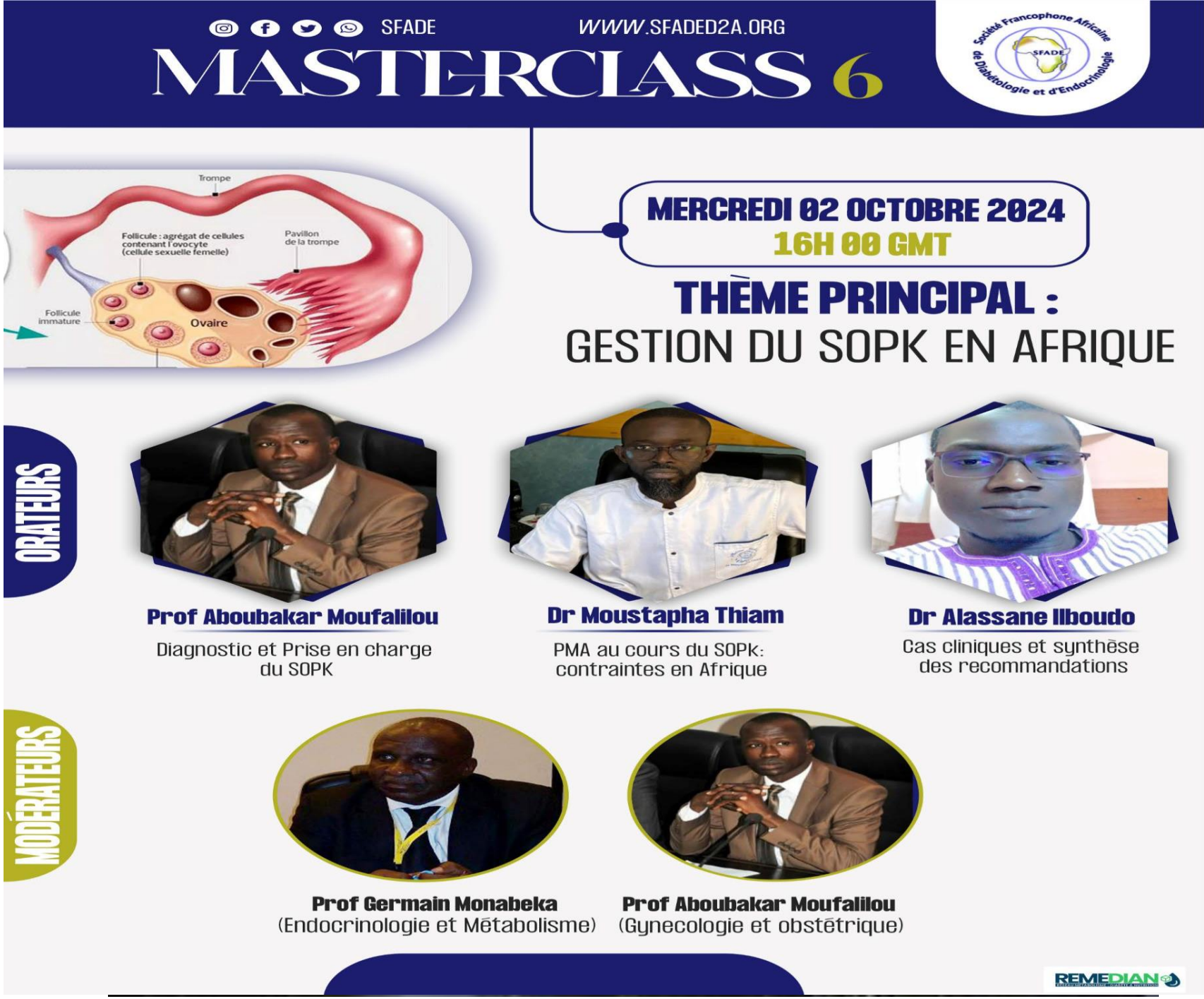
Cas cliniques SOPK

Dr ILBOUDO Alassane

Endocrinologue/ Médecin Interniste

Burkina Faso

+226 76768198



MOTIF D'HDJ

Madame YG, âgée de 26 ans,

HDJ Pitié Salpetrière Médecine de la reproduction

Pour spanioménorrhée avec Infertilité primaire

HABITUDES ET MODE DE VIE

Assistante de direction dans la fonction publique

Pratique la pèche et le bricolage ainsi que de la danse.

Repas du matin et midi souvent non pris par manque de temps ;

Grignotage assez nombreux mais les repas pris sont équilibrés.

