



...The Newsletter of The PCOS Society of India

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Welcoming....

Our New Patron Members



Dr. Aparna Padgaonkar



Dr. Kavita Mantry



Dr. Madhuri Joshi



Dr. Nirja Chawla



Dr. Shreyas Padgaonkar

Our New Life Members

Dr. Amit Tandon

Dr. Arpita Goen

Dr. Janaki Thankam M. Pillai

Dr. Kunjimoideen K.U

Dr. Manju V. K.

Dr. Naina Jaitli

Dr. Padmapriya Paramasivam

Dr. Rachana Jalal

Dr. Rachana Sampathkumar

Dr. Ratnabali Chakravorty

Dr. Remya Menon

Dr. Sandhya Chhasatia

Dr. Sanjukta Sen

Dr. Shashwati Halder Kayal

Dr. Snehaatha Manu Kuris

Dr. Supriya Patil

Dr. Udayan Kundu

Dr. Uma Ram

Dr. Urmila Patil

Dr. Veena M.

Dr. Zohra Mastoor

Our New Associate Member

Dr. Amina Meer

EXPERT

Excellence in PCOS, Experience in Reproductive Technology

RECENTLY
LAUNCHED
MODULES

Excellence in PCOS, Experience in Reproductive Technology

Authors – **Dr. Duru Shah & Dr. Madhuri Patil**



Total of 6 Modules

- Module 1** Ovulation Induction in Polycystic Ovary Syndrome
- Module 2** Polycystic Ovary Syndrome and Endometriosis
- Module 3** Ovarian Aging: Challenges and Therapeutic Options
- Module 4** Role of Adjuvants in Infertility Management: from Physiology to Therapeutics
- Module 5** Male Infertility
- Module 6** Assisted Reproductive Technology

Online content available on the below link
<http://www.pcosindia.org/expert-modules.php>

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Editorial

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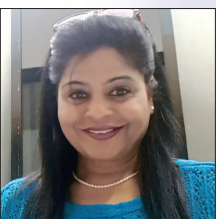
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Dear Friends

"**PANDORA**" the Newsletter, of the PCOS Society of India reaches out to 40,000 physicians globally, and is dedicated to giving you the news from our Society and also some scientific updates.

The PCOS Society of India is a Collective of various disciplines of medicine ie. gynaecology, endocrinology, dermatology, medicine etc. which deal with PCOS. We also have Associate Members who are not physicians but are Nutritionists, physiotherapists, etc. who manage the issues related to PCOS.

Our Website is loaded with educational material which currently is open to all, but very soon we will be restricting access to the educational content, to only members of the Society. To become a Member or Patron of the Society, please download the form from the website <http://www.pcosindia.org/membership.php> and join us in our endeavour to manage our PCOS patients better.

We have started the year 2019 with many academic activities, some of which we reported in our last issue, January-April 2019. In this issue we bring to you what has elapsed between our last report to you and our future scheduled events. Our **Webinar Series with Monash University** have been extremely successful with very meaningful practical discussions. I urge you to check our schedule for further sessions, and if you have missed any of them, you could still see them archived on our website in the "**Education Section**" <http://www.pcosindia.org>. I thank the USV team for making it possible for us to disseminate this brilliant academic initiative to promote the latest International Recommendations on the management of PCOS .

The Course on "**Art of ART in PCOS**" which is a 6 day hands-on course for PCOS and Assisted Reproduction, was held between **March 18th-23rd, 2019**. It was house full with 16 candidates which is all we accept at a time. Please read the details on page 5, and register for the next course in September 2019. I am extremely thankful to our esteemed faculty and to the Torrent team and Origio for supporting our endeavour which is targeted towards upcoming Gynaecologists.

We have completed 2 of our CME's in collaboration with the "**Endocrine Dept. of KEM Hospital**" which focused on the Endocrine aspects of PCOS. We thank the USV team for assisting us in organizing these extremely interactive CME's, of which we have 2 more to go.

We now look forward to our **Annual Conference** between **23rd to 25th August, 2019**, being organized in **Mumbai**, by our Vice President Dr. Shashank Joshi jointly with Dr. Piya Ballani Thakkar, both Endocrinologists. **Do block your dates and you will hear from us soon.**

Also block your dates 1st, 2nd, 3rd November, 2019 for an exciting full day Masterclass on "**PCOS in Puberty and Adolescence**" in collaboration with the International Gynaecological and Endocrine Society (ISGE) with 4 excellent international speakers, followed by a day of solving clinical dilemmas with experts. Please block your dates, you will soon get all details.

The immediate next event which will run from May-October 2019 will be a Series of 6 Webinars of 2 hours each on "**Infertility Management in PCOS**" dedicated to post graduate students and clinicians interested in infertility management.

The webinar will cover 6 topics, with each topic devoted to the current evidence, the new research and the clinical experience of experts on the various aspects of infertility in PCOS. We thank the Torrent team in assisting us in reaching out globally through the digital platform. Please read further details on page 11.

