur. On top of that, the audience was given a great example on how to deal with a study that needs to be stopped before the final inclusion had taken place.

Pim Teunissen was the second key note speaker who gave a talk on his scientific career, scientific integrity and difficulties encountering scientific fraud and fabrication of data by research partners. He addressed the impact of the content of papers being questioned, and what it does to a scientist to have to ask yourself: who can you trust in science? He also provided the audience with tips to help prevent such a situation.

Subsequently, research projects were shared during the plenary and/or parallel pitch sessions. The best pitches of every session were asked to pitch again for a price. Nienke van Welie was voted best by the PI's and Miriam Zagers received the public vote. During the early Thursday evening the brains had to work one more time during the Pubquiz after which a party started themed the Circle of Life with plenty of time for networking. The Friday program focused on personal development i.e. enjoying sports and developing new skills. The early birds were out in the woods during boot camp, showing



their strengths during Jiu Jitsu, or viewing the world through an upside down perspective during yoga.

After sporting, four rounds of workshops were given focusing on "Hakuna Matata" during the mental health workshops: Burn-out prevention and Achievement psychology, working on the "Roaaaar" during the Using theatre skills workshop and learning how to become "Kings in science" during the Presenting/Mindset skills, Grant writing and Getting things done workshops. The first AR&D retreat came to an end after the final words of the board. It was a great success! As indicated by the many positive evaluations. ●

Grants and prizes

○○○ NURSING SCIENCE, OPEN RESEARCH AND TRAVEL GRANTS

In 2019, AR&D awarded 3 types of grants: the Nursing Science Grant, specifically for research performed by nurses with the goal to improve patient care in the field of Reproduction and Development. The Open Research Grant type I, II and III, for all research in the field of Reproduction and Development and the Travel Grant, for young AR&D researchers to travel abroad for a conference or work visit.

Nursing Science Grant



NURSING SCIENCE GRANT

€ 25.000

Anita Bakker - de Jong

Long-term complications resulting from urinary catheters in children: What do we know?

START SMALL, THINK BIG GRANT (TYPE 1)

€ 25.000

Freyja van Lint

The devil is in the details: Skewed paternal inheritance in cardiomyopathies due to selfish spermatogonial selection?

Kelly Nijsten

The effects of in utero undernutrition due to hyperemesis gravidarum on offspring's cardiometabolic disease risk and the possible beneficial effect of maternal early nutritional intervention.

Danai Georgiadou

Discordant Monozygotic Twinning in Beckwith-Wiedemann Syndrome: A Study of Embryonic Pluripotency and Epigenetic Reprogramming – Development of iPSCs.

Douwe Visser

Diagnostic value of soluble CD14 subtype in neonatal sepsis.

Ekaterina Jordanova

Angiogenesis and lymphangiogenesis in uterine adenomyosis.

Marielle Alders

Methylation profiling as a diagnostic test.

IN BETWEEN GRANT (TYPE 2)

€ 50.000

Hamdi Mbarek

The SMAD3 gene and ovarian response to FSH and live birth in IVF.

Callista Mulder

Securing a fertile future for young boys with leukemia: the role of somatic cells in in vitro.

Janneke van 't Hooft

Long-term follow-up of children exposed in-utero to progesterone for prevention of preterm birth.

Anna Landman

Long-term health follow-up of children after in utero exposure to low-dose aspirin, the APRIL follow-up study.

Anke Witteveen

Hair cortisol concentration as a valid indicator of prenatal depression.



Start Small,
Think Big Grant
(Type 1)



Baudewijntje Kreukels

Sex hormones, cognition, and the role of cardiovascular and psychological factors: a study in elderly transgender people receiving gender-affirming hormone therapy.

Maurice van den Hoff

The glycosylation status of Follistatin-like 1 regulates development and growth.

THE BIGGER PICTURE GRANT (TYPE 3)
€ 100.000

Marissa Harmsen

Anti-angiogenesis therapy for adenomyosis: from bench to bedside.

Martijn Finken

Patient-tailored Glucocorticoid Treatment to Prevent Bronchopulmonary Dysplasia and Enhance Neurodevelopmental Outcome in Very Preterm Infants.

Geert Hamer

Role of germ cell-specific genes in the origin and development of cancer.