Pas de tabac ni alcool,

FDCV : Obésité, pas d’activité physique, sédentarité +++

ANTÉCÉDENTS

- Antécédents familiaux :
  - HTA chez les parents.
  - Diabète de type 2 chez le père.
- Antécédents chirurgicaux : Amygdalectomie et strabisme opéré
- Antécédents gynéco-obstétriques :
  - G0P0
  - Ménarche vers 9 ans avec dysménorrhée

HISTOIRE DE LA MALADIE

Au plan gynécologique

Ménarche à 9 ans avec **spanioménorrhée primaire** (cycles de 2-3 mois).

Règles abondantes (6 protections par jour avec surprotections la nuit), douloureuses malgré ANTADYS puis SPASFON.

En parallèle, acné légère, pas d'hirsutisme

Mise sous pilule à l'âge de 10 ans jusqu'à 16 ans pour la dysménorrhée et les ménorragies : efficace. A 16 ans (2010) arrêt de la pilule en raison d'une **prise de poids**.

HISTOIRE DE LA MALADIE

A l'arrêt en 2010 :

Persistance de la spanioménorrhée (2-3 mois). DDR : Novembre 2018, 17/12/2019

- Pas de nécessité d'antalgiques
- Règles d'abondance normale

En **2016 (22 ans)**, **parallèlement à la prise de poids**, apparition d'une **hyperandrogénie clinique** avec

- Pilosité anormale (Lèvres supérieures, menton, bras, dos, seins)
- Acné plus importante au niveau de la parie inferieure du visage
- Pas de modification de la voix ni de clitoridomégalie

HISTOIRE DE LA MALADIE

- **Persistance de la spanioménorrhée (2-3 mois).** DDR : Novembre 2018, 17/12/2019
- - Pas de nécessité d'antalgiques
  - Règles d'abondance normale
- En **2016 (22 ans)**, **parallèlement à la prise de poids**, apparition d'une **hyperandrogénie clinique** avec
  - Pilosité anormale (Lèvres supérieures, menton, bras, dos, seins)
  - Acné plus importante au niveau de la parie inférieure du visage
- - Pas de modification de la voix ni de clitoridomégalie

HISTOIRE DE LA MALADIE

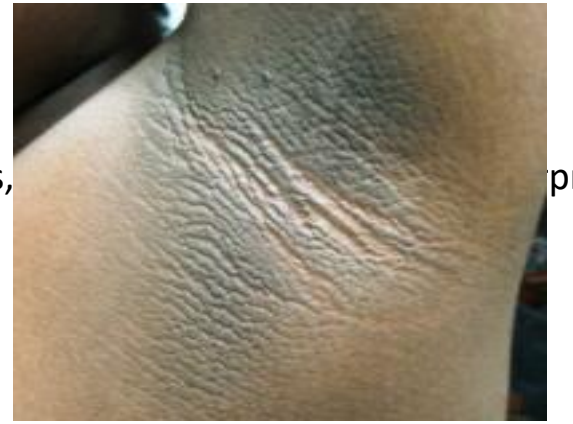
Evolution du poids :
Poids de forme 80-90 kg (avant 22 ans donc 2016) soit un IMC à 29.7 kg/m2
Augmentation progressive du poids depuis l'âge de 22 ans (**2016**) début d'une vie de couple : prise de poids estimée à 10 kg en un an et demi.
Poids actuel = poids maximal 113 Kg soit un IMC à 37.3 kg/m2

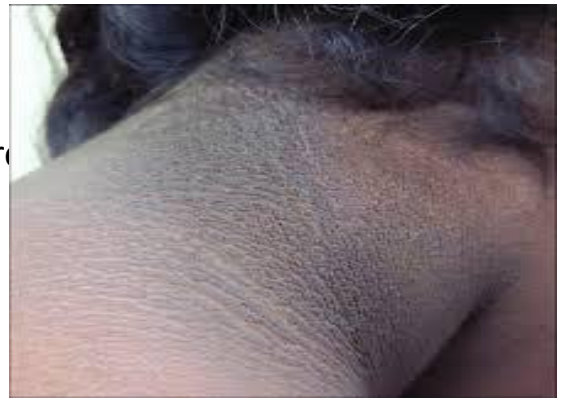
NB: Projet de grossesse depuis 2016

Toujours rechercher un lien chronologique entre l'apparition des signes d'hyper androgénie et la prise de poids.