The educational content on Infertility and Assisted Reproduction has been compressed into 6 brilliant Modules entitled "**EXPERT**" (Experiences in PCOS evidence in Reproductive Technology) which have been supported by Sun Pharma and hard copies delivered to about 3000 gynecologists! The digital version of these are available on the PCOS Society website <http://www.pcosindia.org/expert-modules.php>. The Modules have been developed by Dr. Madhuri Patil and myself and I thank Madhuri for all her support. Please read on page 2 for further details.

I offer my sincere gratitude to our authors who have contributed 2 brilliant articles in this issue of Pandora, which are always the star attractions of Pandora. Please read their articles on pages 6 & 9.

We look forward to you enjoying this 10th issue of **PANDORA** and looking forward to wonderful academic year.

Wishing you all the best

Warm regards,

Duru Shah
Founder President,
The PCOS Society

Events & Updates

CME on "Endocrine Aspects of PCOS" – 3rd Feb 2019, Mumbai



Dr. Sandhya Saharan
Secretary General
Thane OBGY Society

An Interactive CME on "Endocrine Aspects of PCOS" organized by PCOS Society of India in collaboration with Endocrine Department KEM Hospital and The Thane Obstetric Gynaecology Society (TOGS) was held on the 3rd of February 2019, in Thane. It was supported by USV Pharma.

The CME was dedicated to the endocrinological aspects of PCOS, which is a multi factorial complex disorder, requiring multi faculty approach due to its diverse manifestations, which requires strategic treatment and management were tackled with

abundant knowledge and evidence based management guidelines.

Dr. Madhuri Patil, a fertility specialist, who came from Bengaluru, represented the PCOS SOCIETY, gave an exhaustive overview on the diagnosis and investigations of PCOS.

Dr. Lila, an endocrinologist emphasized on the rationale for Metformin treatment, clarifying all doubts.

Dr. Swarupa Iyer, a gynaecologist from Thane spoke on menstrual disorders and infertility.

Dr. Nalini Shah, an endocrinologist from Mumbai gave an extremely informative and lucid presentation on case based approach in ruling out secondary causes of PCOS and Hyperandrogenism.

The Panel discussion moderated by Dr. Rajnish Patel, President of TOGS on the Endocrine perspective of

PCOS was well conducted and well received with practical tips on The Management of Obesity, hypothyroidism and hyperprolactinemia.

The Panelists were Endocrinologists from KEM Hospital, Mumbai, Dr. Tushar, Dr. Swati, Dr. Lila, Dr. Nalini Shah and Gynaecologists from Thane, Dr. Alaka Godbole, Dr. Uma Bansal and Dr. Sandhya Saharan.

It was an extremely interactive panel with enthusiastic audience participation and a touch of humour when it came to management of obesity, which made the atmosphere more lively and interesting.

The CME proved to be one to remember for years to come.

The USV Team did a great job in both organizing and coordinating with TOGS to ensure there was a grand venue with great food and overwhelming attendance by local delegates, numbering 182.



CME on "Adolescent PCOS" – 30th March 2019, Bangalore



Dr. Madhuri Patil
Course Co-ordinator

The PCOS Society (India) held a half day CME on "Adolescent PCOS", on 30th March 2019 at

Bangalore. This was in collaboration with the Bangalore Obstetric and Gynecological Society and saw a participation of experts from varied disciplines like Gynecology, Endocrinology, Cosmetology, Bariatric surgery, Nutrition and Psychology. As it was a multidisciplinary CME it involved discussion on all aspects of adolescent PCOS, from diagnosis to management. Each speaker put forth the different

aspects of adolescent PCOS extremely successfully. The session was attended by 160 delegates with an extremely well attended interactive session. All doubts were clarified on the subject of adolescent PCOS, making the delegates very satisfied.

This CME was supported by an unconditional educational grant from Bayer Zydus Pharma, which was truly appreciated.



The Art of ART in PCOS – 18th-23rd March 2018, Mumbai



Dr. Duru Shah
Course Director



Dr. Madhuri Patil
Course Director

The first hands-on 6 day Certificate course on The Art of ART in PCOS was conducted from the 18th of March to the 23rd of March 2018. The course mainly focused on PCOS Women and had didactic lectures, case discussions and demonstration of sperm preparation techniques, IVF and ICSI procedures with freezing of sperms, oocytes and embryos. The candidates had the opportunity to improve their oocyte retrieval and embryo transfer skills on the Simulators. The course also focused on the medicolegal aspects of ART including third party reproduction, PCPNDT and Adoption. Course



content was provided in the form of Six Modules on various aspects of ART, several E-books and guidelines. The number of candidates was limited to sixteen, hence all the lectures were very interactive, and all queries were resolved.