TRAVEL GRANTS

Ruud van Leutenen

Work visit Politecnico di Milano University, TechRes lab, Milano, Italy
 € 2.450

Marinde van Lennep

Work visit Sydney's children's hospital, pediatric gastroenterology, Sydney, Australia
 € 2.500

Tamara den Harink

Work visit American Society for Reproductive Medicine Congress & Expo, Philadelphia, USA
 € 2.500

Tjitske Zaat

American Society for Reproductive Medicine Congress & Expo, Philadelphia, USA
 € 1.000

Ivy van Dijke

Congress on Controversies in Preconception, Preimplantation and Prenatal Genetic Diagnosis (CoGEN), Paris, France
 € 785

Britt van Keulen

European Society for Paediatric Endocrinology 2019, Vienna, Austria
 € 310

Nienke van Welie

American Society for Reproductive Medicine (ASRM) 2019 Scientific Congress and Expo, Philadelphia, USA
 € 1.000

Sanne Stegwee

European Society for Gynaecological Endoscopy, Thessaloniki, Greece
 € 930

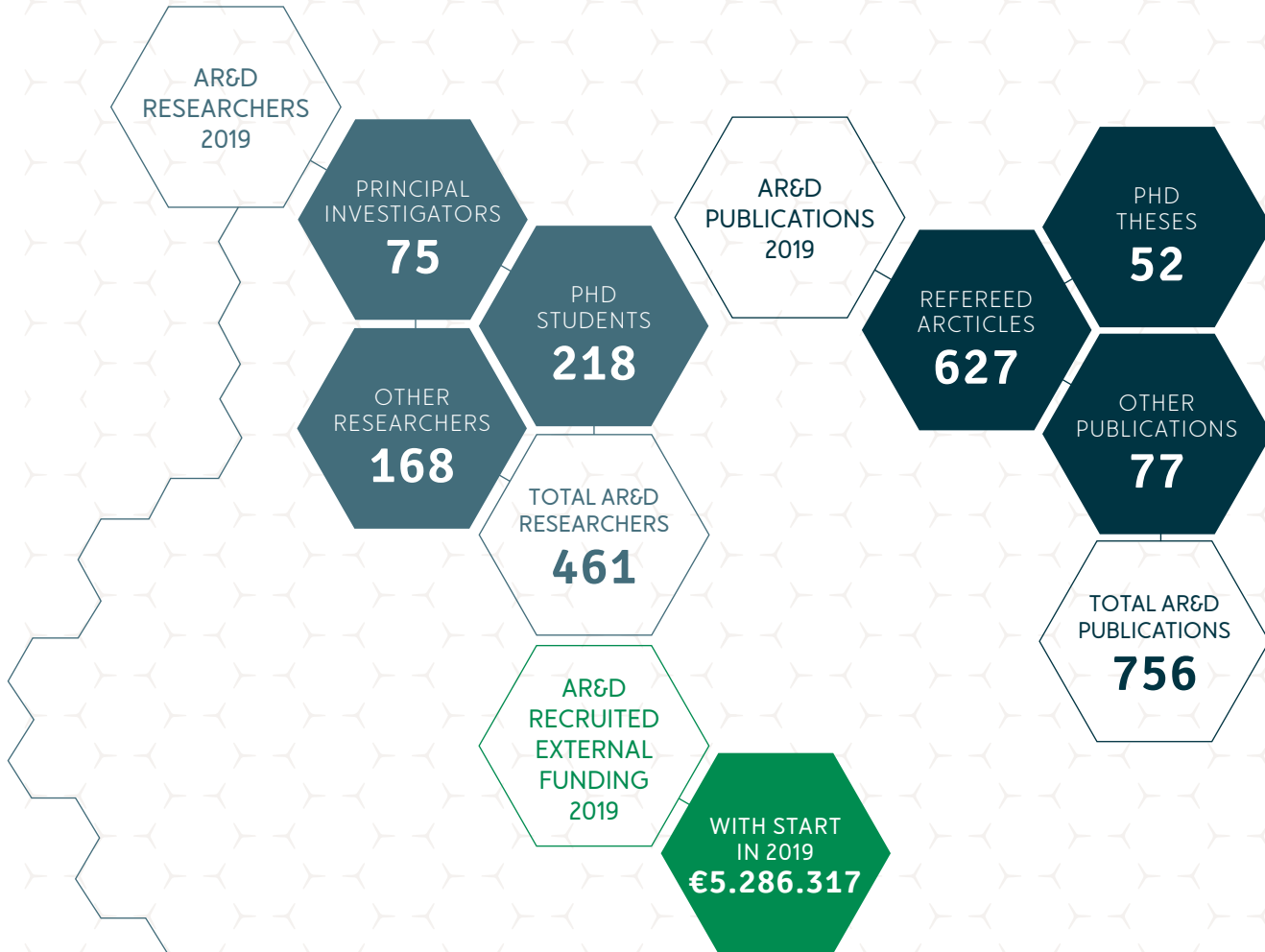
Maud van Muilekom

International Society for Quality of Life Research (ISOQOL), San Diego, USA
 € 1.000

Travel grant reports are available on the AR&D website.