EXAMEN CLINIQUE A L'ENTRÉE

- **Métabolique :**
  Obésité de grade 2 IMC : 37.5 kg/m2
  Tour de taille à 109 cm, tour de hanche à 134 cm
  Acanthosis nigricans au niveau du cou et des aisselles, pr





- **Retentissement de l'obésité :**
  - pas de douleur articulaire
  - Ronflement la nuit
  - Score d'Epworth à 12/24 ==> déficit de sommeil

- **Hyperandrogénie :**
  - Hirsutisme des membres, poitrine et visage épilé à la cire **Ferriman à 18.** - **Acné** persistante en bas du visage.
  - Pas de raucité de la voie ou musculature saillante.
  - Pas d'hypertrophie clitoridienne

- **Hypercortisolisme :**
  - Pas d'obésité faciotronculaire
  - Pas de bosse de Bison
  - Pas d'ecchymose, pas de pétéchies, pas d'érythrose du visage - Pas d'amyotrophie des racines des membres

EXAMENS COMPLÉMENTAIRES
1. Biologie

Bilan métabolique : Insulinoresistance sans diabète, ni intolerance au glucose, pas de dyslipidemie

Glucose	mmol/l	4.9	4.1-6.0
Hémoglobine A1c	%	5.7	4-6

HGPO:

Glucose T0 min	4.8	mmol/l	Insuline T0 min	19.3	mUI/l
Glucose T30 min	5.2	mmol/l	Insuline T30 min	63.0	mUI/l
Glucose T60 min	6.9	mmol/l	Insuline T60 min	181.2	mUI/l
Glucose T90 min	7.7	mmol/l	Insuline T90 min	303.0	mUI/l
Glucose T120 min	7.2	mmol/l	**Insuline T120 min**	**380.5**	**mUI/l**

Cholestérol	g/l	1.76	1.31-2.51
Cholestérol HDL	g/l	0.49	0.40-0.85
Cholestérol LDL	g/l	1.12	0.68-1.60
Triglycérides	g/l	0.77	0.22-1.27

Bilan gonadotrope à J28 du cycle : Inversion du rapport FSH/LH, hyperandrogenie biologique, AMH élevée

Estradiol	pg/ml	58		12-233
Progestérone	ng/mL	: 0.18		:0.06-0.89
FSH	UI/l	6.3		3.5-12.5
LH	UI/l	9.7		2.4-12.6
AMH (u.s.)		9.02 ng/ml	6-30 ans : 0.17 à 7.37 ng/ml	
Testostérone	**ng/ml**	**0.62**	**+**	**0.08-0.48**
Testostérone biod	**ng/ml**	**0.260**	**+**	**0.020-0.220**
Sex hormone bindi	nmol/L	31.2		24.6-122.0

Test au synacthène sur 17 OHP :

T 0 : 0.66 ng/ml

T 60 1.38 ng/ml

Delta 4 anrodstènedione 1.90 ng/ml (0.5-1.5)

Freinage à la dexaméthasone

Cortisol après freinage minute ng/ml 3

Bilan Thyroidien ; euthyroidie

TSH u.s.	mUI/l	1.77	0.27 à 4.2

EXAMENS COMPLÉMENTAIRES RÉALISÉS À L'ENTRÉE
2. Imagerie

Echographie endovaginale

Utérus de situation, de taille et d’aspect normal

Endomètre d’aspect normal

Aspect des ovaires compatible avec la définition d'ovaires micropolykystiques (ESHRE 2018)

Absence d'éléments en faveur d'endométriose ou d'hydrosalpinx

CFA =26 + 27, absence de corps jaune ou de follicule dominant

Autres

CR Diététicienne:
Absence de petit déjeuner
contrôle qualitativement son déjeuner par : association de légumes et de féculents / limite l'ajout de sauce avec les VO / a besoin d'une note sucrée en dessert mais se limite a un yaourt sucré ou quelques carrés de chocolat.
Tachyphagie lors des repas pris sur le lieu de travail.
Pas de prises extra prandiales dans la matinée
Dans l'après midi fait un goûter dont les quantités sont très variables en fonction de la faim.
Compulsions si stress sur des produits sucrés (chocolat / un paquet de biscuits)
Dîner identique en prenant plus de temps
Alimentation riche en lipides par les modes de cuisson, toutefois essai de limiter les graisses d'assaisonnements (1 l d'huile d'olive et 1 l d'huile de sésame en 1.5 mois + 750 g de beurre en 1 mois pour 2 personnes **sans prendre tous les repas a domicile**).