We had an excellent faculty including fertility specialists Drs Padma Rekha Jirge, Shreyas Padgaonkar, Sujata Kar, Pratap Kumar, Ameet



Patki, Kanthi Bansal, Parikshit Tank; embryologists Rajvi Mehta and Kersi Avari and Medico legal expert Hitesh Bhatt. The entire faculties for the course were stalwarts in the field of ART. All the candidates have been offered a complimentary observational week at any of the ART centers approved by the PCOS society (India).

The feedback from all the candidates was very good as all of them thought they would be able to improvise on their present practice of managing infertile PCOS patients.

The next course has been scheduled on 16th September to the 21st of September 2019. Registration can be completed by direct online payment on the PCOS Society website or by sending your cheque or Demand Draft to the PCOS Society office or through net banking.



The Art of ART in PCOS

Feedback from the ART Course delegates

"One of the finest ART Course I have attended"

"Very informative Sessions"

"The hardwork, dedication and knowledge of the teachers have inspired me to excel and work hard. Would like to attend further courses."

"Excellent workshop! Very Practical"

ART Centres for Observership

Faculty, Email id	Centers & Dates
Dr. Kanthi Bansal kanthibansal@gmail.com	Allahabad 24 th April to 27 th April Varanasi 28 th April to 2 nd May Ahmedabad 6 th May to 10 th May
Dr. Kersi Avari kersiavari@hotmail.com	Mumbai 6 th -10 th May
Dr. Duru Shah durushah@gmail.com	Mumbai Gynaecworld, Dates to be confirmed as per mutual convenience.
Dr. Madhuri Patil drmadhuripatil59@gmail.com	Bangalore , Dates to be confirmed as per mutual convenience.
Dr. Sujata Kar suju63@yahoo.com	KCHPL, Bhubaneswar – based on the candidates requirements
Dr. Rekha Jirge rekha.jirge@gmail.com	Kolhapur

International evidence-based guideline for the assessment and management of PCOS 2018



Professor Helena Teede
Co-Director, Centre for Research
Excellence in Polycystic Ovary Syndrome
Director, Evidence-based guideline in
PCOS project.

Download the full version of the guideline and translation resources for women and health professionals at <https://www.monash.edu/medicine/sphpm/mchri/pcos/guideline>

Introduction

We have led the development of the first international evidence-based guideline for the diagnosis and management of polycystic ovary syndrome (PCOS), with an integrated translation program incorporating health professional and consumer resources. The development process involved an extensive Australian-led international and multidisciplinary collaboration of health professionals and consumers over two years. The guideline aims to support both health professionals and women with PCOS in improving care, health outcomes and quality of life.

Context and background

Polycystic ovary syndrome (PCOS) is a significant public health issue with reproductive, metabolic and psychological features. PCOS is one of the most common conditions in reproductive aged women affecting 8-13% of reproductive-aged women¹⁻⁴ with up to 70% of affected women remaining undiagnosed³. Presentation varies by ethnicity and in high-risk populations, prevalence and complications are higher^{4,5}. Women with PCOS present with diverse features including psychological (anxiety, depression, body image)⁶⁻⁸, reproductive (irregular menstrual cycles, hirsutism, infertility and pregnancy complications)⁹ and metabolic features (insulin resistance (IR), metabolic syndrome, prediabetes, type 2 diabetes (DM2) and cardiovascular risk factors).^{10,11}

Diagnosis and treatment of PCOS remain controversial with challenges defining individual components within the diagnostic criteria, significant clinical heterogeneity generating a range of phenotypes with or without obesity, ethnic differences and variation in clinical features across the life course. These factors contribute to variation in diagnosis and care across geographical regions and health professional groups.¹² This culminates in delayed diagnosis, poor diagnosis experience and dissatisfaction with care reported by women internationally.¹³ These challenges are exacerbated by a lack of recognition of the diverse features of PCOS, inadequate funding for quality research and a lack of comprehensive international evidence-based guidelines.¹⁴ In this context, there was a compelling need for development and translation of an international evidence-based guideline for assessment and management of PCOS, addressing psychological, metabolic and reproductive features of PCOS, promoting consistent evidence-based care and guiding and encouraging research in PCOS.

The extensive international guideline network across our partners and collaborators engaged in prioritization of clinical questions and outcomes, identification of gaps in knowledge and care and into translation preferences and information needs for health professionals and consumers. This stakeholder engagement directly informed the

guideline and translation program and involved over 3000 health professionals and consumers with PCOS. Our partners and collaborators contributed members to the guideline governance, development and translation committees and formed special interest groups with considerable expertise in PCOS to provide feedback during the public consultation process and are engaged in translation and evaluation.

Governance

Governance included international representation across the Advisory Committee, Project Board, Consumer Reference Group, Translation Committee and five multidisciplinary Guideline Development Groups comprising partner and collaborator nominated experts, practicing clinicians and consumers. Guideline development groups and special interest groups/experts were nominated by the partner and collaborator organizations. The Australian Centre for Research Excellence in PCOS (CREPCOS), funded by the National Health and Medical Research Council (NHMRC), led and primarily funded the guideline development. In this endeavour, we partnered with the European Society of Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM). Thirty five other societies partnered in the development of the guideline including the PCOS Society of India with Dr.Duru Shah involved as an expert guideline developer.

