

AE-PCOS

ANDROGEN EXCESS & PCOS SOCIETY

NEWSLETTER

Strengthening care for women with Androgen Excess Disorders



Photo of the Erasmus Bridge in Rotterdam by Niel Hunnensen from Pexels.com

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FOREWORD FROM THE PRESIDENT



Looking back at the last few months I and most of you as well witnessed the publication of the new International Guideline on PCOS in 4 different major journals covering endocrinology as well as reproduction and women's health. So again, a major step forward especially since there is also attention drawn to the fact that although PCOS is the most common endocrine disorder in women of reproductive age it is the lowest funded entity in the US and Europe as well as in other parts of the world. Hopefully all of you will prioritize this and see that we get it on the agenda of funding and political bodies in all our countries across the globe. I am counting on our members concerning this endeavor.

We are also looking back at a very successful annual meeting at the former cruise ship the SS Rotterdam. It was the best attended AE PCOS meeting ever with a total number of registered attendees approaching 200! I would like to express my sincere gratitude to all of you that attended and contributed either as a speaker, poster presenter or thoughtful listener interacting with the presenters. I as well as many board members received an enormous number of compliments about how the meeting was organized as well as what the content was. Many thanks also on behalf of the board of AE-PCOS. Personally, I would like to thank Anju Joham, the program director, for her efforts which made that meeting such a success!

We had a historic overview presented by very established leaders in the field celebrating the 20-year anniversary of the Rotterdam consensus and all the consensus meetings that followed the first one in 2003. During the second day we paid attention to the major changes in the new guideline and some knowledge gaps were addressed.

We closed that day with some award ceremonies and oral presentations from (young) scientists from all over the world. And finally, we had an interactive poster session which was very well attended.

The last day we had sessions addressing what we still need to know about PCOS and the session in which the patients contributed in an exceptional manner. That session was full of emotions, and I learned again that there are still many unmet patient needs that we should address in the near future.

I also enjoyed very much the interaction with the early career members during the speed dates we had as well as in a session led by Helena Teede and Anju Joham on Saturday morning. We will definitely continue organizing such sessions in future meetings and I will meet on a quarterly basis with most of the early career SIG members.

Last but not least, the most exciting and probably also the most controversial session at the last day was the one on the name change. It was determined that we really need to decide on whether we are going to keep the abbreviation PCOS but we might fill in the letters with other words better describing the issues associated with PCOS. I sensed that the majority of the audience on that last day as well as the patients were in favor of such a name change. How it will look at the end of the day has to be seen, but this was the beginning.

Hope this as well as the newest version of the guideline and our latest AE PCOS meeting might inspire you as it did me!

Cheers,

Joop Laven MD PHD REI

President, AE-PCOS Society

Early Career Special Interest Group

BY JAMIE BENHAM

The Early Career Special Interest Group (EC-SIG) aims to support the professional development of early career professionals who have an interest in androgen excess disorders and polycystic ovary syndrome.

The EC-SIG objectives set by the Leadership Committee in collaboration with EC-SIG members are:

- 1) To expand collaborations between EC-SIG members.
- 2) To increase social media presence of EC-SIG to promote members and connect with early career professionals internationally.
- 3) To improve EC-SIG members knowledge about PCOS awareness initiatives.

The EC-SIG holds four meetings annually over Zoom. In addition, several Meet the Professor sessions are planned each year and in person events at AEPCOS meetings.

Join EC-SIG!

Please contact EC-SIG if you're interested in joining:
aepcos.ecsig@gmail.com

2023 Leadership Committee

Faculty Lead
Marla Lujan

Chairs
Snigdha Alur-Gupta
Nour El Houda Mimouni

Secretary
Sharmin Abbasi



**The next EC-SIG meeting is
February 20, 2024.**

EC-SIG CORNER

EC-SIG AT THE ANNUAL AEPCOS CONFERENCE

BY SNIGDHA ALUR-GUPTA

The EC-SIG had a fantastic turnout at the annual AEPCOS conference in Rotterdam. The EC-SIG leadership worked with Program Chair Dr. Anju Joham to organize this meeting's events.