Autres

DEXA :
% graisse androïde 55.54%
% graisse gynoïde 41.62
Rapport graisse androïde/ Graisse gynoïde : 1.33 Besoin énergétique 1946 Kcal/j

Épreuve d'effort
ECG de repos normal
Performance normale
Réponse FC à l'effort normale
Réponse TA à l'effort normale
Pas de douleur thoracique, pas d'arythmie Pas de modification du segment ST Épreuve d'effort normale

Échelle de somnolence d'Epworth 12/24

NB : Entretien spy au besoin

Diagnostic de sortie

1/ Confirmation d'un syndrome des ovaires polykystiques (SOPK) :

- Spanioménorrhée primaire
- Hyperandrogénie clinico-biologique (acné et hirsutisme)
- Aspect échographique évocateur
- Elimination des diagnostics différentiels :
  - ✓ absence de bloc en 21 hydroxylase,
  - ✓ absence de syndrome de Cushing,
  - ✓ absence d'hyperprolactinémie

Diagnostic de sortie

2/ Compliqué d'une infertilité primaire du couple sur dysovulation :

- E2 58 pg/mL à J28 du cycle
- AMH 9.02 ng/mL et CFA à 26+27
- TSH à l'objectif, immunisée contre la rubéole, FCV à vérifier

3/ Cet SOPK est associé à une obésité de grade 2 (poids 113.5 kg)

- Poids actuel = poids maximal, en phase stable
- Sur alimentation hyperlipidique et compulsions sucrées en cas de stress
- Et absence d'activité physique
- Il s'y associe une insulinorésistance, sans diabète ni dyslipidémie ni stéatose hépatique. L'épreuve d'effort est normale.
- Et un déficit en sommeil (score d'Epworth à 12/24)

Traitement de sortie

ETP +++

MHD (alimentation équilibrée)

Activité physique régulière +++

Metformine 500 mg 1 cp matin et soir pendant 10 jour

Metformine 850 mg 1 cp matin et soir pendant 10 jours

Metformine 1000 mg 1 cp matin et soir en continue

Parcours de soins

Bilan complémentaire du conjoint

Consultation de suivi >>> évolution du poids, régularité des cycles, bilan hormonal ….

Absence de grossesse ou évolution défavorable >>> suivi RENON

Cycles de stimulation Gonadotrophine +/- Metformine

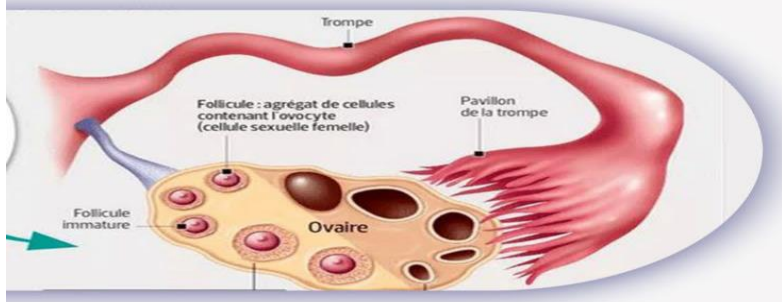
Clomid rarement utilisé

En cas d'échec >>> pompe GnRh

En absence de résultat >>> transfert autres service pour FIV/ICSI

SFADE WWW.SFADED2A.ORG

MASTERCLASS 6



MERCREDI 02 OCTOBRE 2024
16H 00 GMT

THÈME PRINCIPAL :
GESTION DU SOPK EN AFRIQUE

ORATEURS

Prof Aboubakar Moufalilou
Diagnostic et Prise en charge du SOPK

Dr Moustapha Thiam
PMA au cours du SOPk: contraintes en Afrique

Dr Alassane Ilboudo
Cas cliniques et synthèse des recommandations

MODÉRATEURS

Prof Germain Monabeka
(Endocrinologie et Métabolisme)

Prof Aboubakar Moufalilou
(Gynecologie et obstétrique)

REMEDIAN

Synthèse des recommandations 2023

OXFORD

human reproduction

Human Reproduction, 2023, **38(9)**, 1655–1679

https://doi.org/10.1093/humrep/dead156

Advance Access Publication Date: August 14, 2023

ESHRE Pages

Recommendations from the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome†

Helena J. Teede [1,2,*], Chau Thien Tay[1,2], Joop Laven[2,3], Anuja Dokras[4], Lisa J. Moran [1,2], Terhi T. Piltonen [5], Michael F. Costello[2,6], Jacky Boivin [7], Leanne M. Redman[8], Jacqueline A. Boyle[2,9], Robert J. Norman [2,10], Aya Mousa [1], Anju E. Joham[1,2], on behalf of the International PCOS Network[#]