Methods

Guideline development engagement and processes were extensive and followed best practice. Four project board and 15 guideline development group face to face meetings occurred across Europe, USA and Australia over 15 months. Sixty prioritized clinical questions were addressed with 40 systematic and 20 narrative reviews, generating 166 recommendations and practice points.

Recommendations were formulated using the considered judgement process in the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework¹⁵ across the quality of available evidence, integrating clinical expertise and consumer preference, and considering the applicability, feasibility, equity, cost effectiveness, implementation and value for consumers and health professionals through the GRADE framework. Implementation issues and international health systems and settings were also considered.

Community and consumer engagement

Extensive engagement and formative research on unmet needs of women with PCOS was a key driver for this work. Far-reaching engagement included focus groups and then surveys of over 1500 women with PCOS. We adopted the International Association for Public Participation (IPA), Public Participation Spectrum framework, in which

consumer's capacity to participate was built and enhanced throughout the process. Consumers were engaged in all phases as active contributors within a distributed decision making environment, ensuring that the lived experiences of women with PCOS were prioritized. Consumer representatives were informed about the process of participation and at GDG meetings were present to embed consumer perspectives within the GRADE decision-making process. Consumers were empowered to ensure that all decisions optimised participation in care. Consumer organizations proactively participated in feedback and public consultation processes and have co-designed and will continue to guide and influence the implementation, translation and dissemination program.

Guideline recommendations

Recommendations and practice points cover the following broad areas: diagnosis, screening and risk assessment depending on life stage; emotional well being; healthy lifestyle; pharmacological treatment for non-fertility indications; and assessment and treatment of infertility.

Summary of clinical changes in the recommendations

- Endorsement of the Rotterdam PCOS diagnostic criteria in adults (two of clinical or biochemical hyperandrogenism, ovulatory dysfunction, or polycystic ovaries on ultrasound).
- Where irregular menstrual cycles and hyperandrogenism are present, ultrasound not necessary in diagnosis .
- In adolescents and those within 8 years of menarche, both hyperandrogenism and ovulatory dysfunction are required, with ultrasound not recommended, as it over-laps with the normal physiology around puberty .
- The definition of irregular cycles is more clearly defined based on gynaecological age .
- Androgens to be measured in diagnosis are specified along with optimal assays.
- Ultrasound criteria are tightened with advancing technology.
- Anti-mullerian hormone levels, although promising, are not recommended for diagnosis.
- Once diagnosed, assessment and management includes reproductive, metabolic, and psychological features.
- Education, self-empowerment, and multi-disciplinary care are important.
- Healthy lifestyle is vital for all with PCOS for prevention of excess weight gain, and lifestyle .Intervention is needed for those who are of unhealthy weight. Depressive and anxiety symptoms should be screened, assessed, and managed with the need for awareness of other impacts on emotional well-being.
- Combined oral contraceptive pills are First-line pharmacological management for menstrual irregularity and hyperandrogenism, with no specific recommended preparations and a preference for lower dose preparations .

Continued on page 8

Webinar on International PCOS Guidelines



The PCOS Society of India
in collaboration with
Monash University

Brings to you a series of **12 FREE Webinars** based on the **latest**

International PCOS Guidelines

One Webinar every 15 days for 1 hr duration

Dates
Feb. to Aug. 2019

A unique opportunity to solve your queries by
the experts who helped in creating the Guidelines

Month	Date	Topic	Speaker	Timings
Feb	12 th Feb., Tuesday	Are women with PCOS at a higher risk of cardiovascular disease? How should we screen and monitor CV risk?	Dr. Kurt Barnhart	7.30 pm Indian Standard Time
March	28 th March, Thursday	How should we diagnose PCOS? Is it different for adolescents?	Dr. Kathy Hoeger	7.30 pm Indian Standard Time
April	11 th April, Thursday	Does PCOS impact fertility?	Dr. Michael Costello	2 pm Indian Standard Time
May	16 th May, Thursday	What are the principles of drug therapy in PCOS? What should we prescribe and when?	Dr. Helena Teede	2 pm Indian Standard Time
	28 th May, Tuesday	What contributes to weight gain in PCOS women? Is it her genes, her altered metabolic function, her psychological morbidity, obesogenic environment or her lifestyle?	Dr. Anuja Dokras	7.30 pm Indian Standard Time
June	13 th June, Thursday	What exactly do we mean by "Lifestyle modifications" in PCOS? Do they really help?	Dr. Rob Norman	2-4 pm Indian Standard Time
	25 th June, Tuesday	What is insulin resistance, why does it occur and how should it be managed?	Dr. Elisabet Stener-Victorin	7.30 pm Indian Standard Time
July	11 th July, Thursday	Use of Gonadotropins in Infertility Management in PCOS Women	Dr. Clare Boothryd	To be announced
	30 th July, Tuesday	What should we expect during pregnancy in PCOS? Any precautions before, during and after pregnancy?	Dr. Roger Hart	2 pm Indian Standard Time
August	12 th Aug., Monday	Hyperandrogenism in PCOS	Dr. Joop Laven	2 pm Indian Standard Time
	29 th Aug., Thursday	To be announced		