We first hosted an informal Meet and Greet prior to the start of the meeting that was kindly sponsored by the AEPCOS.

On Day 2 of the conference, we hosted a Mini Mentorship session with a record 31 mentees in attendance! During this "speed dating" type of session, mentees were able to meet with 4 mentors each and have 1 on 1 time to discuss mentorship and research goals.

On Day 3 Dr. Helena Teede and Dr. Joham organized a universally loved EC-SIG session discussing the importance of leadership efforts, mentorship, and pearls of advice for early career members.

We are looking forward to putting together more great programs for AEPCOS 2024!



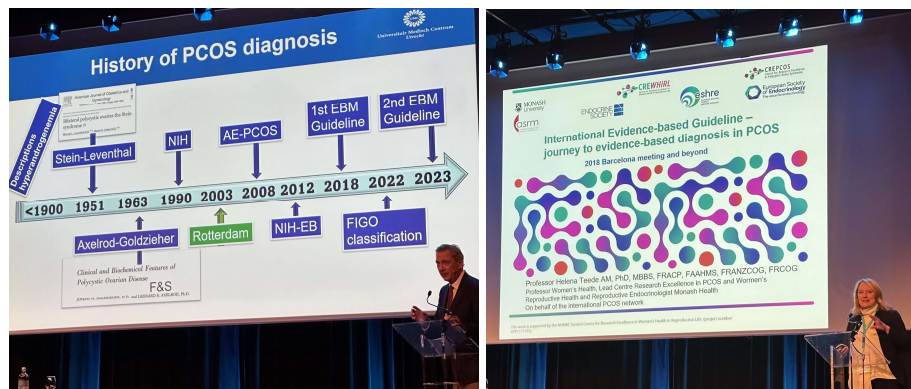
AE-PCOS

21th ANNUAL MEETING

Oct 2023 Rotterdam

By Alyse Goldberg

- Dr. Johan put together a rigorous syllabus to highlight research advances.
- The first afternoon event highlighted reflections of the past 20 years since the 2003 Rotterdam diagnostic criteria were established.



Day 2: Focus on the 2023 PCOS Evidence based guidelines

It was highlighted that these guidelines focused on consumer set priorities and are intended to be living guidelines that will update as evidence continues to emerge.

PCOS diagnosis:

- Dr. Azziz discussed indication to measure serum androgens as well as relationship of hyperandrogenism and cardiometabolic outcomes. Dr. Lujan reviewed sonographic ovarian markers of PCOS.
- Dr. Louwers reviewed the new potential role of AMH to the diagnostics of PCOS, She advised considering individualized cutoffs of AMH as a PCOM biomarker.
- Dr. Joham took us through the current data on CVD outcomes in those with PCOS. Although there is an increased risk of MACE, the incidence is low overall in this population, especially related to CVD mortality

What's new?

- Dr. Vanky highlighted that pregnancy outcomes in PCOS suggest increased risk of miscarriage, GDM, HTN, Low birth weight, preterm birth and cesarian sections. Metformin was only associated with reduction in preterm birth.
- Metformin's role in non pregnant individuals with PCOS was discussed by Dr Melin. Although there were no changes from the 2018 recommendations, there has been increased data to support benefits of metformin for those with PCOS and BMI>25.
- Dr. Forslund reviewed the oral contraceptive pill recommendations highlighting that various combinations of COCP did not show definite benefits for symptoms of hyperandrogenism. However, combination of OCP and metformin may have anthropometric benefits.
- Hirsutism pharmacologic and laser therapy were reviewed by Dr. Romualdi. Although there is limited data on combination anti androgen and OCP therapy, OCP and Laser did improve hair reduction rather than laser alone.
- Dr. Hoeger reminded up that lifestyle management goals and priorities should be first line and developed with women with PCOS. Further, there are benefits to lifestyle even in the absence of weight loss
- Lastly, Dr. Costello highlighted the changes in fertility recommendation since 2018 and reviewed the updated algorithm for fertility therapy and advances in levels of evidence of the current recommendations.