1.1		**Irregular cycles and ovulatory dysfunction**	
1.1.1	CR	Irregular menstrual cycles are defined as: • Normal in the first year post menarche as part of the pubertal transition. • 1 to < 3 years post menarche: < 21 or > 45 days. • 3 years post menarche to perimenopause: < 21 or > 35 days or < 8 cycles per year. • 1 year post menarche > 90 days for any one cycle. • Primary amenorrhea by age 15 or > 3 years post thelarche (breast development). When irregular menstrual cycles are present a diagnosis of PCOS should be considered and assessed according to these PCOS Guidelines.	❖❖❖❖
1.2		**Biochemical hyperandrogenism**	
1.2.1	EBR	Healthcare professionals should use total and free testosterone to assess biochemical hyperandrogenism in the diagnosis of PCOS; free testosterone can be estimated by the calculated free androgen index.	❖❖❖❖ ⊕◯◯◯
1.2.2	EBR	If testosterone or free testosterone is not elevated, healthcare professionals could consider measuring androstenedione and dehydroepiandrosterone sulfate (DHEAS), noting their poorer specificity and greater age associated decrease in DHEAS.	❖❖❖ ⊕◯◯◯
1.2.3	EBR	Laboratories should use validated, highly accurate tandem mass spectrometry (LC-MS/MS) assays for measuring total testosterone and if needed, for androstenedione and DHEAS. Free testosterone should be assessed by calculation, equilibrium dialysis or ammonium sulfate precipitation.	❖❖❖❖ ⊕⊕◯◯
1.2.4	EBR	Laboratories should use LC-MS/MS assays over direct immunoassays (e.g., radiometric, enzyme-linked, etc.) for assessing total or free testosterone, which have limited accuracy and demonstrate poor sensitivity and precision for diagnosing hyperandrogenism in PCOS.	❖❖❖❖ ⊕⊕◯◯

	Clinical hyperandrogenism	
EBR	The presence of hirsutism alone should be considered predictive of biochemical hyperandrogenism and PCOS in adults.	❖❖❖ ⊕○○○
EBR	Healthcare professionals could recognize that female pattern hair loss and acne in isolation (without hirsutism) are relatively weak predictors of biochemical hyperandrogenism.	❖❖❖ ⊕○○○
CR	A comprehensive history and physical examination should be completed for symptoms and signs of clinical hyperandrogenism, including acne, female pattern hair loss and hirsutism in adults, and severe acne and hirsutism in adolescents.	❖❖❖❖
CR	Healthcare professionals should be aware of the potential negative psychosocial impact of clinical hyperandrogenism and should consider the reporting of unwanted excess hair growth and/or female pattern hair loss as being important, regardless of apparent clinical severity.	❖❖❖
CR	A modified Ferriman Gallwey score (mFG) of 4 – 6 should be used to detect hirsutism, depending on ethnicity, acknowledging that self-treatment is common and can limit clinical assessment.	❖❖❖❖
CR	Healthcare professionals should consider that the severity of hirsutism may vary by ethnicity but the prevalence of hirsutism appears similar across ethnicities.	❖❖❖

Ultrasound and polycystic ovarian morphology

EBR	Follicle number per ovary (FNPO) should be considered the most effective ultrasound marker to detect polycystic ovarian morphology (PCOM) in adults.	❖❖❖❖ ⊕⊕○○
EBR	Follicle number per ovary (FNPO), follicle number per cross-section (FNPS) and ovarian volume (OV) should be considered accurate ultrasound markers for PCOM in adults.	❖❖❖❖ ⊕⊕○○
CR	PCOM criteria should be based on follicle excess (FNPO, FNPS) and/or ovarian enlargement.	❖❖❖❖
CR	Follicle number per ovary (FNPO) ≥ 20 in at least one ovary should be considered the threshold for PCOM in adults.	❖❖❖❖
TYPE	**RECOMMENDATION**	**GRADE/QUAITY**
CR	Ovarian volume (OV) ≥ 10 ml or follicle number per section (FNPS) ≥ 10 in at least one ovary in adults should be considered the threshold for PCOM if using older technology or image quality is insufficient to allow for an accurate assessment of follicle counts throughout the entire ovary.	❖❖❖❖

	Anti-Müllerian Hormone in the diagnosis of PCOS	
EBR	Serum anti-Müllerian hormone (AMH) could be used for defining PCOM in adults.	❖❖❖ ⊕⊕⊕○
EBR	Serum AMH should only be used in accordance with the diagnostic algorithm, noting that in patients with irregular menstrual cycles and hyperandrogenism, an AMH level is not necessary for PCOS diagnosis.	❖❖❖❖ ⊕⊕⊕○
EBR	We recommend that serum AMH should not be used as a single test for the diagnosis of PCOS.	❖❖❖❖ ⊕⊕⊕○
EBR	Serum AMH should not yet be used in adolescents.	❖❖❖❖ ⊕⊕⊕○

