Nouvelle classification des désordres ovulatoires de la FIGO

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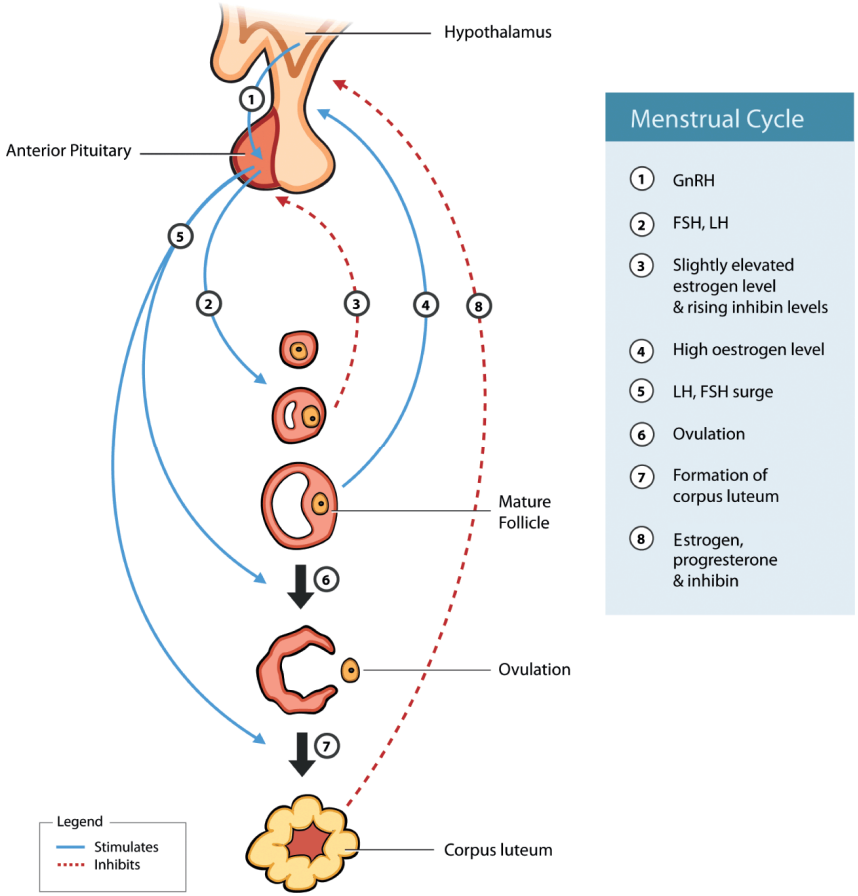
XVII èmes Journées Liégeoises de Gynécologie-Obstétrique

Définition

Trouble ovulatoire

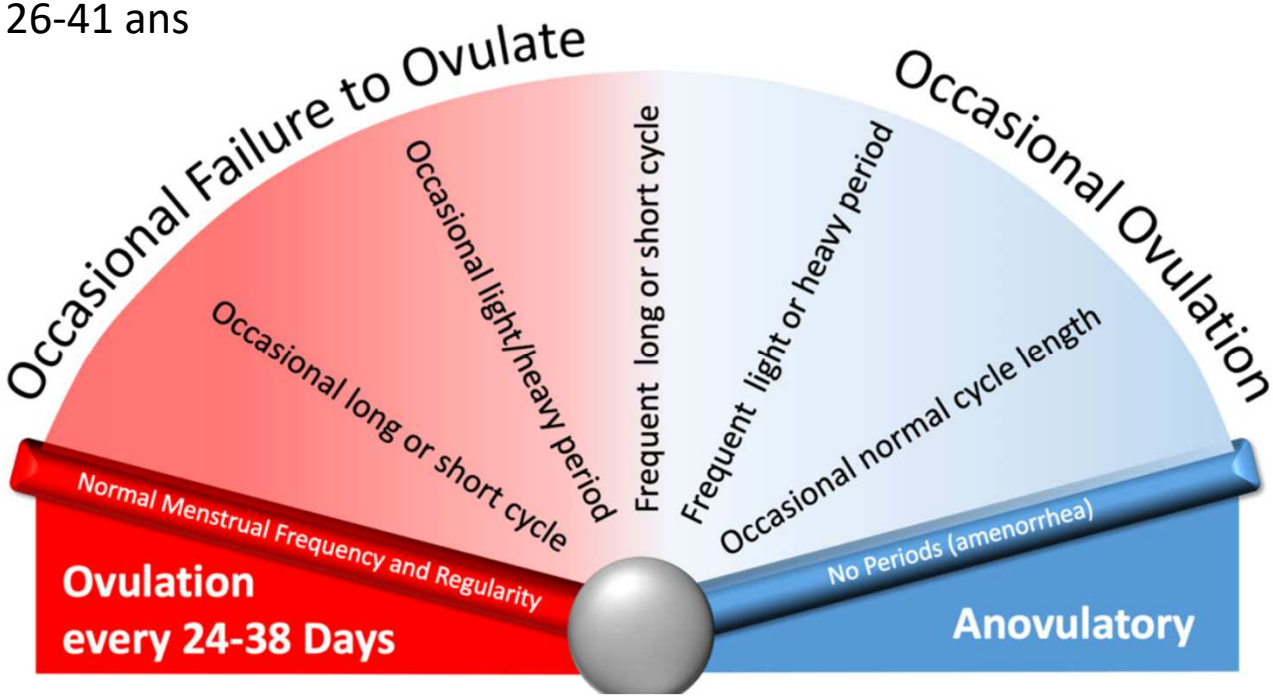
Toute altération de la fonction ovulatoire chez les femmes non enceintes en âge de procréer



Critères diagnostiques

Cycles réguliers si la différence entre le cycle le plus long et le cycle le plus court est :

- ≤ 9 jours entre 18-25 ans et entre 42-45 ans
- ≤ 7 jours entre 26-41 ans



M.G. Munro, Human Reproduction, The FIGO Ovulatory Disorders Classification System, pp. 1–19, 2022