Congratulations to our award winners and oral presenters. The poster session highlighted over 100 posters.

Congratulations to the Verity and AE PCOS society Poster award winners:

Dr Heidi Vanden Brink: Emergence of Phenotypic Differences in Adolescents who Develop in the Early Post -Menarcheal Years

Dr. Haojiange Lu: Maternal Hyperandrogenism Causes Pregnancy Failure through Improper Placentation via Androgen Related Pathway



Day 3: After the guidelines: What do we still need to know?

- Dr. Laven focused on diagnostic challenges and shared his data on AMH values and assays in those with PCOS. Dr. Dokras elaborated on the need to focus on psychological and psychosexual aspect of PCOS since these factors affect quality of life in this population.
- Dr. Moran reviewed physiological, behavioural and psychosocial predictors of weight gain and emphasized the high prevalence of eating disorders in this population.
- Dr. Piltonen discussed future priorities in clarifying rolls of all medical treatments including Cocc, anti androgens, metformin and inositol There is high need of unbiased research in all these areas.
- Dr. Norman raised suspicions of PCOS trials. He also eloquently discussed both positives and drawback of the current infertility algorithm and invited discussion on roll of big data and prediction models for choice of fertility interventions.

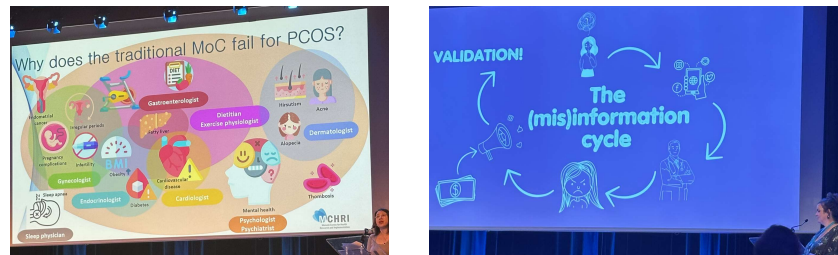
Patient advocacy and Support panel- Supported by the Waterloo Foundation

- We were fortunate to have representatives from Korento (Finland), PCOS challenge (USA), PCOS network Sweden, POSAA (Australia), SOPK (Europe) and Verity (UK) to remind us of the patient perspectives and need to focus on patient concerns when we pursue research questions and clinical studies



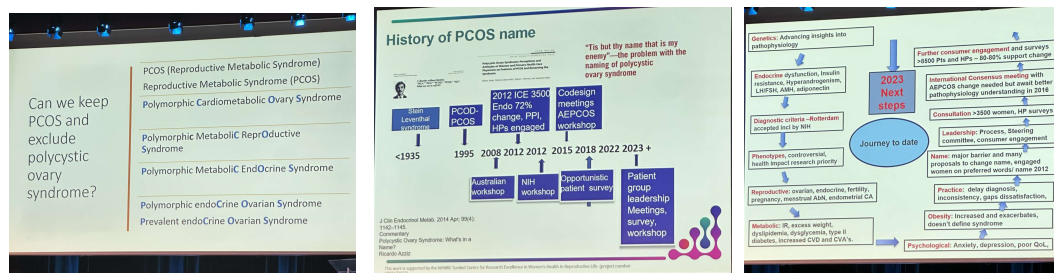
Partnering with Women with PCOS

- Dr. Tay discussed the need for further establishment of best practice for models of care for patients with PCOS
- Dr Cooney and Rachel Morman (verity) highlighted the consumer perceptions and dissatisfaction with current management of PCOS and implication of social networking on support misinformation but all potential rolls of establishing a therapeutic network together.



Name change:

- Dr. Norman focused on the implications and qualities of an effective name of a medical condition and walked us through the previous names for PCOS.
- Dr Teede reminded us that the call for a name change is driven by imperative for diagnosis, recognition and improved care. Further, that a name should keep up with all the physiological advancement that have been discovered
- The consumer voice was expressed as well which illustrated the different stakeholders with some varied opinions and concerns. Dr. Teede shared the preliminary results from the ongoing survey on name change as well as next steps.