	Cardiovascular disease risk	
EBR	Women with PCOS should be considered at increased risk of cardiovascular disease and potentially of cardiovascular mortality, acknowledging that the overall risk of cardiovascular disease in pre-menopausal women is low.	❖❖❖ ⊕○○○
EBR	All women with PCOS should be assessed for cardiovascular disease risk factors.	❖❖❖❖ ⊕○○○
CR	All women with PCOS, regardless of age and BMI, should have a lipid profile (cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and triglyceride level) at diagnosis. Thereafter, frequency of measurement should be based on the presence of hyperlipidaemia and additional risk factors or global cardiovascular risk.	❖❖❖❖
CR	All women with PCOS should have blood pressure measured annually and when planning pregnancy or seeking fertility treatment, given the high risk of hypertensive disorders in pregnancy and the associated comorbidities.	❖❖❖❖
CR	Funding bodies should recognize that PCOS is highly prevalent with multisystem effects including cardiometabolic disease and should diversify and increase research support accordingly.	❖❖❖❖
CR	Cardiovascular general population guidelines could consider the inclusion of PCOS as a cardiovascular risk factor.	❖❖❖
CR	Healthcare professionals, women with PCOS and other stakeholders should all prioritize preventative strategies to reduce cardiovascular risk.	❖❖❖❖

	Impaired glucose tolerance and type 2 diabetes risk	
EBR	Healthcare professionals and women with PCOS should be aware that, regardless of age and BMI, women with PCOS have an increased risk of impaired fasting glucose, impaired glucose tolerance and type 2 diabetes.	❖❖❖❖ ⊕⊕○○
EBR	Glycaemic status should be assessed at diagnosis in all adults and adolescents with PCOS.	❖❖❖❖ ⊕⊕○○
CR	Glycaemic status should be reassessed every one to three years, based on additional individual risk factors for diabetes.	❖❖❖❖
CR	Healthcare professionals, women with PCOS and other stakeholders should prioritize preventative strategies to reduce type 2 diabetes risk.	❖❖❖❖
CR	Funding bodies should recognize that PCOS is highly prevalent, has significantly higher risk for diabetes, and should be funded accordingly.	❖❖❖❖
CR	Diabetes general population guidelines should consider the inclusion of PCOS as an independent risk factor for diabetes.	❖❖❖❖
	Glycaemic testing	
EBR	Healthcare professionals and women with PCOS should recommend the 75-g oral glucose tolerance test (OGTT) as the most accurate test to assess glycaemic status in PCOS, regardless of BMI.	❖❖❖❖ ⊕○○○
EBR	If an OGTT cannot be performed, fasting plasma glucose and/or glycated haemoglobin (HbA1c) could be considered, noting significantly reduced accuracy.	❖❖❖ ⊕○○○
EBR	An OGTT should be considered in all women with PCOS and without pre-existing diabetes, when planning pregnancy or seeking fertility treatment, given the high risk of hyperglycaemia and the associated comorbidities in pregnancy. If not performed preconception, an OGTT could be offered at the first prenatal visit and all women with PCOS should be offered the test at 24–28 weeks gestation.	❖❖❖ ⊕○○○

	Obstructive Sleep Apnea	
EBR	Healthcare professionals should be aware that women with PCOS have significantly higher prevalence of obstructive sleep apnea compared to women without PCOS, independent of BMI.	❖❖❖❖ ⊕⊕⊕○
EBR	Women with PCOS should be assessed for symptoms of obstructive sleep apnea (i.e., snoring in combination with waking unrefreshed from sleep, daytime sleepiness or fatigue) and if present, screen with validated tools or refer for assessment.	❖❖❖❖ ⊕⊕⊕○

	Depression and Anxiety	
EBR	Healthcare professionals should be aware of the high prevalence of moderate to severe depressive symptoms and depression in adults and adolescents with PCOS and should screen for depression in all adults and adolescents with PCOS, using regionally validated screening tools.	❖❖❖❖ ⊕⊕⊕⊕
EBR	Healthcare professionals should be aware of the high prevalence of moderate to severe anxiety symptoms and anxiety disorders in adults and should screen for anxiety in all adults with PCOS, using regionally validated screening tools.	❖❖❖❖ ⊕⊕⊕⊕
CR	If moderate or severe depressive or anxiety symptoms are detected, practitioners should further assess, refer appropriately, or offer treatment.	❖❖❖❖
PP	Severity of symptoms and clinical diagnosis of depression or anxiety should guide management. The optimal interval for anxiety and depression screening is not known. A pragmatic approach could include screening at diagnosis with repeat screening based on clinical judgement, risk factors, comorbidities, and life events, including the perinatal period. Screening for mental health disorders comprises assessment of risk factors, symptoms, and risk of self-harm and suicidal intent.	
	Body Image	
EBR	Healthcare professionals should be aware that features of PCOS can have a negative impact on body image.	❖❖❖❖ ⊕⊕○○
	Eating disorders	
EBR	Eating disorders and disordered eating should be considered in PCOS, regardless of weight, especially in the context of weight management and lifestyle interventions (see sections 2.4 and 3.6).	❖❖❖ ⊕⊕○○