Webinars with Speaker's consent
will be archived on the PCOS Society
Website www.pcosindia.org

Register on www.pcosindia.org

Supported by 

BLOCK YOUR DATE

THE PCOS SOCIETY | MONASH UNIVERSITY

brings a Series of Webinar based on the latest
"International PCOS Guidelines"

The 1st live session
will be moderated by Dr. Duru Shah
and will be conducted by:



Dr. Kurt Thomas Barnhart
MD, MPH



Dr. Snigaha Akur-Gupta
MD, MSc

Topic: Are women with PCOS at a higher risk of cardiovascular disease? How should we screen and monitor CV risk?

Date: Tuesday, Feb 12, 2019 | Time: 7:30 pm - 9:00 pm

THE PCOS SOCIETY | MONASH UNIVERSITY

The forum will see
two eminent speakers

brings a series of Webinar based on the latest
"International PCOS Guidelines"

The 2nd live session is scheduled on



MARCH 28
THURSDAY



SPEAKER
Dr. Kathleen Hoeger MD MPH

- Professor of OBGYN
- Division Chief, Reproductive Endocrinology and Infertility
- Associate Chair of Academic Affairs
- University of Rochester Medical Center, Rochester, New York, USA



MODERATOR
Dr. Duru Shah

- Founder President, The PCOS Society (India)
- Director, Gynaecworld, the Center for Women's Health & Fertility

Topic: How should we diagnose PCOS? Is it different for adolescents?

7:30 pm - 9:00 pm Indian Standard Time

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THE PCOS SOCIETY | MONASH UNIVERSITY

The forum will present
2 Eminent Speakers

brings a series of Webinar based on the latest
"International PCOS Guidelines"

The 3rd live session is scheduled on



APRIL 11
THURSDAY



SPEAKER
Dr. Michael Costello

- University of New South Wales, Royal Hospital for Women and IVF Australia in Sydney, Australia
- Chaired the GDO in the topic area of Screening, Diagnostic Assessment and Management of Infertility in PCOS for the International Evidence-based Guidelines for the Assessment and Management of PCOS published in 2018
- Editor for the Cochrane Menstrual Disorders & Subfertility Group



MODERATOR
Dr. Duru Shah


- Founder President, The PCOS Society (India)
- Director, Gynaecworld, the Center for Women's Health & Fertility
- Member of the GDO in the topic Screening, diagnostic assessment, risk assessment & life-stage
- Past President of Indian Society of Assistant Reproduction

Topic: Does PCOS Impact Fertility?

2:00 pm - 3:30 pm Indian Standard Time

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[CLICK HERE to view the Webinar](#)



International evidence-based guideline for the assessment and management of PCOS 2018

Continued from page 6

- Metformin recommended in addition or alone, primarily for metabolic features
- Letrozole, where permitted by national bodies, is First-line pharmacological infertility therapy with, clomiphene and metformin having a role alone and in combination.
- Gonadotrophins and laparoscopic surgery are second line and in vitro fertilization third line in isolated PCOS.

Guideline translation

A comprehensive, international translation program is disseminating, translating and amplifying the impact of the guideline. Central to the translation and dissemination program is active engagement of 37 international partners and collaborator organizations and leading health experts, across 71 countries, who are leveraging their extensive reach and influence to promote guideline uptake. Leading consumer groups internationally and translation organizations are strongly engaged and committed to translation and impact.

The guiding principles of the comprehensive international translation and dissemination program are:

- components are informed by the needs and preferences of women with PCOS;
- resources are co-created with, and attuned to, the needs of end-users; and
- dissemination strategies are multi-faceted, multi-modal and refined to the communication channels of end-users.

The research translation program uses a multi-model approach-delivering individual, community and system level impact. It targets a range of stakeholders including; consumers and their significant others and those who serve consumers such as specialist physicians (endocrinologists, obstetricians and gynaecologists, fertility specialists) primary care practitioners, allied health professionals (dietitians, exercise physiologists, psychologists) public health professionals, nurses, midwives and policy makers.

The aims of the program are:

- To guide implementation of the guideline recommendations.
- To build the capability of health professionals to deliver high-quality, consistent, evidence-based assessment and management of PCOS.
- To augment the health literacy of PCOS health consumers, leading to early diagnosis and improved health outcomes;
- To promote best-practice PCOS models of care .
- To influence health policy towards an evidence-based, best practice approach.