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 as well as Hora Finita for VUmc PhD-students on June 22nd, 2020. Registration of research institute affiliation was done by the researchers themselves, by personnel from the Medical Library AMC 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 June 22nd, 2020. 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 2019, 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.



VIDI GRANT NWO

€ 800.000

Unraveling the mechanisms of intestinal anastomotic healing and leakage

nwo.nl/onderzoeksprogrammas/nwo-talentprogramma/projecten-vidi/2018

Joep Derikx, Department of Pediatric surgery

VENI GRANT NWO

€ 250.000

Development of a novel wound-healing implant with mechano-stimulation and localized delivery

nwo.nl/onderzoek-en-resultaten/programmas/nwo/vernieuwingsimpuls/toekenningen-veni-2019.html

Zeliha Guler Gokce, Department of Obstetrics and Gynecology

“TRANSLATIONEEL ONDERZOEK 2” GRANT ZONMW

€ 742.150

An evidence-based, open source embryo culture medium for in vitro fertilization

amc.nl/web/nieuws-en-verhalen/verhalen/community/embryos-kweken-in-de-beste-vloeistof.htm

Sebastiaan Mastenbroek, Center for Reproductive Medicine

“GOED GEBRUIK GENEESMIDDELEN” GRANT ZONMW

€ 2.200.000

Doxapram to protect preterm newborns: an international double blinded multicenter randomized placebo controlled trial

zonmw.nl/In/onderzoek-resultaten/doelmatigheidsonderzoek/programmas/project-detail/goed-gebruik-geneesmiddelen/doxapram-to-protect-preterm-newborns-an-international-double-blinded-multicenter-randomized-placebo

Jeroen Hutten, Department of Neonatology together with a.o. Sophia Children's Hospital Rotterdam (national study)

“GOED GEBRUIK GENEESMIDDELEN” GRANT ZONMW

€ 122.060

Oil-based versus water-based contrast media for hysterosalpingography (HSG) in infertile women with unevaluated indications: a randomized controlled trial (H2Oil-2 study)

zonmw.nl/In/onderzoek-resultaten/doelmatigheidsonderzoek/programmas/project-detail/goed-gebruik-geneesmiddelen/oil-based-versus-water-based-contrast-media-for-hysterosalpingography-hsg-in-infertile-women-with/verslagen/

Velja Mijatovic, Department of Obstetrics and Gynaecology

“PROGRAMMA ZWANGERSCHAP EN GEBOORTE” GRANT ZONMW

€ 250.000

Psychosocial aspects (expanded) newborn screening (PANDA)

zonmw.nl/In/onderzoek-resultaten/preventie/onbedoelde-zwangerschap-en-kwetsbaar-jong-ouderschap/programmas/project-detail/zwangerschap-en-geboorte-2/psychosocial-aspects-of-newborn-bloodspot-screening-evaluating-perspectives-on-the-current-program/

Lidewij Henneman, Department of Clinical Genetics together with TNO

“TAKE-OFF” GRANT NWO

€ 40.000

Development of a supportive monitoring system for children and neonates

nwo.nl/onderzoeksprogrammas/toekenningen/2019

Job van Woensel, Department of Pediatric Intensive Care

AMSTERDAM UMC PHD THESIS AWARD € 2.000

3D Atlas of Human Embryology - New insights in human development

amc.nl/web/leren/graduate-school/phd-1/phd-thesis-awards.htm

Bernadette de Bakker, Department of Medical Biology

○○○ KEY PUBLICATIONS

2019 was a very productive year. Here is a selection of peer-reviewed publications that were highlights for our researchers.



Nausea and vomiting of pregnancy and hyperemesis gravidarum

Fejzo et al.

Nat Rev Dis Primers. 2019;5(1):62.