Outside of the lecture program, many collaborations and mentorships were established. The EC Sig group had the opportunity to explore mentorship and meet with society leaders (highlighted in the EC sig section)



Highlights from the 2023 Conference

Interviews with: AWARD LECTURE AND EARLY CAREER AWARD WINNERS

Ricardo Azziz Distinguished Researcher Award: **Prof. Daniel Dumesic,**

University of California, U.S.A.

Our research views PCOS as an evolutionary metabolic adaptation that developed in antiquity during times of famine to balance energy storage with use for reproduction. This altered metabolic adaptation, however, makes women with hyperandrogenic PCOS susceptible to excess weight gain in today's obesogenic environments.

What is a highlight of the research presented?

One highlight of our research is that subcutaneous abdominal adipose stem cells obtained from healthy normal-weight women with hyperandrogenic PCOS show a programmed, accelerated lipid accumulation during their development into fat cells *in vitro*.

How will your research impact individuals with PCOS?

Our research emphasizes that women with hyperandrogenic PCOS are susceptible to excess weight gain over time. It suggests that they should prepare a personalized, preventive healthcare strategy in coordination with their healthcare providers to optimize metabolic and reproductive health beginning in adolescence.



Azziz-Baumgartner Family Early Career Investigator Travel Award: Overactivation of GnRH Neurons is Sufficient to Promote PCOS-like Cardinal Traits in Female Mice

Dr Mauro Silva, Harvard Medical School



My research focus is primarily rooted in understanding how neuroendocrine systems in the brain control ovarian function and female fertility from a developmental and brain perspective. Particularly, I am interested in understanding how disturbances in female hypothalamic circuitry are key to the pathogenesis of polycystic ovary syndrome (PCOS).

What is a highlight of the research presented?

We know that many PCOS women suffer from neuroendocrine alterations altering luteinizing hormone (LH) secretion, which might be a key culprit trigger leading to ovarian dysfunction and hyperandrogenism in these patients. We also know that LH levels are a proxy of gonadotropin-releasing hormone (GnRH) secretion from hypothalamic GnRH neurons; thus, suggesting that high LH secretion in PCOS might indicate an abnormally high GnRH neuronal activation. These pieces of evidence have been described since primary human studies from the 1980s and 1990s to the most recent work using PCOS animal models. However, we still miss the direct connection between high GnRH neuronal activity to the reproductive impairments in PCOS. Here, our work showed that by chronically enhancing GnRH neuronal activity in young adult female mice, we can observe all cardinal PCOS-like symptoms in these animals such as hyperandrogenism, impairment of reproductive cycles, and ovarian dysfunction.

We used the powerful tools of chemogenetics and mouse transgenic technology to specifically target hypothalamic GnRH neurons, manipulate their neuronal activity in a chronic way, and model PCOS-like endocrine imbalance. Remarkably, even when we removed the chemogenetic treatment, both neuroendocrine and hormonal impairments remained in these animals suggesting that alterations leading to high GnRH neuronal activity might occur before ovarian dysfunction in PCOS and lead to a vicious cycle of endocrine imbalance throughout the women's reproductive life.

How will your research impact individuals with PCOS?

I believe that our work is primarily important for us to give more attention to neuroendocrine disturbances in PCOS and their role in PCOS pathogenesis. Our field would greatly benefit from more discussions on this topic as other groups have found preclinical and clinical evidence that aberrant GnRH secretion in PCOS seems to be a primary drive to the disease's manifestation over pubertal development. The present research also suggests that therapeutically targeting GnRH neuronal activity might be a beneficial route to treat PCOS patients.



Azziz-Baumgartner Family Early Career Investigator Travel Award: **Dr. Thaís P. Rocha** University of Birmingham, U.K.