Reach

1. Consumers

Over 1,70,000 consumers have been directly reached via a range of modalities such as; web-based platforms, national media coverage (TV, radio, conventional media and digital platforms), collaborating organization reach and App based platforms such as AskPCOS. A range of strategies were employed to reach PCOS consumers. The

primary dissemination strategy of the translation program was to engage with consumer representative organizations and associations both in Australia and internationally (Appendix 1: Collaborating organizations).

All consumer focused translation resources were co-created with consumers. In addition, the comprehensive media campaign achieved national coverage with an estimated number of exposures per consumer of up to three across mainstream and digital platforms.

2. Health professionals

Up to 40,000 health professionals were directly reached in presentations and up to 800,000 indirectly. A range of modalities were used such as; an international conference program, high-impact journals, health media (conventional media, web-based and social media) with deep penetration achieved within collaborating societies. Multi-disciplinary health professionals (endocrinologists, obstetricians and gynaecologists, exercise physiologists, nurses, psychologists, fertility specialists and dietitians) from 37 societies across 7 continents that formed an international collaboration to develop the PCOS guideline and sign up to participate in the translation program. Health professionals were consulted on knowledge and clinical gaps and had input into the research questions informing the rigorous evidence-synthesis undertaken. Health professionals also formed part of the five guideline-development-groups (GDGs) with active input into the consensus process informing the guideline recommendations. All practice tools and decision-making support tools were co-created with health professionals. In addition, the comprehensive media campaign with the health media sector had extensive reach and penetration.

Impact

The guideline and translation program impact the following areas:

- Cost reduction to the health system.
- Improved patient satisfaction.
- Early diagnosis rates increased.
- Improved feasibility of implementation.
- Increased health professional capacity to deliver evidence-based care.
- Consistency in the assessment and management of PCOS.
- Increased consumer awareness and PCOS related health literacy.
- Guidance to health professional on interdisciplinary care.
- Uptake and implementation of best practice models of care.
- Policy outcomes supporting evidence-based care.
- Feasibility and clinical care improvements will have significant impacts on reducing costs and improving the patient experience and on health outcomes.

Outputs

The following translation outputs were informed by extensive consultation with end-users:

- co-designed practice algorithms promoting evidence-based practice (covering assessment and diagnosis, emotional wellbeing, lifestyle management, pharmacology and fertility)
- consumer info-graphs to increase consumer PCOS related health literacy and enhance self-management (covering self-diagnosis, emotional wellbeing, lifestyle management, pharmacology and fertility)

- co-designed digital booklets catering to low and medium health literacy levels
- a consumer booklet co-designed with and for Aboriginal and Torres Strait Islander women
- an internationally accessible, accredited health professional learning module hosted on the UK based Futurelearn platform
- an innovative, consumer PCOS App (AskPCOS) providing comprehensive evidence-based PCOS health information, a self-diagnostic function, a Question Prompt List (QPL) to optimize health practitioner engagement and a commonly asked questions list

We would like to acknowledge and thank Professor Duru Shah for her expert guidance and participation in the Centre for Research Excellence in PCOS International Advisory Panel. We also thank the PCOS Society India, one of the international collaborating partners in this guideline. Additionally, The Society is actively participating in the dissemination of the guideline through the delivery of a series of webinars. The webinars will feature leading members within the PCOS guideline development groups and focus on a range of topics of interest to health professionals. The aim of the webinars is to increase the capacity of health practitioners within India to deliver evidence-based PCOS care.

The full guideline, including 166 recommendations and practice points can be downloaded at <https://www.monash.edu/medicine/sphpm/mchri/pcos/guideline>

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Estrogen – "Angel or the devil in guise?"



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Estrogens or female sex hormones are important for sexual and reproductive development in women. It's primary source are the ovaries but it is also produced by fat cells and the adrenals. The term "estrogen" refers to all of the chemically similar hormones in this group, which are estrone, estradiol and estriol.

Estrogen as a hormone has different roles to play in each aspect of a woman's life starting from puberty to menopause and beyond. Natural menopause is defined as the permanent cessation of menstrual periods, determined retrospectively after a woman has experienced 12 months of amenorrhea without any other obvious pathological or physiological cause. It occurs at a median age of 51.4 years in normal women and is a reflection of complete, or near complete, ovarian follicular depletion, with resulting hypoestrogenemia and high follicle-stimulating hormone (FSH) concentrations.

The hypoestrogenic state of menopause may lead to various symptoms such as depression, vaginal dryness and subsequent atrophy, sexual dysfunction, mastalgia, migraines. The long term consequences of estrogen deficiency include bone loss, loss of collagen in the skin, higher risk of CVD, dementia and a possibility of it acting as a contributing factor to the development of osteoarthritis. In the early postmenopausal years, women who do not take estrogen therapy typically gain fat mass and lose lean mass. Some, but not all, studies, suggest that postmenopausal hormone therapy is associated with a decrease in central fat distribution.