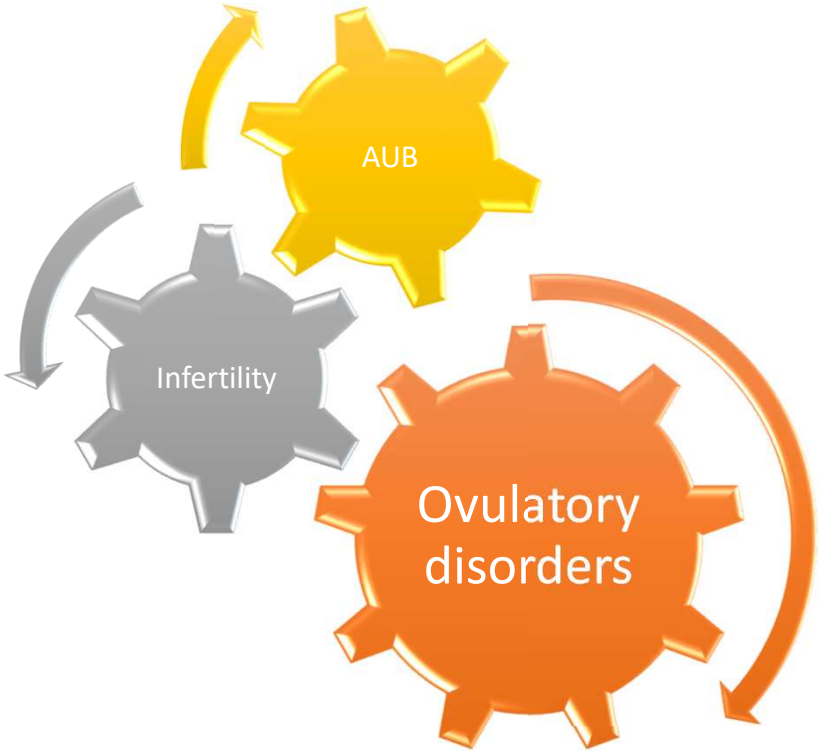
Critères diagnostiques

Parameter	Normal	Abnormal	☑
Frequency	Absent (no bleeding) = amenorrhea		☐
	Infrequent (>38 days)		☐
	Normal (≥24 to ≤38 days)		☐
	Frequent (<24 days)		☐
Duration	Normal (≤8 days)		☐
	Prolonged (>8 days)		☐
Regularity	Normal or "Regular" (shortest to longest cycle variation: ≤7-9 days)*		☐
	Irregular (shortest to longest cycle variation: ≥8-10 days)*		☐
Flow Volume (patient determined)	Light		☐
	Normal		☐
	Heavy		☐

Intermenstrual Bleeding (IMB) Bleeding between cyclically regular onset of menses	None		☐
	Random		☐
	Cyclic (Predictable)	Early Cycle	☐
		Mid Cycle	☐
		Late Cycle	☐

Unscheduled Bleeding on Progestin ± Estrogen Gonadal Steroids (birth control pills, rings, patches or injections)	Not Applicable (not on gonadal steroid medication)	☐
	None (on gonadal steroid medication)	☐
	Present	☐

Implications

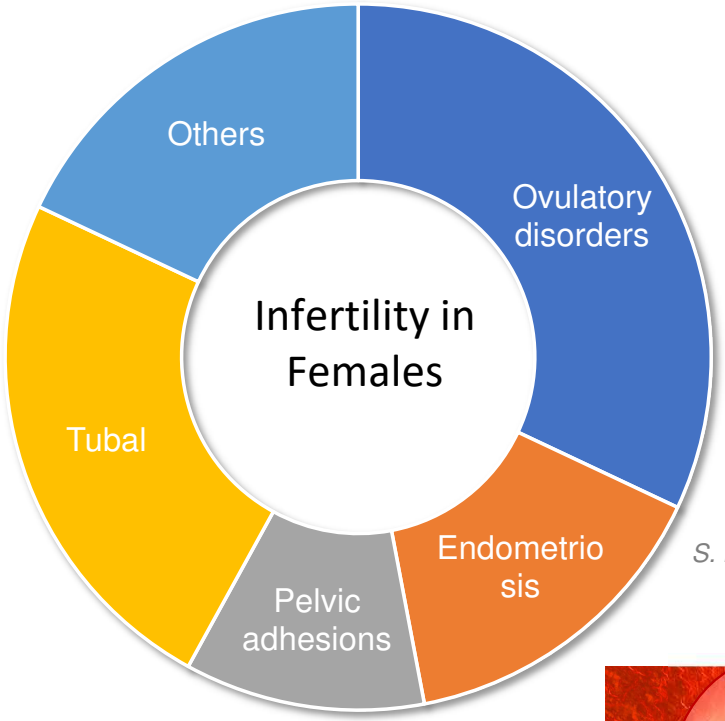


Implications - Infertilité

Table 2.5 Own fresh cycles: Indications of ART: female and male causes

	Statistic	All Centres
Female pathology	N	6893
Tubal	n/N (%)	2116/6466 (32.73%)
Endometriosis	n/N (%)	1657/5816 (28.49%)
Ovulatory	n/N (%)	2305/6668 (34.57%)
Premature Ovarian Failure	n/N (%)	691/6623 (10.43%)
Genetic anomaly	n/N (%)	866/5801 (14.93%)
Uterine factor	n/N (%)	609/6692 (9.10%)
Male pathology	N	7135
Genetic anomaly	n/N (%)	597/6106 (9.78%)
Sperm abnormality	n/N (%)	6674/7085 (94.20%)

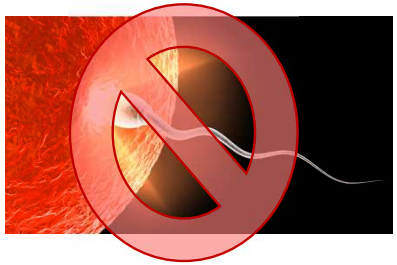
Some patients have more than one cause identified per cycle.