Polycystic ovary syndrome (PCOS) affects 10% of women and is associated with a 2-3 fold risk of type 2 diabetes, hypertension, fatty liver disease, and cardiovascular risk in PCOS. Androgen excess has been implicated as a major contributor to metabolic risk in PCOS. We aimed to identify PCOS sub-types with distinct androgen profiles and compare their cardiometabolic risk.

What is a highlight of the research you presented?

Unsupervised cluster analysis revealed three PCOS subtypes with distinct androgen excess profiles, implicating 11-oxygenated androgens as associated with a high metabolic risk profile in women with PCOS.

How will your research impact individuals with PCOS?

Our results provide proof of principle for a novel metabolic risk prediction tool in PCOS and have the potential to guide future preventative and therapeutic approaches.

Walter Futterweit Award in Clinical Research: Prof. Zi-Jiang Chen

We have established the largest PCOS cohort and pioneered the PCOS GWAS study, as well as conducted functional research on the newly discovered genes. Simultaneously, based on clinical issues, we have carried out multiple randomized controlled trials (RCTs) to obtain high-quality evidence for transforming clinical guidelines. Leveraging the cohort, we have also conducted follow-up analyses on maternal and offspring health.

What is a highlight of the research presented?

- 1) The genetic susceptibility loci discovered through our GWAS have been extensively validated worldwide.
- 2) PCOS susceptibility SNPs from 14 populations showed significant positive selection signals.
- 3) The newly discovered genes have been found to affect metabolism and reproductive function. For example, THADA is involved in the development of PCOS by influencing insulin secretion, while DENND1A is involved in the development of PCOS by affecting FSH sensitivity.
- 4) Androgen-induced gut dysbiosis disrupts glucolipid metabolism and endocrinal functions in PCOS. Alleviation of *Limosilactobacillus reuteri* in polycystic ovary syndrome protects against circadian dysrhythmia-induced dyslipidemia via capric acid and GALR1 signaling.
- 5) In response to common clinical issues such as indications for frozen embryo transfer, we have conducted a series of multi-center randomized controlled trials (RCTs) that provide evidence supporting the use of the "freeze-all" strategy in certain cases, including traditional indications, PCOS and Single blastocyst transfer cycles.
- 6) The cohort follow-up study revealed decreased insulin sensitivity in boys with PCOS and increased anti-Müllerian hormone (AMH) levels in girls with PCOS.

How will your research impact individuals with PCOS?

Our study systematically unravelled the role of genetic and environmental factors in the development of PCOS, enriching the etiological theory of PCOS. Additionally, we provided Class I clinical evidence for the precise diagnosis and treatment of PCOS, facilitating clinicians in formulating rational treatment plans. Moreover, it raised awareness among PCOS patients regarding the health status of their offspring.



ORAL PRESENTATIONS:



Prof. Han Zhao Shandong University, China

Unsupervised Clustering-based Reclassified Subtypes of Polycystic Ovary Syndrome: a Large Cohort Study

We identified four novel PCOS subtypes (HA-PCOS, OB-PCOS, SHBG-PCOS, and LH-PCOS) in a large discovery cohort and replicated in validation cohorts from China, America, Singapore, and Europe. Distinct reproductive and metabolic outcomes were investigated among four subtypes through prospective follow-up.

What is a highlight of the research presented?

- 1) Our study used the largest PCOS cohorts in the world.
- 2) A novel and interpretable disease classification model has been developed, and it has been well validated in populations from different regions around the world.
- 3) For each subtype, we identified their respective characteristics, particularly highlighting the similarities and differences in the risk of pregnancy complications and the variations in ART outcomes.
- 4) Through long-term follow-up, we have unveiled the prognostic features of each subtype, providing crucial scientific evidence for early disease prevention.

How will your research impact individuals with PCOS?

Our study will make a notable contribution to the field of reproductive endocrinology, which can enable physicians to better understand the PCOS patient's condition and characteristics, increase diagnostic accuracy, adjust treatment plans promptly, develop personalized prevention strategy, and enhance treatment efficacy and diagnosis of PCOS.