	Dietary Intervention	
EBR	Healthcare professionals and women should consider that there is no evidence to support any one type of diet composition over another for anthropometric, metabolic, hormonal, reproductive or psychological outcomes.	❖❖❖ ⊕○○○
CR	Any diet composition consistent with population guidelines for healthy eating will have health benefits and, within this, healthcare professionals should advise sustainable healthy eating tailored to individual preferences and goals.	❖❖❖❖
PP	Tailoring of dietary changes to food preferences, allowing for a flexible, individual and co-developed approach to achieving nutritional goals, and avoiding unduly restrictive and nutritionally unbalanced diets, are important, as per general population guidelines.	
PP	Barriers and facilitators to optimize engagement and adherence to dietary change should be discussed, including psychological factors, physical limitations, socioeconomic and sociocultural factors, as well as personal motivators for change. The value of broader family engagement should be considered. Referral to suitably trained allied healthcare professionals needs to be considered when women with PCOS need support with optimizing their diet.	
	Exercise Intervention	
EBR	Healthcare professionals and women could consider that there is a lack of evidence supporting any one type and intensity of exercise being better than another for anthropometric, metabolic, hormonal, reproductive or psychological outcomes.	❖❖❖ ⊕○○○

	Combined Oral Contraceptive Pills	
EBR	Combined oral contraceptive pills (COCP) could be recommended in reproductive age adults with PCOS for management of hirsutism and/or irregular menstrual cycles.	❖❖❖ ⊕○○○
EBR	The COCP could be considered in adolescents at risk or with a clear diagnosis of PCOS for management of hirsutism and/or irregular menstrual cycles.	❖❖❖ ⊕○○○
EBR	Healthcare professionals could consider that there is no clinical advantage of using high dose ethinylestradiol (≥ 30 μg) versus low dose ethinylestradiol (< 30 μg) when treating hirsutism in adults with PCOS.	❖❖❖ ⊕○○○
EBR	General population guidelines should be considered when prescribing COCP in adults and adolescents with PCOS as specific types or doses of progestins, estrogens or combinations of COCP cannot currently be recommended.	❖❖❖ ⊕○○○
EBR	The 35μg ethinyl estradiol plus cyproterone acetate preparations should be considered as second-line therapy, versus other COCPs, balancing benefits and adverse effects, including venous thromboembolic risks.	❖❖❖ ⊕○○○
EBR	Progestin only oral contraceptives may be considered for endometrial protection, based on general population guidelines, acknowledging that evidence in women with PCOS is limited.	❖❖❖ ⊕○○○

	Metformin	
EBR	Metformin alone should be considered in adults with PCOS and a BMI $\geq$ 25 kg/m^2 for anthropometric, and metabolic outcomes including insulin resistance, glucose, and lipid profiles.	❖❖❖ ⊕○○○
EBR	Metformin alone could be considered in adolescents at risk of or with PCOS for cycle regulation, acknowledging limited evidence.	❖❖❖ ⊕○○○
CR	Metformin alone may be considered in adults with PCOS and BMI < 25 kg/m^2, acknowledging limited evidence.	❖❖❖
PP	Where metformin is prescribed the following need to be considered: • Shared decision making needs to consider feasibility and effectiveness of active lifestyle intervention. Women should be informed that metformin and active lifestyle intervention have similar efficacy. • Mild adverse effects, including gastrointestinal side-effects are generally dose dependent and self-limiting. • Starting at a low dose, with 500 mg increments 1–2 weekly and extended-release preparations may minimize side effects and improve adherence. • Suggested maximum daily dose is 2.5 g in adults and 2g in adolescents. • Use appears safe long-term, based on use in other populations, however indications for ongoing requirement needs to be considered. • Use may be associated with low vitamin B12 levels, especially in those with risk factors for low vitamin B12 (e.g., diabetes, post bariatric / metabolic surgery, pernicious anaemia, vegan diet etc.), where monitoring should be considered.	