S. L. Corson *2002*

Prévalence

- 1/7 couples dans le monde occidental
- 1/4 des couples dans les pays en voie de développement



Implications - AUB

- Prévalence :
  - Probablement sous-déclarée
  - 3 % à 30 % chez les femmes en âge de procréer
  - Prévalence des saignements menstruels abondants: 27 à 53 %

Fraser I. et al., 2015

Schoep M. et al., 2018

Polyp
Adenomyosis
Leiomyoma
Malignancy & Hyperplasia

FIGO
International Federation of Gynecology and Obstetrics
the Global Voice for Women's Health

Coagulopathy
Ovulatory Dysfunction
Endometrial
Iatrogenic
Not Otherwise Classified

Evolution des classifications FIGO

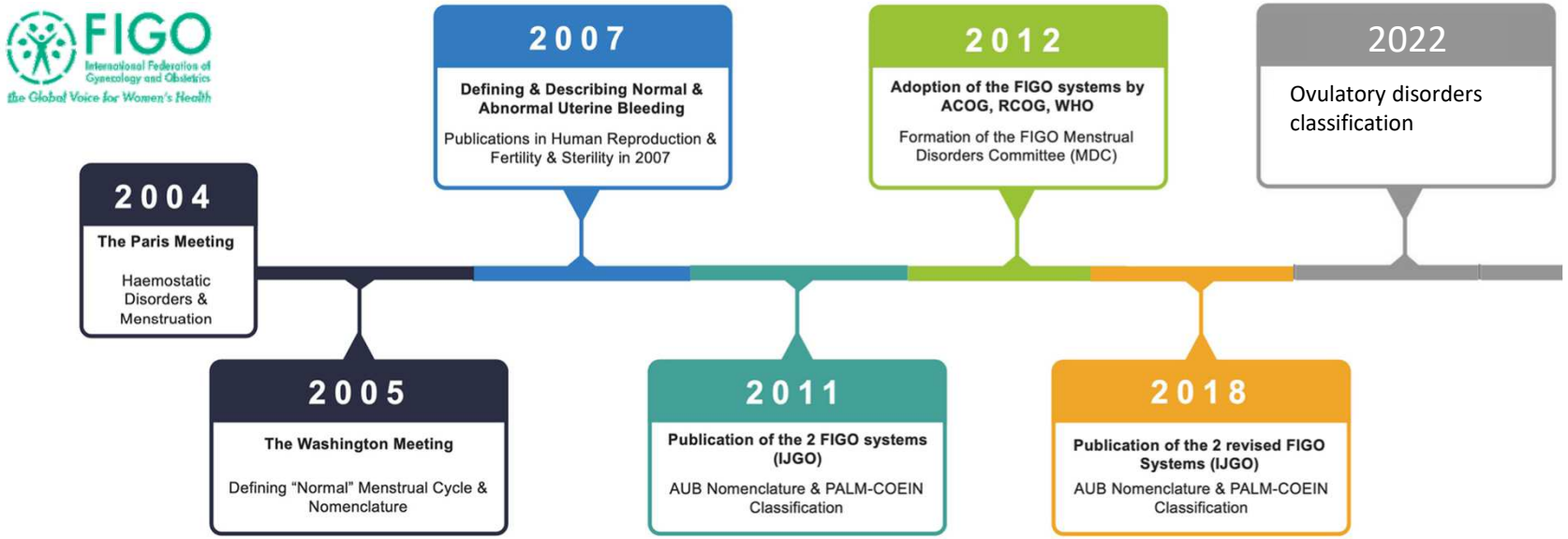


FIGURE 1 | Evolution of the two FIGO Systems. Relevant publications include 2005 (13–15), 2007 (16, 17), 2008 (6), 2011 (11), and 2018 (12). FIGO, International Federation of Gynecology and Obstetrics; IJGO, International Journal of Gynecology & Obstetrics; ACOG, American College of Obstetricians & Gynecologists; RCOG, Royal College of Obstetricians & Gynecologists; WHO, World Health Organization; AUB, Abnormal Uterine Bleeding; MDC, Menstrual Disorders Committee.

Chodankar RR, Munro MG, Critchley HOD. Historical Perspectives and Evolution of Menstrual Terminology. Front Reprod Health. 2022

Classification(s) OMS

1973:

- Groupe I: aménorrhée et peu ou pas d'activité œstrogénique endogène
  - Insuffisance ovarienne hypogonadotrophique
  - Hypopituitarisme complet ou partiel
  - Dysfonctionnement hypothalamo-hypophysaire
- Groupe II: troubles du cycle menstruel, y compris l'aménorrhée, qui présentent une activité œstrogénique distincte (œstrogènes urinaires généralement <10 mg/24 h), dont les gonadotrophines urinaires et sériques se situent dans la plage normale et fluctuent, et qui peuvent également avoir des saignements menstruels spontanés assez réguliers mais sans ovulation
- Groupe III: insuffisance ovarienne primaire associée à une faible activité œstrogénique endogène et à des gonadotrophines sériques et urinaires pathologiquement élevées

World Health Organization

Classification(s) OMS

1976:

- Groupe I : Insuffisance hypothalamo-hypophysaire
- Groupe II : Dysfonctionnement hypothalamo-hypophysaire
- Groupe III : Insuffisance ovarienne
- Groupe IV : Troubles congénitaux ou acquis de l'appareil génital
- Groupe V : Hyperprolactinémie (macro)
- Groupe VI : Hyperprolactinémie (micro)
- Groupe VII : Tumeurs hypothalamiques/hypophysaires non fonctionnelles

Classification(s) OMS

- Group I: Hypogonadotropic hypogonadal anovulation disorders

These women present clinically with primary or secondary amenorrhoea due to reduced or absent gonadotrophin-releasing hormone (GnRH) release from the hypothalamus or gonadotrophin release from the anterior pituitary. Causes can be either hypothalamic or pituitary.

Hypothalamic

- Low body weight, stress or exercise-related amenorrhoea
- Craniopharyngioma or other tumours affecting the hypothalamus
- Amenorrhoea combined with anosmia - Kallmann's syndrome
- Idiopathic.

Pituitary

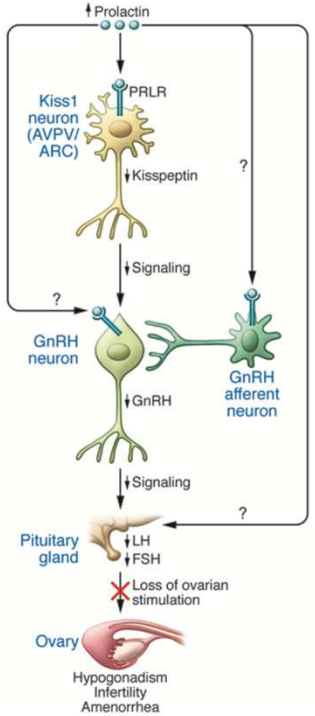
- Sheehan's syndrome (panhypopituitarism, typically infarction of pituitary after an episode of substantial hypovolaemia e.g. postpartum haemorrhage)
- Functioning tumours of the pituitary (prolactinoma)
- Non-functioning tumours of the pituitary or affecting the pituitary (space-occupying but not hormone-producing tumours)
- Brain radiotherapy
- Post-pituitary surgery.