Activation of the HIF Pathway Alleviates Metabolic Defects in Pre-pubertal PCOS Mouse Model

My research is centered around using PCOS mouse models to discover novel ways to alleviate the metabolic defects found in PCOS, specifically using the cellular hypoxia response.

What is a highlight of the research presented?

The highlight of my research so far was the discovery that activation of the HIF - pathway, central regulator of the hypoxia response, does indeed provide significant metabolic benefits in PCOS mice.

How will your research impact individuals with PCOS?

These are still early days in this line of investigation, but should any new treatment approaches eventually arise from our work, it could provide great relief to PCOS patients struggling with metabolic problems.



Nikke Virtanen University of Oulu, Finland



Lena Luyckx
University of Oulu, Finland

Abnormal Endometrial Calcium Signalling in PCOS-like Obese Mice Might Contribute to Subfertility in PCOS

My research focusses on how PCOS affects the endometrial function during key reproduction events such as decidualization and embryo implantation. For this, I used an obese prenatally androgenized PCOS mouse model, from which I isolated endometrial cells.

What is a highlight of the research presented?

We report in our studies endometrium-related abnormalities in a PCOS mouse model. Our preliminary data showed that endometrial epithelial cells have elevated intracellular calcium concentrations and aberrant expression of genes related to ion channel function. This data suggests that endometrial calcium signalling, and by extension the embryo selection mechanism it regulates, might by function improperly in PCOS.

How will your research impact individuals with PCOS?

Calcium signalling is a key player in the epithelial selection process of good/bad quality embryos for implantation. Disturbances in this mechanism can cause implantation of poor quality embryos, leading to suboptimal embryo development and pregnancy complications later on. This research can increase our understanding of PCOS-related subfertility and the possible underlying mechanism(s) relating to adverse reproductive outcomes. The studies may pave way for improved fertility and pregnancy outcomes.

Circulating Anti-Müllerian Hormone Levels in PreMenopausal Women: Novel Genetic Insights From a GWAS Meta-Analysis

We performed the largest (n=9,668) genome-wide association study (GWAS) meta-analysis for circulating anti-Müllerian hormone (AMH levels) in premenopausal women to date, including a large sample from a founder population from Northern Finland. This has aided to identify three novel genetic loci influencing AMH levels and provide insights into biological pathways and tissues involved in AMH regulation.

What is a highlight of the research presented:

One of these genetic loci is in complete linkage disequilibrium with c.1100delC in *CHEK2*, which is found to be 4-fold enriched in the Finnish population compared to other European populations. *CHEK2* has a role in culling defecting oocytes. AMH is secreted from the small antral and preantral follicles in the ovary and is a marker of ovarian reserve. Recently, mice lacking *CHEK2* showed elevated levels of AMH and it is valuable to see the same now in women through a GWAS discovery.

How will your research impact individuals with PCOS?

The research described, which includes the largest sample size in a GWAS for AMH levels, identifies novel genetic insights associated with AMH levels, a marker often elevated in women with PCOS. By shedding light on the genetic factors influencing AMH levels, we provide a valuable dataset that can contribute to a better study of the connection between AMH and PCOS. It opens the door to further investigations such as genetic correlation analysis and Mendelian randomization approaches, that could help us better understand the relationship between AMH and PCOS. However, further research is needed to directly link these findings to women with PCOS and its clinical management.



Natàlia Pujol-Gualdo University of Oulu, Finland



D.
University of Oulu, Finland

The Risk for Diabetic Complications in Women with Polycystic Ovary Syndrome and Matched Control Women

My main research interest is the cardiometabolic health of women with PCOS.

I am presenting at AE-PCOS 2023 conference our novel findings about the risk of diabetic complications in women with PCOS and type 2 diabetes. The risk of diabetic complications has not been previously investigated even though women with PCOS have markedly increased risk for type 2 diabetes. Opposite to our hypothesis, we found that when compared to women with matching diabetes duration and age at disease onset, women with PCOS had a slightly smaller risk for diabetic complications during eight-year follow-up

Our results may bring relieving information to women living with PCOS and type 2 diabetes: even though the risk of type 2 diabetes is increased, the risk of diabetic complications is not increased when diabetes is detected early and managed properly.