Pediatric Perceived Cognitive Functioning: Psychometric Properties and Normative Data of the Dutch Item Bank and Short Form

Marchal et al.

J Int Neuropsychol Soc . 2019;25(8):845-856.

Role of angiogenesis in adenomyosis-associated abnormal uterine bleeding and subfertility: a systematic review

Harmsen et al.

Hum Reprod Update. 2019;25(5):647-671.

Genomics of human aggression: current state of genome-wide studies and an automated systematic review tool

Odintsova et al.

Psychiatr Genet. 2019;29(5):170-190.

Effectiveness of Routine Third Trimester Ultrasonography to Reduce Adverse Perinatal Outcomes in Low Risk Pregnancy [The IRIS Study]: Nationwide, Pragmatic, Multicentre, Stepped Wedge Cluster Randomised Trial

Henrichs et al.

BMJ. 2019;367:l5517.

Effect of Hydrocortisone Therapy Initiated 7 to 14 Days After Birth on Mortality or Bronchopulmonary Dysplasia Among Very Preterm Infants Receiving Mechanical Ventilation: A Randomized Clinical Trial

Onland et al.

JAMA. 2019;321(4):354-363.

Validation of noninvasive focal depth measurements to determine epithelial thickness of the vaginal wall

Kastelein et al.

Menopause. 2019;26(10):1160-1165.

Assessment of fresh and cryopreserved testicular tissues from (pre)pubertal boys during organ culture as a strategy for in vitro spermatogenesis

Portela et al.

Hum Reprod. 2019;34(12):2443-2455.

An enhancer cluster controls gene activity and topology of the SCN5A-SCN10A locus in vivo

Man et al.

Nat Commun. 2019;10(1):4943.

Human Fetal TNF- α -Cytokine-Producing CD4 + Effector Memory T Cells Promote Intestinal Development and Mediate Inflammation Early in Life

Schreurs et al.

Immunity. 2019;50(2):462-476.e8.

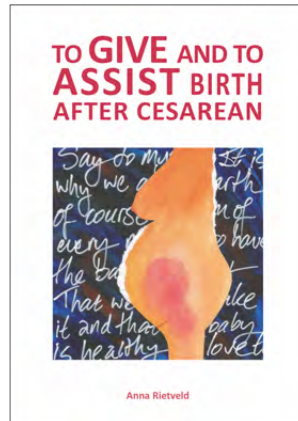
○○○ PHD THESIS

In 2019, 52 researchers obtained their PhD in the area of Reproduction & Development.

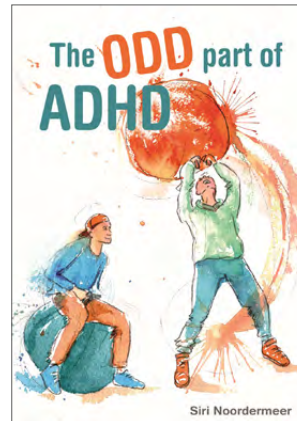
Here below a cross section of the PhD theses.



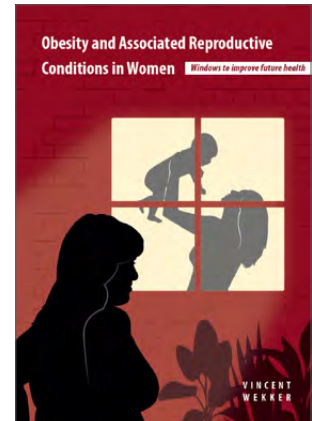
Preconception dietary intake and physical activity
Tessa M. van Elten



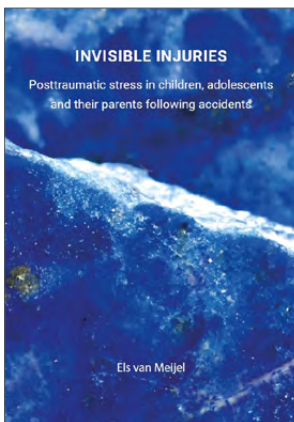
To give and to assist birth after cesarean
Anna Rietveld



The odd part of ADHD
Siri Noordermeer



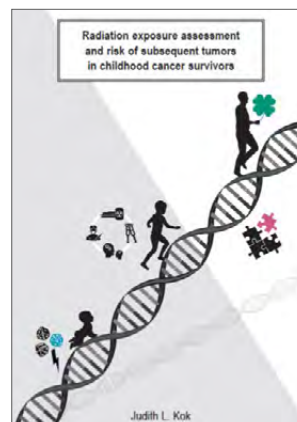
Obesity and associated reproductive conditions in women
Vincent Wekker