	Letrozole	
EBR	Letrozole should be the first-line pharmacological treatment for ovulation induction in infertile anovulatory women with PCOS, with no other infertility factors.	⧫⧫⧫⧫ ⊕⊕⊕⊕
PP	The use of letrozole is still off- label in many countries. Where it is not allowed, clinicians could use other ovulation induction agents.	
PP	Letrozole should not be given where there is any possibility of a pre-existing pregnancy, though there is no evidence for increased teratogenicity compared to other ovulation induction agents.	

	Clomiphene citrate verses metformin	
EBR	Clomiphene citrate could be used in preference to metformin in women with PCOS with anovulatory infertility and no other infertility factors, to improve ovulation, clinical pregnancy and live birth rates.	❖❖❖ ⊕⊕○○
PP	The risk of multiple pregnancy is increased with clomiphene citrate use (alone or in combination with metformin) and therefore clomiphene cycles may require ultrasound monitoring.	
	Clomiphene citrate and metformin verses clomiphene citrate alone	
EBR	Clomiphene citrate combined with metformin could be used rather than clomiphene citrate alone in women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation and clinical pregnancy rates.	❖❖❖ ⊕⊕○○
	Clomiphene citrate and metformin versus metformin alone	
EBR	Clomiphene citrate combined with metformin could be used rather than metformin alone in women with PCOS with anovulatory infertility and no other infertility factors to improve live birth rates.	❖❖❖ ⊕⊕○○
PP	Monitoring of combined cycles will need to be equivalent to clomiphene citrate alone.	
	Clomiphene citrate versus Letrozole	
EBR	Letrozole should be used rather than clomiphene citrate in women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation, clinical pregnancy and live birth rates.	❖❖❖❖ ⊕○○○
PP	Current evidence demonstrates no difference in fetal abnormality rates between letrozole or clomiphene citrate ovulation induction or natural conception.	

	Gonadotrophins	
EBR	Gonadotrophins alone could be considered rather than clomiphene citrate in therapy naïve women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation, clinical pregnancy and live birth rates (refer to PP 5.5.6).	❖❖❖ ⊕⊕○○
EBR	Gonadotrophins alone could be used over gonadotrophins combined with clomiphene citrate in women with PCOS who are anovulatory and infertile with clomiphene citrate resistance or failure, and no other infertility factors.	❖❖❖ ⊕⊕○○
EBR	Gonadotrophins could be considered rather than the combination of clomiphene citrate and metformin in women with PCOS who are anovulatory and infertile, with clomiphene citrate-resistance and no other infertility factors.	❖❖❖ ⊕○○○
EBR	Either gonadotrophins or laparoscopic ovarian surgery could be used in women with PCOS who are anovulatory and infertile, with clomiphene citrate-resistance and no other infertility factors, following counselling on higher live birth rate and higher multiple pregnancy rates with gonadotrophins.	❖❖ ⊕⊕○○
EBR	Gonadotrophins could be second-line pharmacological therapy for women with PCOS who are anovulatory and infertile, with no other infertility factors and who have failed first line oral ovulation induction.	❖❖❖ ⊕⊕○○

	Pregnancy outcomes	
EBR	Women with PCOS have higher risk pregnancies, and healthcare professionals should ensure that PCOS status is identified during antenatal care, and appropriate monitoring and support is provided.	❖❖❖❖ ⊕○○○
EBR	Healthcare professionals should recognize that pregnant women with PCOS have an increased risk of: • Higher gestational weight gain. • Miscarriage. • Gestational diabetes. • Hypertension in pregnancy and preeclampsia. • Intrauterine growth restriction, small for gestational age babies and low birth weight. • Preterm delivery. • Caesarean section.	❖❖❖❖ ⊕○○○
EBR	Assisted reproductive technology in women with PCOS should be considered as not conferring additional risk of miscarriage, preterm birth, impaired fetal growth, and caesarean section, over that observed in women without PCOS.	❖❖❖ ⊕○○○
EBR	Women with PCOS should be considered as not having an increased risk of large for gestational age babies, macrosomia and instrumental delivery.	❖❖❖ ⊕○○○

Algorithm 1: Diagnostic algorithm for polycystic ovary syndrome (PCOS)

Step 1: Irregular cycles + clinical hyperandrogenism
(exclude other causes)* = diagnosis
Step 2: If no clinical hyperandrogenism
Test for biochemical hyperandrogenism (exclude other causes)* = diagnosis
Step 3: If ONLY irregular cycles OR hyperandrogenism
Adolescents ultrasound is not indicated = consider at risk of PCOS and reassess later
Adults - **request ultrasound for PCOM***, if positive (exclude other causes)* = diagnosis

Algorithm 2: Infertility algorithm for polycystic ovary syndrome (PCOS)
Central Blue Pathway follows best practice evidence and is preferred