Menopause and HRT

The reasoning behind the use of HRT as a preventative treatment for menopausal women was based on the evidence for its protective effect on the cardiovascular system as well as wide range of studies dating back to the 1960s showing estrogen deficiency may have a causal role in postmenopausal osteoporosis. The mechanism whereby estradiol-17 β prevented osteoporosis was shown to involve augmenting osteoblast survival and decreasing pro-osteoclastic signals.

In 2002 Writing Group for the Women's Health Initiative (WHI) published a multi-center double-blind, placebo-controlled trial which was initiated to assess the effect of HRT on decreasing cardiovascular events in women between ages of 50-79 yrs. The outcome of the study was widely publicized because the results of one arm of the trial where the women were given E+P, showed that there was a significant overall increase in the risk of CVD, breast cancer, stroke and dementia. In the other arm of the trial where more than 10,000 women were only given 0.625 of conjugated estradiol, there was found to be an increased risk of stroke similar to E+P, increased dementia, but no change in risk of coronary vascular diseases and an overall decrease in the incidence of hip and vertebral fractures. These outcomes were backed by another 'Million women retrospective cohort study' where 1,804,100 women between ages of 50-64 were recruited to assess the association between specific types of HRT and risk of breast cancer. The outcomes suggested increased risk with increased duration of HRT, ie, 10 years of use led to 19 cases per 1000 users of combination HRT.

These two studies made the world of HRT stop in its heels as 65% women on HRT stopped treatment. But 2 yrs later, 1 in 4 women restarted HRT.

Does the formulation of estrogen make a difference in clinical use?

Synthetic conjugated Estradiol (Ethinyl Estradiol)

- Most potent
- Most commonly used in oral contraception
- Animal derived (Conjugated equine estrogen)
- Mostly estronesulphate and 10 minor components

Plant derived

- 17 β Estradiol – micronized
- Estradiol valerate – better absorbed

Estradiol valerate

Is a natural estrogen and is found to be safer than the synthetic counterparts. It contains the most active estrogen i.e 17 β estradiol. It is available in the micronized form and is convenient for oral administration. It has increased dissolution and bioavailability when taken orally as esterification prevents extensive first pass metabolism in liver and GI tract. It is safe even for long-term use (adherence is good even after 7 yrs. of therapy).

When compared to other forms of estrogen such as ethinyl estradiol, there has been no significant effect on the breast density, blood pressure, lipid profile. Doses as low as 17 β estradiol 0.25 mgms, appear to be effective for vasomotor symptoms and to prevent bone loss.

Estradiol valerate vs other conjugated estrogens

Parameters	Estradiol valerate	Conjugated estrogen (CE)
Vasomotor symptoms	Hot flushes, severe throbs, and breast tenderness is lower	Presence of vasomotor symptoms are higher with CE
Lipid profile and cardio-protective effect	Offers favorable lipid profile	Lesser favorable lipid profile
Endothelial function	EV improves endothelial function and reduces plasma levels of endothelin	Vasoprotective effect not reported
Plasma homocysteine level	EV has no effect on plasma homocysteine level	Effect on homocysteine level not reported

Only E or P as well?

Endometrial hyperplasia and cancer can occur after as little as six months of unopposed estrogen therapy; as a result, a progestin should be added in women who have not had a hysterectomy. Women who have undergone hysterectomy should not receive a progestin.

Route of administration

Once a decision has been made to treat a woman with menopausal hormone therapy (MHT), consideration should be given not only to the type of estrogen but also to the route by which it is to be given. The route of administration is significant as transdermal estrogen is as effective as oral estrogen for preserving bone density and is associated with a lower risk of venous thrombosis and stroke, and it has less of an effect on serum lipid concentrations when compared with a comparable dose of oral estrogen. Women being treated for menopausal symptoms such as hot flashes require systemic estrogen. Vaginal estrogen is most commonly used in very low doses for the management of vaginal atrophy. Higher doses of vaginal estrogen can be used to treat vasomotor symptoms, much like any of the preparations for systemic use.

Current recommendations for HRT

American heart association

- HRT should not be initiated for the sole purpose of primary prevention of CVD
- HRT should not be initiated for the purpose of secondary prevention
- HRT should not be initiated within one year of a cardiac event even for other indication, since increased risk from HRT is seen in the first year a pro inflammatory state
- If there is a CVD event or immobilization for a women on HRT – it should be discontinued

International menopause society

- Antimuscarinic drugs, combined with local estrogens, constitute first-line medical treatment in postmenopausal women with symptoms suggestive of an overactive bladder. [A]
- MHT is the most appropriate therapy for fracture prevention in the early menopause. [A]
- Oral estrogen therapy is contraindicated in women with personal history of VTE. [A]
- Transdermal estrogen therapy should be the first choice in obese women suffering from climacteric symptoms. [B]