Invisible injuries
Els van Meijel



Well begun is half done
Jacomine E. Hogewind-Schoonenboom



Radiation exposure assessment and risk of subsequent tumors in childhood cancer survivors
Judith L. Kok



Tracing tubal factor infertility
Eleanne Frederike van Ess

○○○ SOCIETAL IMPACT

In 2019, AR&D researchers have been contributing to the Societal Impact of research. A selection of societal impact events is presented.



Arne Popma winner of the Amsterdam UMC Societal Impact Award 2019, Tessa Roseboom runner-up.



[For more information click here](#)

National implementation of genome-wide non-invasive prenatal testing as a first-tier screening test in the Netherlands.

Publication on NOS.nl, Erik Sistermans and Karuna van der Meij:

[For more information click here](#)

Based on publication: TRIDENT-2: National Implementation of Genome-wide Non-invasive Prenatal Testing as a First-Tier Screening Test in the Netherlands
Van der Meij et al.
Am J Hum Genet. 2019;105(6):1091-1101.

[For more information click here](#)

AR&D performance on Lowlands music festival



Ellen Laan on the difference between sexual pleasure between females and and males

[For more information click here](#)

Oil-based versus water-based contrast media for hysterosalpingography (HSG).

Article in a supplement of The Guardian (UK Fertility Campaign), Velja Mijatovic:
Tubal flushing during HSG with oil contrast – from diagnostics to fertility enhancement

Based on publication: Oil-based or Water-Based Contrast for Hysterosalpingography in Infertile Women: A Cost-Effectiveness Analysis of a Randomized Controlled Trial
Van Rijswijk et al.
Fertil Steril. 2018;110(4):754-760.

[For more information click here](#)

AR&D research on television at Jinek.



- Tessa Roseboom about health care for children (Kansrijke start!):
[For more information click here](#)

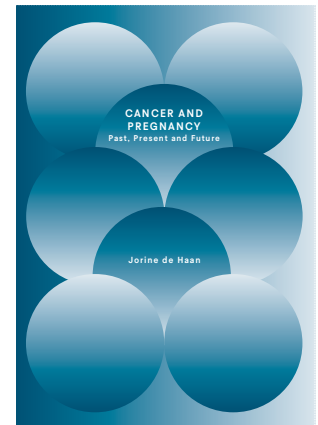
- Ellen Laan about the book: Van vulva tot vagina
[For more information click here](#)

Ellen Laan nominated for Joke Smit Oeuvreprijs.

A reward for a person or organization committed to female emancipation

[For more information click here](#)

Jorine de Haan about cancer and pregnancy.



- Interview on NPO Radio 1:
[For more information click here](#)

- Article in newspaper AD:
[For more information click here](#)

- PhD thesis Jorine de Haan:
[For more information click here](#)

Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior.

- Article in newspaper NRC, Karin Verweij:
[For more information click here](#)
- Large-scale GWAS reveals insights into the genetic architecture of same-sex sexual behavior
Ganna et al.
Science. 2019;365(6456):eaat7693.
[For more information click here](#)

- **Geert Hamer:**
Mens op bestelling, article in popular science magazine Quest:
[For more information click here](#)
- **Martina Cornel:**
Is the designer baby coming?
article in newspaper Financieel Dagblad

Laveren tussen God en wetenschap.
Komt de designbaby eraan?
[For more information click here](#)

Kids watch too much tv; they think so themselves.



Jeugdjournaal, Mai Chin a Paw:
[For more information click here](#)

3D models of embryos Bernadette de Bakker, Antoon Moorman en Roelof-Jan Oostra



Part of the Exhibition Humania in Nemo Science Museum
[For more information click here](#)

Participation in National Public Dialogues (initiated by Ministry of Health)

[For more information click here](#)

- **Sebastiaan Mastenbroek:**
Is the Designer baby coming?
Can we use embryo's for research?

Article in newspaper Trouw:
[For more information click here](#)

Interview on NPO Radio 1:
[For more information click here](#)



The Amsterdam Science & Innovation Award 2019 in the category Life Sciences went to the team of Bernadette de Bakker of Amsterdam Reproduction & Development:
[For more information click here](#)

Article on student magazine folia.nl:
[For more information click here](#)



Newly appointed professors



In 2019, three professors were appointed at the Amsterdam UMC in the field of AR&D.