Classification(s) OMS

- Group I: Hypogonadotropic hypogonadal anovulation disorders

  - Hyperprolactinémie?

    Groupe 1 ou 4?



Classification(s) OMS

- Group II: Normogonadotropic, normoestrogenic ovulatory disorders
  - Endocrine: hypothalamo–pituitary–ovarian axis Inability to generate LH surge in response to an estrogen challenge
  - Lack of maturation at puberty (failure of positive feedback)
  - Interference by 'ectopic' steroids, e.g. adrenal androgens, progestogens (e.g. Congenital Adrenal Hyperplasia)
  - Dysfunction of follicle maturation
  - Premature acquisition of LH receptors by a small antral follicle
  - Relative lack of FSH at the critical point when follicles are selected for final ovulatory maturation
  - Failure of follicle rupture [LRF?]
  - Inappropriate LH surge
  - Drugs (non-steroidal anti-inflammatory drugs, clomiphene citrate, progesterone antagonists)

Other

- PCO / PCOS (Four Phenotypes)
- Weight/BMI
- Endocrinopathies (hyperprolactinemia, hypothyroidism, hyperthyroidism?, hyperandrogenic not PCOS?)

Classification(s) OMS

- Group III: Hypergonadotropic, hypoestrogenic ovulatory disorders
  - idiopathic
  - surgical removal (ovariectomy/oophorectomy)
  - environmental
  - chemotherapy
  - radiotherapy (in proximity to the pelvic area)
  - autoimmune (thyroiditis, antiovarian, autoimmune polyglandular syndrome, adrenal (Addison's), DM, Celiac)
  - chromosomal (most common is Turner syndrome 45X0)
  - pure gonadal dysgenesis
  - androgen-insensitivity syndrome (absent ovaries and uterus with a 46XY karyotype).
  - ?Endometriosis
  - Infectious – tuberculosis, other?

Pourquoi une nouvelle classification?

- Limites de la classification de l'OMS →Absence de documents de base ou de processus de développement
- Pathologie très fréquente chez les jeunes filles et les femmes en âge de procréer
- Infertilité et AUB = Problèmes de santé publique
- Pathogenèse/étiologie multifactorielle
- Il était nécessaire de mettre en place un système de classification internationalement accepté afin de normaliser :
  - la recherche (fondamentale, translationnelle, clinique, épidémiologique)
  - les soins cliniques
  - l'éducation

Processus

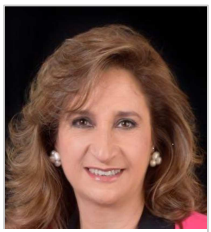
- Accord des deux comités de la FIGO : Troubles menstruels & Médecine de la reproduction, de l'endocrinologie et d'infertilité
  - Steering committe
  - *Co-Chairs

FIGO
Ovulatory Disorders Classification


Adam Balen
United Kingdom


Si Hyun Cho
South Korea


Hilary Critchley
United Kingdom


Ivonne Diaz*
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Rui Ferriani
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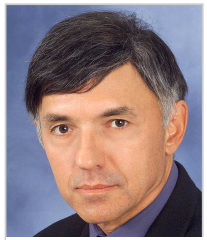
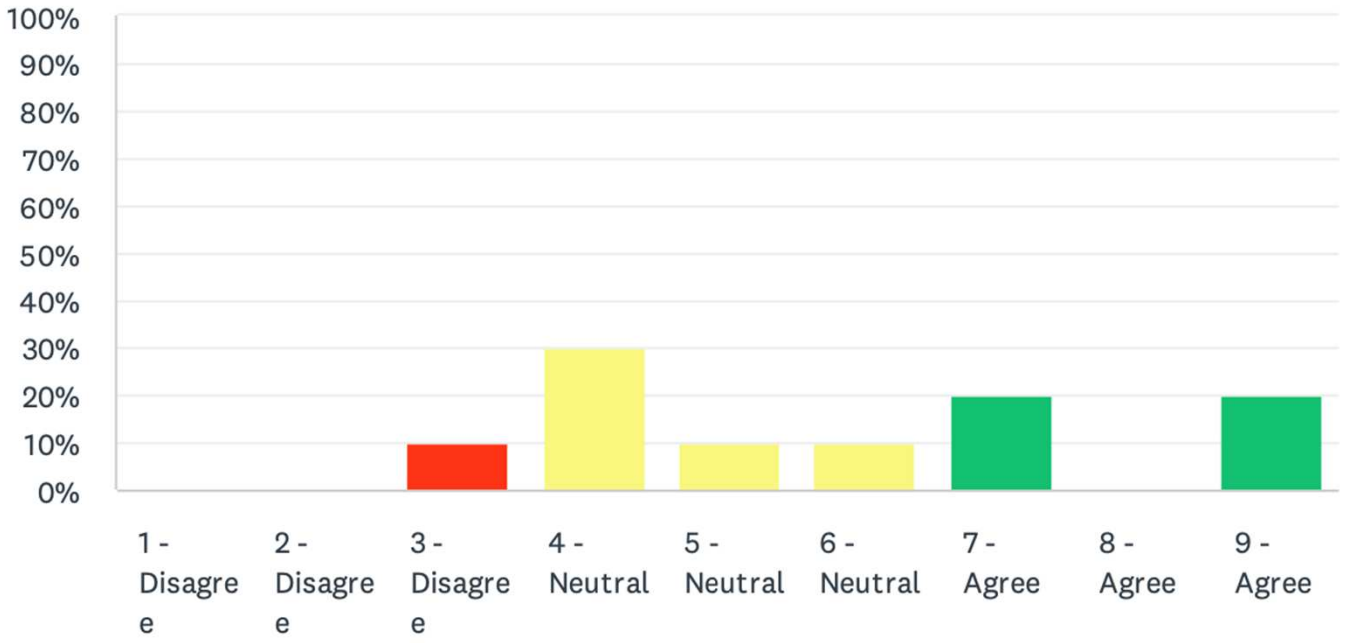

Malcolm Munro*
USA


Zephne Van Der Spuy
South Africa

Processus

- Procédure RAND Delphi
  - Développée par la société RAND pour obtenir un consensus parmi les experts
  - Anonyme
  - Principes généraux
    - Parties prenantes/experts
    - Plusieurs tours
    - Retour d'information entre les tours
    - Définition prédéterminée du consensus

Processus


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1 - Disagree
2 - Disagree
3 - Disagree
4 - Neutral
5 - Neutral
6 - Neutral
7 - Agree
8 - Agree
9 - Agree