Hypertension and Hyperlipidaemia in Women with Polycystic Ovary Syndrome: a Population Based Multi-register Matched Cohort Study in Sweden

My main research is as follows: According to the findings from our research group, women with PCOS have a two-fold risk to develop hypertension as well as dyslipidemia later in life, a risk that is independent of their body weight. These risks can be up to six times higher among women with the hyperandrogenic PCOS phenotype.

What is a highlight of the research presented:

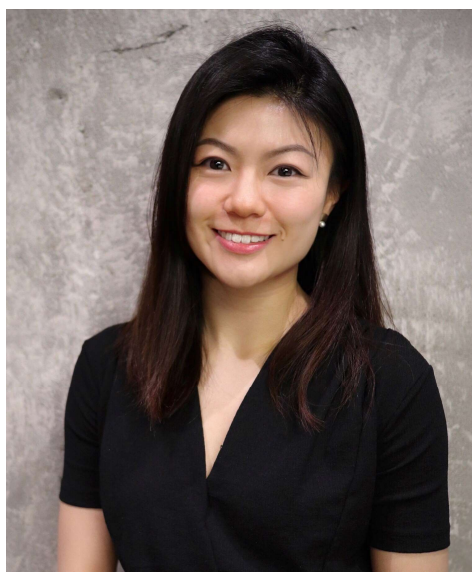
Androgen excess among PCOS women confers a risk for hypertension and dyslipidemia that is independent and higher than that of obesity.

How will your research impact individuals with PCOS?

The implication of the research is that we recommend incorporating PCOS and more specifically the hyperandrogenic PCOS phenotype among the factors included in the risk estimates for (fatal) cardiovascular disease, and advocate for life-style interventions and potentially preventive pharmacotherapy among those with PCOS that have additional cardiovascular risk factors.



Dr. Evangelia Elenis Uppsala University,
Sweden



The Effects of Maternal PCOS on the Cardiometabolic Risk and Liver Steatosis in Daughters and Sons

My study is about initiating a mother-offspring cohort to examine the intergenerational effects of PCOS and the potential differential impact of maternal PCOS on male and female offspring.

What is a highlight of the research presented:

By conducting comprehensive assessments for the offspring, we have demonstrated that daughters of PCOS mothers have increased risk of menstrual irregularity and higher androgen profile compared to daughters of healthy controls. Worsen cardiometabolic traits were observed daughters of PCOS mothers. Moreover, maternal history of PCOS is significantly associated with the moderate to severe liver steatosis in female offspring.