- MHT should not be used to enhance cognitive function. [A] Estrogen therapy may be of short-term cognitive benefit to surgically menopausal women when initiated at the time of oophorectomy. [B]
- The increased risk of breast cancer is primarily associated with the addition of a synthetic progestogen to estrogen therapy (CEE + MPA continuous combined therapy) and related to the duration of use. [B] The risk may be lower with micronized progesterone or dydrogesterone than with a synthetic progestogen. [C]
- Based on the evidence to date, the association between MHT use and ovarian cancer remains unclear.
- MHT use may be associated with a reduced risk of gastric cancer. [C]
- When Vulvo-vaginal atrophy is the sole symptom, local estrogen treatment should be the first choice. [B]
- FDA approved indications for HRT
- Vasomotor symptoms
- Prevention of bone loss
- Hypo estrogenism – primary hypo-hypo / POI / Postsurgical
- Genito urinary syndrome of menopause

Absolute contraindications for HRT

- Breast cancer
- Previous venous thromboembolism
- Active liver disease
- Coronary heart disease
- Stroke

Conclusion

- The benefits of HRT outweigh the risks for the treatment of menopausal symptoms if prescribed before the age 60 or within 10 years after menopause.
- HRT potentially prevents osteoporosis-related fractures in at-risk women before the age of 60 or within 10 years after menopause.
- HRT using standard-dose monotherapy with estrogen may decrease CHD and all-cause mortality in women younger than 60 years and within 10 years of menopause.
- Oral HRT increases the risk for VTE and ischemic stroke, but the absolute risk is rare in women younger than 60 years
- Increased risk for breast cancer may be a concern with combination HRT (E + P) and may be related to duration of use. The risk is small and after treatment is discontinued.

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INDCFT191674-09 Apr 2019

PCOS- Polycystic Ovary Syndrome, MI- Myo-Inositol, DC- D-Chiro-Inositol, *Modified as per Indian regulation.

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Quiz

- I. How dose L-carnitine have an impact on male infertility?
 - a. Leads to adnosine triphosphate depletion.
 - b. Epididymal maturation of spermatozoa.
 - c. Act as a donor of acetyl group facilitation transfer of fatty acid from mitochondria to cytosol.
 - d. All of the above.
- II. Source of L-carnitine:
 - a. Red meat
 - b. Legumes
 - c. Lysine methylation in kidney and liver
 - d. A & C
 - e. B & C
- III. How dose L-carnitine improve the reproductive functions?
 - a. Free radical scavenging.
 - b. Increases the action of capases 3,7,8.
 - c. Increase the cytokines like TNF- α INF- γ IL-6 and IL-2.
 - d. All of the above.
- IV. L-carnitine has proven to be beneficial for some PCOS women by:
 - a. Lower ring the blood glucose levels and improveing insulin sensitivity.
 - b. Helps in weight loss.
 - c. Increases the response to ovarian stimulation.
 - d. All the above.
- V. Highest concentration of myoinositol is found in:
 - a. Beans.
 - b. Corns.
 - c. Nuts.
 - d. All the above.
- VI. What is the MI/DCI ratio in follicular fluid of normal and PCOS women respectively?
 - a. 1 : 1 / 1 : 50.
 - b. 100:1 / 0.2 : 1.
 - c. 0.2 : 1 / 1 : 100.
 - d. 1 : 50 / 0.2 : 1.
- VII. How dose L-carnitine help in male factor fertility?
 - a. Epididymal maturation of spermatozoa.
 - b. Energy for sperm respiration and motility.
 - c. Increase the viability of sperm.
 - d. All the above.
- VIII. Action of myoinositol in PCOS women:
 - a. Dichiroinositol decreases the insulin sensitivity.
 - b. Improves FSH signalling
 - c. Oocyte maturation
 - d. All of the above.
 - e. None of the above
- IX. Better action of myoinositol is seen after ----- weeks of treatment.
 - a. 8
 - b. 6
 - c. 12
 - d. Immediately
- X. Clinical studies have shown that both myo-inositol and D-chiro-inositol may also:
 - a. Have no effect on serum androgens (male hormones)
 - b. Decrease triglycerides
 - c. Increase HDL cholesterol (the good cholesterol)
 - d. Lower systolic and diastolic blood pressure
- XI. Myoinositol has been used in the treatment of:
 - a. Panic disorder and depression
 - b. Diabetic neuropathy
 - c. PCOS (polycystic ovarian syndrome)
 - d. Alzheimer's disease
 - e. All of the above

- Answers
- I. B
II. A
III. D
IV. D
V. D
VI. E
VII. C and D
VIII. X
IX. B
X. B and C
XI. E

Quiz Answers

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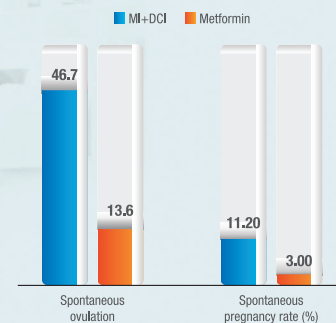
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Weight reduction

Resumption of spontaneous ovulation

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*A Mera et al. JAPI • VOL. 57 • FEBRUARY 2009
Amr Mohamed S. et al. Evidence Based Women's Health Journal 2015, 5:61-66



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