Processus

- Invitation d'experts

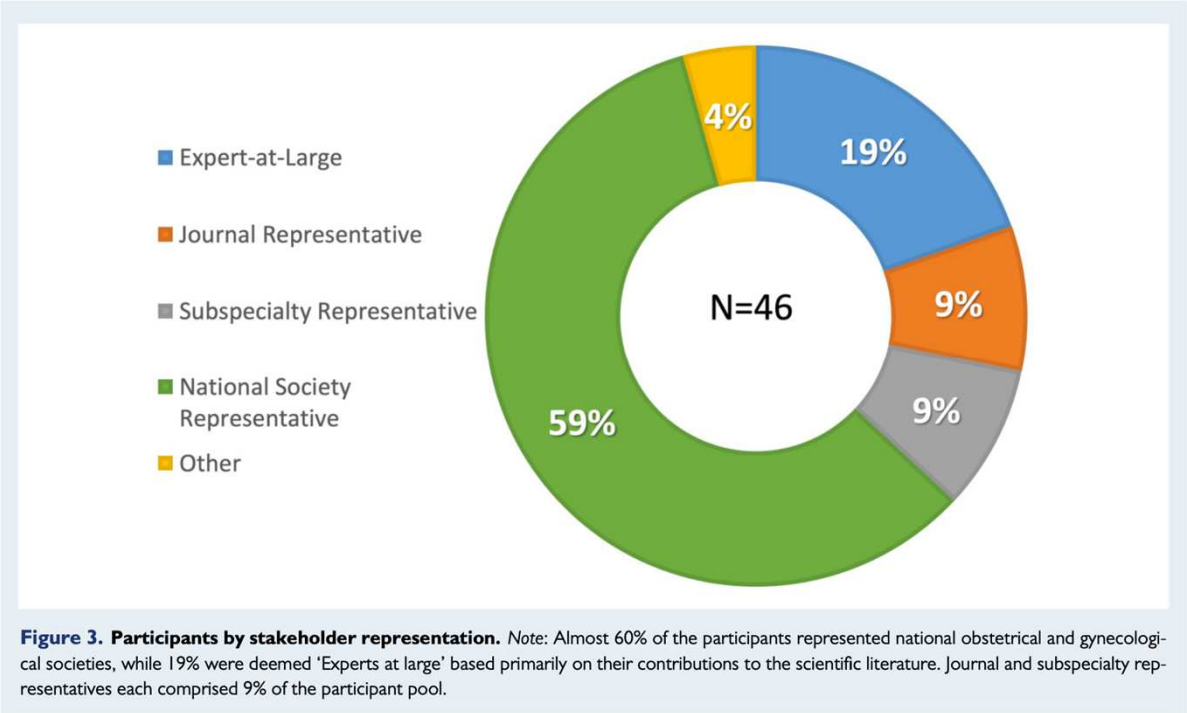


Figure 3. Participants by stakeholder representation. *Note*: Almost 60% of the participants represented national obstetrical and gynecological societies, while 19% were deemed 'Experts at large' based primarily on their contributions to the scientific literature. Journal and subspecialty representatives each comprised 9% of the participant pool.

Processus

- Invitation d'experts

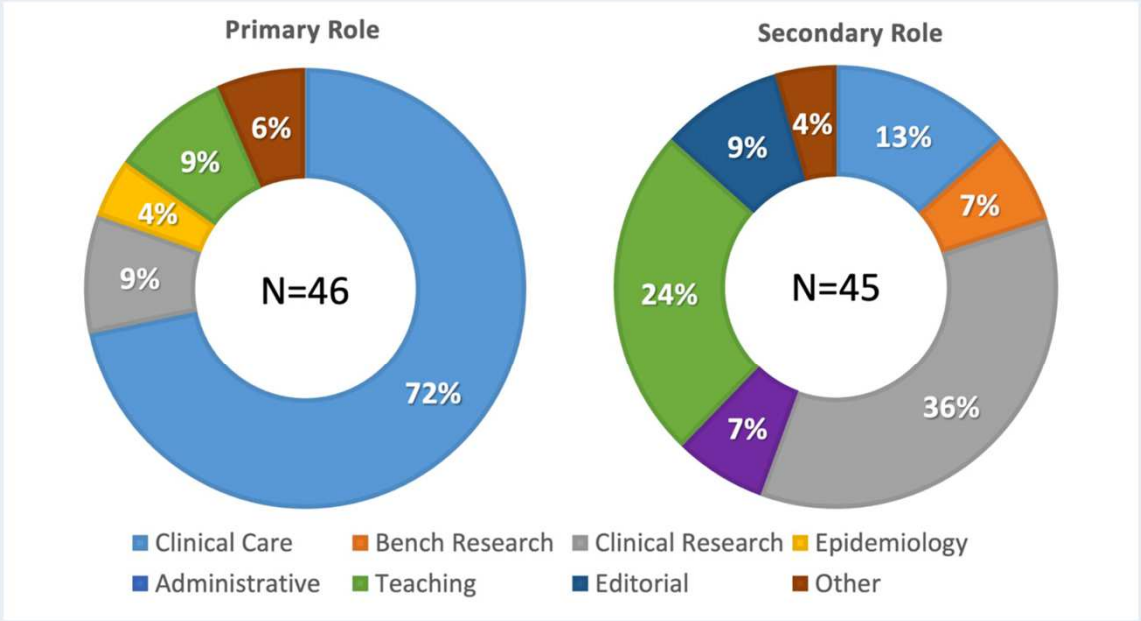
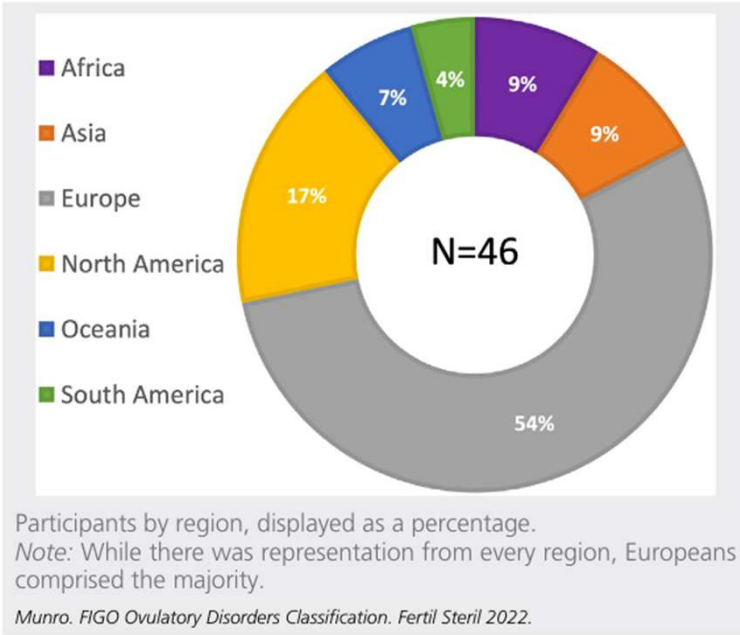