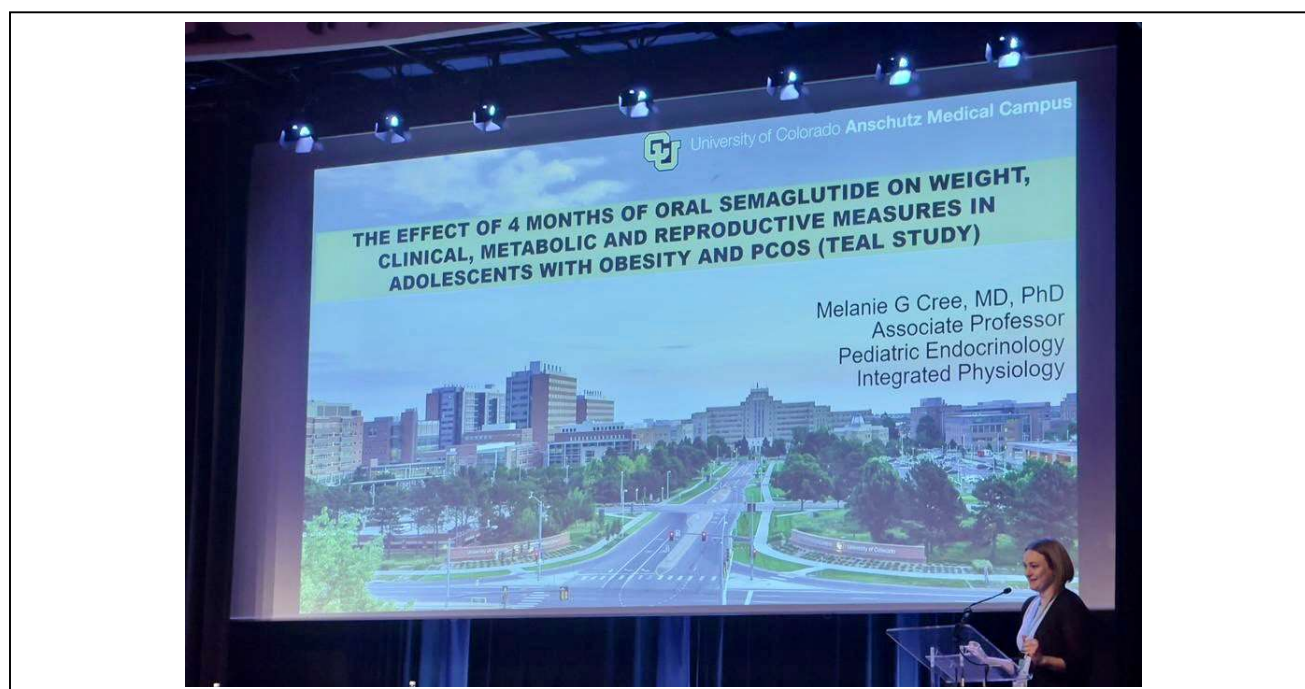
How will your research impact individuals with PCOS?

Our preliminary results shed some light on the potential long-term cardiometabolic burden on daughters of PCOS mothers.

Dr. Noel Ng The Chinese University
of Hong Kong, Hong Kong

The Effect of 4 Months of Oral Semaglutide on Weight, Clinical,
Metabolic and Reproductive Measures in Adolescents with Obesity
and PCOS

Dr. Melanie Cree
Children's Hospital, Colorado,
U.S.A.



AE PCOS Society is happy to announce the Waterloo Foundation AEPCOS Award



Objective: To help early career AE PCOS society members to gain experience performing independent basic or clinical PCOS research

Recipients:

- **Mauro Silva PhD**, Harvard Medical School, Boston MA
 - Investigating disordered brain autonomic ovary communications in PCOS
- **Rosie Bauer**, Northwestern University, Chicago USA
 - Impact of genetic variation in PCOS
- **Congru Li**, Karolinska Institute, Stockholm Sweden
 - Dissect molecular dysfunction in adipose tissue of IR Women with PCOS



MEMBER ENGAGEMENT

We are pleased to share news from our members:

Dr. Stephanie Mohammed

The University of the West Indies, St. Augustine, WI

The **PCOS Challenge Early Stage Investigator Award** as well as the **Ricardo Azziz Advocacy Leadership Award** was awarded to Dr Stephanie Mohammed for her leadership carrying out the Trinidad PEP study and bringing PCOS awareness to the Trinidad and the Caribbean,

CALL FOR NEWSLETTER CONTENT

Share with us any news or announcements.

We want to hear from you!

Interested members please email newsletter@ae-society.org.

Use the subject line "Member engagement".

We suggest the content to be around 200-300 words with 1-3 accompanying images

CALENDER OF EVENTS

March 1–3, 2024, **21st International Congress of Endocrinology** Dubai, UAE

AE-PCOS Scientific Update Meeting: *Immune function in PCOS* Friday May 10 2024, ECE Stockholm, Sweden



September 2024 **62nd Annual Meeting of the European Society for Paediatric Endocrinology** Liverpool, UK

Save the date:

22nd annual Meeting of AEPCOS Society
Queenstown, New Zealand
7-9 Nov 2024



More information at: <https://ae-society.org/meetings/>