PROF. DR. VELJA MIJATOVIC

Prof. dr. Velja Mijatovic is a consultant gynecologist, subspecialist in reproductive medicine and principle investigator at the department of Reproductive Medicine of the Amsterdam UMC. Since 2014, he is head of the multidisciplinary endometriosis center, one of three academic endometriosis referral centers in the Netherlands. As head of the endometriosis center he is responsible for the patient care within a dedicated team of 16 medical specialists originating from 10 disciplines, 2 fertility doctors and two endometriosis nurses. His research is focused on several theme's related to endometriosis (imaging/ biomarkers of endometriosis, infertility due to endometriosis, pregnancy related complications of endometriosis, surgical treatment of endometriosis and organization of endometriosis care) as well as to tubal dysfunction and implantation. The goal of his endometriosis research activities is to lower the delay in diagnosis, to improve fertility outcomes, to introduce innovations in treatment and to increase patient

centeredness in endometriosis care. This work is done in close collaboration with the Dutch patient association for endometriosis (Endometriose Stichting) with the common aim to promote awareness of the disease and to improve patient care. The challenge for the future will be to collaborate more in regional networks and to be distinctive in research, training, innovation and quality of care. Velja Mijatovic wants to commit himself to this with the ambition to further develop an excellent center for endometriosis care in the Netherlands. Apart from his clinical & research work, he fulfilled the following positions: past president of the Dutch Menopause Society (2010-2014), Editor-in-Chief of the Dutch Journal of Obstetrics & Gynecology (2013-now) and member of the Scientific Board of the Dutch Society of Obstetrics & Gynecology (2014-now).

PROF. DR. RIEKELT HOUTKOOPER

In February 2019 Riekelt Houtkooper was appointed professor of Translational Metabolism at the University of Amsterdam.

After a PhD on Barth syndrome in the laboratory Genetic Metabolic Diseases (Location AMC), under supervision of Prof. Ronald Wanders and Dr. Fred Vaz, and a postdoctoral project in the laboratory of prof. Johan Auwerx at EPFL Lausanne (Switzerland), Houtkooper established his group at the laboratory Genetic Metabolic Diseases of location AMC. The work in his group covers a range of metabolic diseases from rare inherited metabolic diseases to age-related metabolic diseases such as diabetes and cardiovascular disease. Moreover, they work on fundamental mechanisms regulating aging and lifespan. Houtkooper's group uses a variety of

“Ank de Jonge set up the first university department of Midwifery Science in the Netherlands.”

model systems including *C. elegans* and mice, but also works in close collaboration with clinical departments (e.g. pediatrics, internal medicine, clinical genetics) to identify new biomarkers and treatment options for patients with acquired or inborn metabolic diseases. To achieve these goals, his group together with the Core Facility Metabolomics develops and uses state-of-the-art technology to measure metabolic changes in detail, including Seahorse respirometry, lipidomics, metabolomics, and stable-isotope tracing through fluxomics.

PROF. DR. ANK DE JONGE

Ank de Jonge is the first Dutch midwife that has been appointed as a professor. She is a professor in Midwifery Science at the VU. Together with colleagues, she set up the first university department of Midwifery Science in the Netherlands, which is located in Amsterdam and Groningen. The research of her department focuses on organisation of care, evaluation of midwifery care and perinatal psychology. Client participation and care for women in vulnerable situations are important aspects of this research. Ank de Jonge did her PhD on birthing positions during the second stage of labour. She received a VENI grant which enabled her to

examine the associations between care setting and care provider at the onset of labour as exposures and maternal and perinatal morbidity and women’s experiences as outcomes. Topics for future research include detection of growth restriction, integrated maternity care, the implementation of continuity of care and supporting women to become more resilient. Much of the work is carried out through the Childbirth Network, an academic network in which client representatives, midwifery practices, research and education are combined. Within Amsterdam UMC researchers of Midwifery Science work together with several departments, such as obstetrics, general practice, public and occupational health and medical humanities. ●



Velja Mijatovic

Riekelt Houtkooper



Ank de Jonge



**“The ambition
of AR&D is to
enhance the field
of reproduction
and development
nationwide, and
to sustainably
improve health
care for mother
and child
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”