Figure 4. Participants' roles in their local institution or organization. *Note*: Each participant was asked to reveal their primary (left) and secondary (right) roles or responsibilities in their local institution or organization. Almost three-quarters were primarily involved in clinical care, and there were no individuals who reported that bench research or editorial activity was their primary role. More than one-third saw clinical research as their secondary role, while almost one-quarter reported teaching as their secondary responsibility.



Participants by region, displayed as a percentage.
Note: While there was representation from every region, Europeans comprised the majority.

Munro. FIGO Ovulatory Disorders Classification. Fertil Steril 2022.

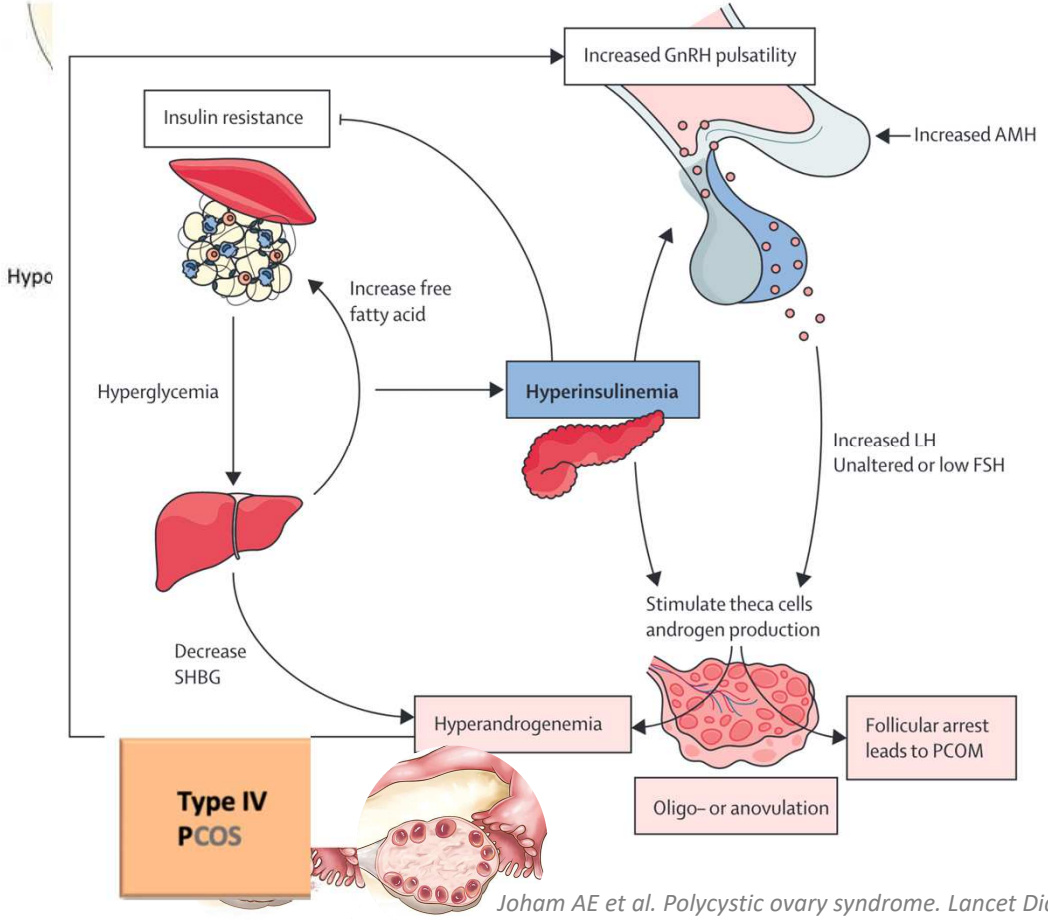
Classification HyPo-P

Type I
Hypothalamic

Type II
Pituitary

Type III
Ovarian

Type IV
PCOS



Joham AE et al. Polycystic ovary syndrome. Lancet Diabetes Endocrinol. 2022

Classification HyPo-P

Type I
Hypothalamic

Type II
Pituitary

Type III
Ovarian

Type IV
PCOS

Diagnosis and categorization as recommended by the International PCOS Network

G A I N

F I T

P I E

Classification HyPo-P

Hypothalamic	Genetic	Kallman's
		Gene mutations
		Other
	Autoimmune	
	Iatrogenic	Pharmacological
		Radiation
		Surgery
	Neoplasm	Craniophyringioma
		Glioma
		Other
	Functional	Pubertal or Constitutional delay
		Stess
		Weight-related
		Exercise
	Infectious/Inflammatory	Sarcoid
		TB
		Other
	Trauma and Vascular	Head injury
	Physiological	Pregnancy
		Breast feeding
		Other
	Idiopathic	
	Endocrine	Thyroid dysfunction
		Hyperandrogenism (not PCOS)
		Cushings
		Other

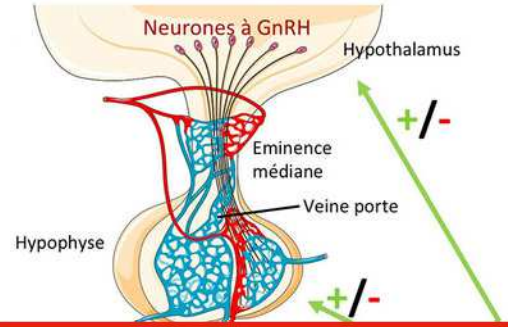


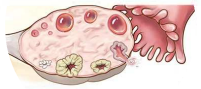
TABLE 4

Ovulatory Disorders Classification Delphi results: Round 4.

Question No.	Round 4 questions	Mean score (1–9)	Disagree (%)	Neutral (%)	Agree (%)
1	There should be a category for both benign and malignant ovarian neoplasms, including those that may secrete gonadal steroids (e.g. granulosa cell tumors) because they are possible causes of ovulatory disorders.	7.1	7.7	12.8	79.5
2	There should be a category for bacterial (example tuberculosis) and viral (example mumps) infections because, in some instances, they may affect some aspect of the hypothalamic-pituitary-ovarian axis and, therefore, could be potential causes of ovulatory disorders.	6.3	17.9	17.9	64.1
3	There should be a category for inflammatory conditions such as sarcoidosis that are not infectious but could potentially cause or contribute to ovulatory disorders.	6.4	12.8	25.6	61.5
4	Please answer with your opinion of the following statement understanding that, if adopted, the system will be subjected to periodic review and appropriate revision: "I support the adoption of the proposed FIGO Ovulatory Disorders Classification System."	8.0	2.6	2.6	94.9

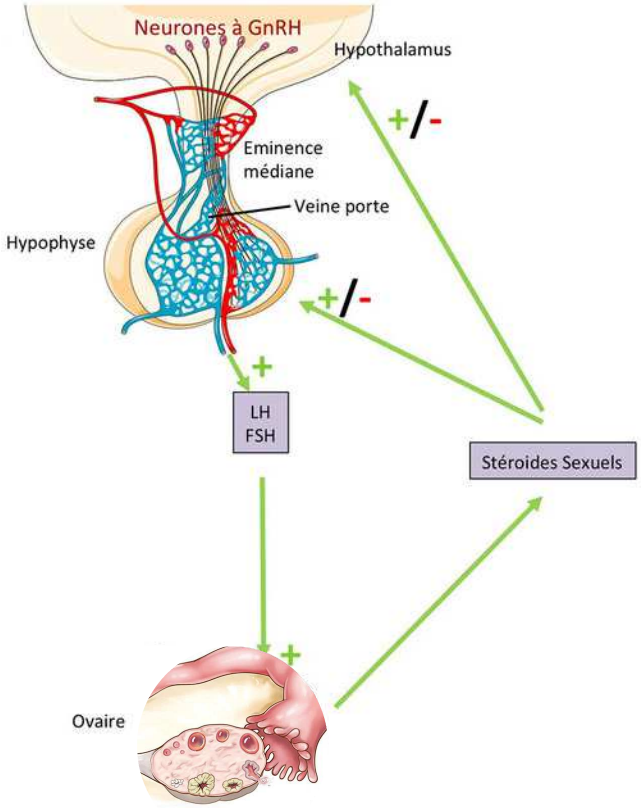
Note: Delphi round 4 followed the live meeting. There were 46 invitations and 39 respondents. For agreement, a mean score of 7 was required (green) with fewer than 15% disagreeing with a statement. Here there was strong support for the system design, although there was a lack of consensus (yellow) regarding the role of infections and inflammatory conditions as contributors to the genesis of ovulatory disorders. There was now consensus support for the potential role of ovarian neoplasms as a potential cause of ovulatory disorders.

Munro. FIGO Ovulatory Disorders Classification. Fertil Steril 2022.



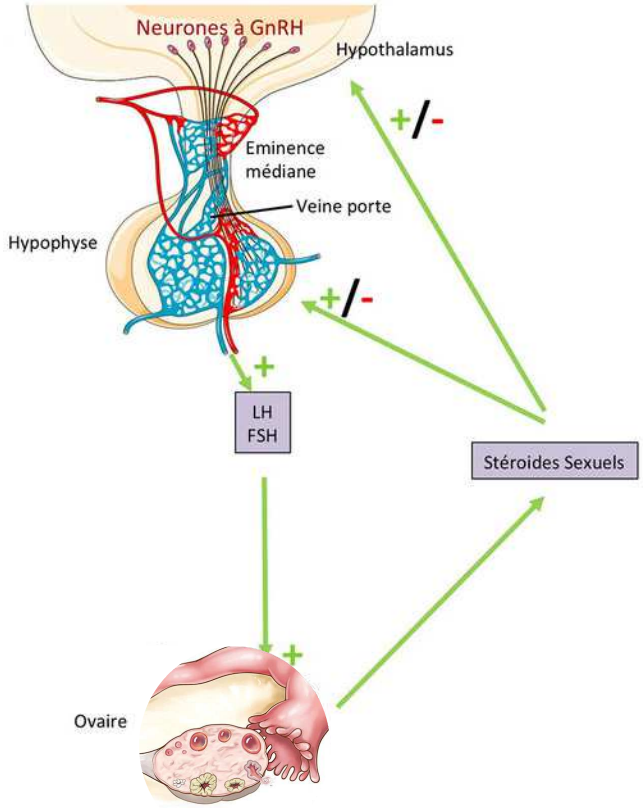
Classification HyPo-P

Pituitary	Genetic	Hypopituitarism
		Receptor polymorphisms
		Other
	Autoimmune	
	Iatrogenic	Pharmacological
		Radiation
		Surgery
		Other
	Neoplasm	Endocrine secreting (functioning)
		Non-endocrine secreting (non-functioning)
	Functional	Absent LH Surge
	Infectious/Inflammatory	Sarcoid
		TB
		Other
	Trauma and Vascular	Infarction (Sheehan's)
		CVA
		Head injury
		Other
	Physiological	Hyperprolactinemia (pregnancy, breast feeding)
	Idiopathic	
	Endocrine	Hyperprolactinemia
		Hypothyroidism



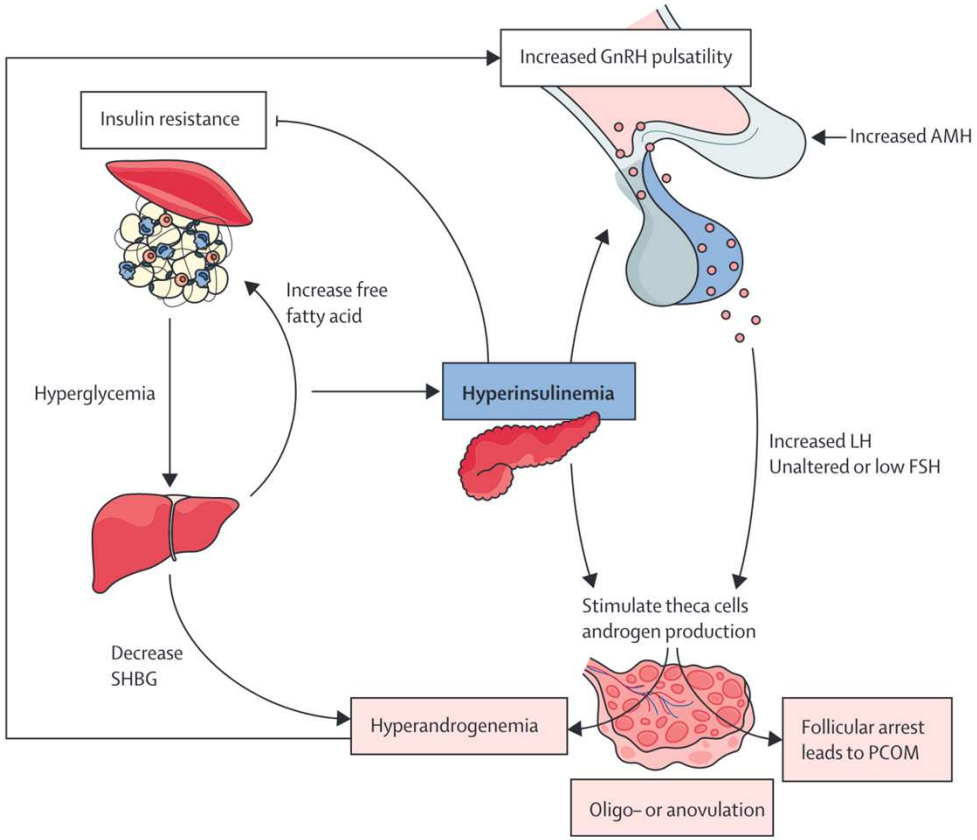
Classification HyPo-P

Ovarian	Genetic	Turner syndrome including mosaics
		Other gonadal dysgenesis
	Autoimmune	Anti-ovarian
		Autoimmune polyglandular
		Other
	Iatrogenic	Pharmacological
		Radiation
		Surgical
		Vascular
	Neoplasm	Benign
		Malignant; primary or secondary
	Functional	Luteinzed unruptured follicle (LUF)
		Luteal out of phase (LOOP)
		Other
	Infectious/Inflammatory	Bacterial
		Viral
		Other
	Trauma and Vascular	Surgical (which is iatrogenic)
	Physiological	Menopause
	Idiopathic	Idiopathic (premature) ovarian failure
	Endocrine	



Classification HyPo-P

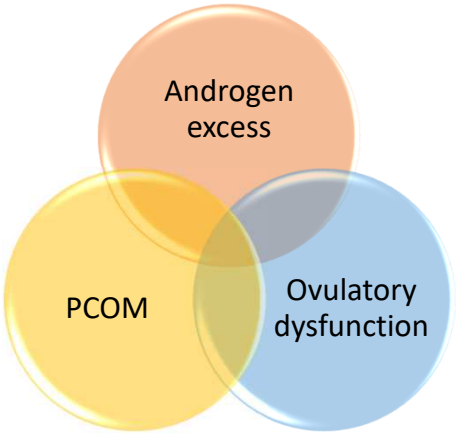
PCOS	Refer to ESHRE/ASRM system for guidance

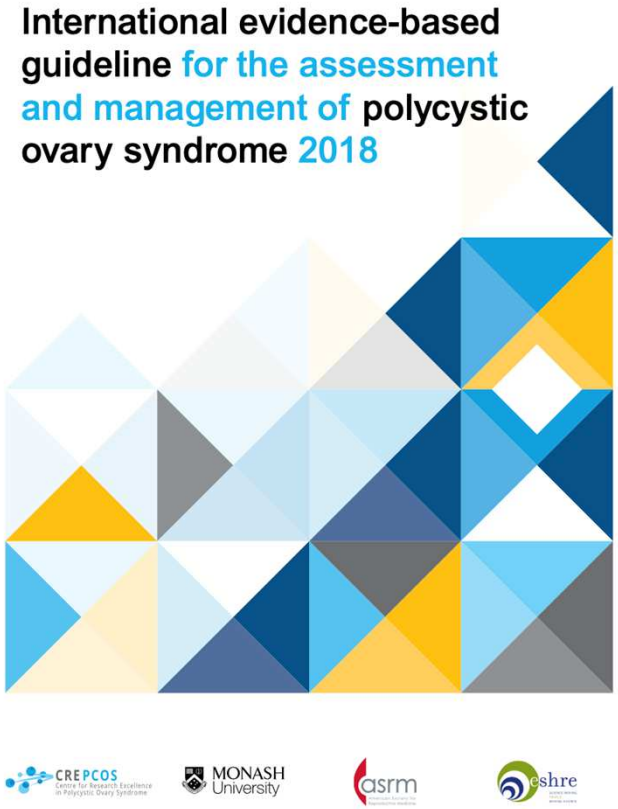


Joham AE et al. Polycystic ovary syndrome. Lancet Diabetes Endocrinol. 2022

Classification HyPo-P

PCOS	Refer to ESHRE/ASRM system for guidance	Defined by Rotterdam criteria - 2 of 3 (1. menstrual cycle disturbance - either amenorrhea or infrequent or irregular bleeding; 2. Hyperandrogenism; 3. Polycystic ovaries)
		Heterogenous condition; number of phenotypes and ethnic variation
		Multifactorial with different etiologies and hypotheses about pathogenesis and genetics
		For adolescents with features of PCOS but who do not meet diagnostic criteria, an "increased risk" category could be considered with reassessment advised at or before full reproductive maturity (8 years post menarche)





Publication

DOI: 10.1002/ijgo.14331

ORIGINAL ARTICLE: INFERTILITY

International Journal of Gynecology & Obstetrics FIGO WILEY

The FIGO Classifica

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Disorders and Related Health
Infertility

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Human Reproduction, pp. 1–19, 2022
https://doi.org/10.1093/humrep/deac180

human reproduction **ORIGINAL ARTICLE** ***Reproductive endocrinology***

The FIGO Ovulatory Disorders Classification System†

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Submitted on July 29, 2022; editorial decision on July 29, 2022

n system

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[8] | Zephne M. van der Spuy[9] |

lealth Impacts, and FIGO
rtility

Publication

FIGO Ovulatory Disorders Classification System collaborators.

First name	Last name	Category	Representing organization/society
Laurie	Henry	Steering Committee	n/a
Michelle	Nisolle	Journal	Fertility Sterility
Axelle	Pintiaux	National Society	Collège Royal des Gynécologues de Langue Française Belges

LIÈGE université

Merci pour
votre attention