



The Global  
Aware Group

Appropriate Care For Women  
With Androgen Excess

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# Recognition and diagnosis of androgen excess

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Educational Slide Kit  
Module 2

The AWARE group is a panel of independent physicians with an expert interest in androgen excess in women. Formation of the AWARE group and its ongoing work is supported and funded by Bayer AG.

October 2018  
PP-DIA-ALL-0044-01

# Testing your knowledge



1. Which of the following could be a non-hormonal cause of acne?
  - A. Genetic predisposition
  - B. Medication use
  - C. Cosmetics
  - D. All of the above

# Testing your knowledge



## 2. What is SAHA syndrome?

- A. SAHA – Skin, Acne, Hyperandrogenism, Alopecia
- B. Simultaneous presentation of seborrhea, acne, hirsutism and alopecia
- C. SAHA - Serum, Androgens, Hair loss, Acne
- D. Simultaneous presentation of specifically distributed acne and hirsutism in androgen excess

# Testing your knowledge



3. In addition to androgen-secreting tumours which of the following conditions can also cause androgen excess
- A. Polycystic ovary syndrome (PCOS)
  - B. Thyroid dysfunction
  - C. Non-classic congenital adrenal hyperplasia (NCAH)
  - D. All of the above

# Testing your knowledge




4. Why is early recognition and treatment of androgen excess important?
- A. Hyperandrogenic skin symptoms cause significant quality of life and psychological impairment
  - B. Androgen excess due to biochemical hyperandrogenism may have a long-term impact on general health
  - C. Androgen excess represents a significant health economic burden
  - D. All of the above

# Module content



- Challenges in the recognition of androgen excess
- Rationale for early diagnosis and treatment
- A diagnostic pathway:
  - Ask, Assess, Consider, Test
- Further investigations
- Resources



# Challenges in the recognition of androgen excess

# Global and ethnic differences in prevalence and primary presentation of androgen excess<sup>1,2</sup>



- Women in far-East Asia present less frequently with hirsutism than Western women<sup>1</sup>
- Thickness of body hair is greater in Caucasian women than Asian women<sup>2</sup>
- Increased risk of insulin resistance in African-American women<sup>2</sup>





# Women can present with a combination of non-specific symptoms<sup>1,2</sup>



In some cases, women present with all four hyperandrogenic skin symptoms, described as the **SAHA syndrome**<sup>3,4</sup>

# Sometimes skin symptoms are mistakenly seen as just a cosmetic problem



- Women with hirsutism and some practitioners, still believe this abnormality to be primarily a cosmetic disturbance<sup>1</sup>
- Many women therefore seek help from a beautician, cosmetologist or electrologist in preference to a physician<sup>2,3</sup>
- Acne can be seen as an 'adolescent problem' that will resolve with age<sup>4</sup>

# Not all acne is specific to a disorder of androgen metabolism



Hormonal influences	Non-hormonal influences
<ul style="list-style-type: none"><li>• Menstrual cycle</li><li>• Pregnancy (+/- effect)</li><li>• Polycystic ovary syndrome (PCOS)</li><li>• Androgen excess is the cause of acne in approximately <b>1</b> in <b>6</b> women<sup>1</sup></li><li>• Hormone treatment (e.g. oral contraceptives)</li></ul>	<ul style="list-style-type: none"><li>• Genetic predisposition</li><li>• Medication use (e.g. iodine, lithium, isoniazid, phenytoin, cyclosporine)</li><li>• Cosmetics (e.g. oil- or cocoa butter-containing products)</li><li>• Competitive sport</li><li>• Lifestyle aspects (e.g. smoking or diet, the latter possibly related to consumption of dairy products or foods with a high glycemic index)</li><li>• Pressure or friction on the skin (e.g. bike helmet straps)</li></ul>

# Although hirsutism is a recognised marker of androgen excess...<sup>1</sup>



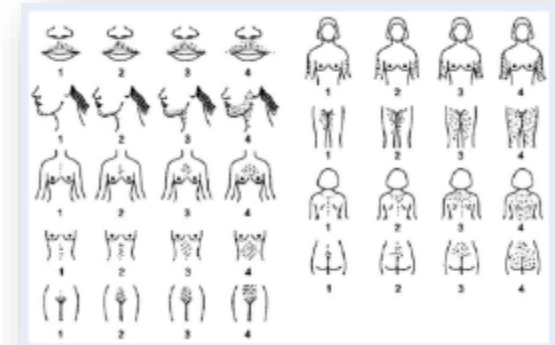
...less frequently, it can also be caused by **ovarian**  
**or adrenal dysfunction**<sup>2,3</sup>

Etiology	Frequency (%) <sup>1</sup>
Polycystic ovary syndrome (PCOS)	71
Idiopathic hyperandrogenism	15
Idiopathic hirsutism	10
Non-classic congenital adrenal hyperplasia (NCCAH)	3
Androgen-secreting tumors	0.3

# Assessment of skin symptoms is not always straightforward<sup>1</sup>



- Women may present in a variety of settings.
- Use of validated assessment tools outside dermatology or clinical trial settings is rare<sup>2</sup>
- When they are used, confirmation of hirsutism for example can be further complicated by:<sup>1</sup>
  - The semi-quantitative approach of the modified Ferriman-Gallwey (mF-G) scale<sup>1</sup>
  - High inter-observer variability
  - Lack of consensus regarding the score that defines hirsutism
- Self-care such as shaving or waxing may limit full assessment of severity



- 0 = Normal, clear skin with no evidence of acne vulgaris
- 1 = Skin is almost clear: rare non-inflammatory lesions present, with rare non-inflamed papules (papules must be resolving and may be hyperpigmented, though not pink-red)
- 2 = Some non-inflammatory lesions are present, with few inflammatory lesions (papules/pustules only, no nodule-cystic lesions)
- 3 = Non-inflammatory lesions predominate, with multiple inflammatory lesions evident: several to many comedones and papules/pustules, and these may or may not be one small nodule-cystic lesion
- 4 = Inflammatory lesions are more apparent: many comedones and papules/pustules, there may or may not be a few nodule-cystic lesions
- 5 = Highly inflammatory lesions predominate: variable number of comedones, many papules/pustules nodule-cystic lesions

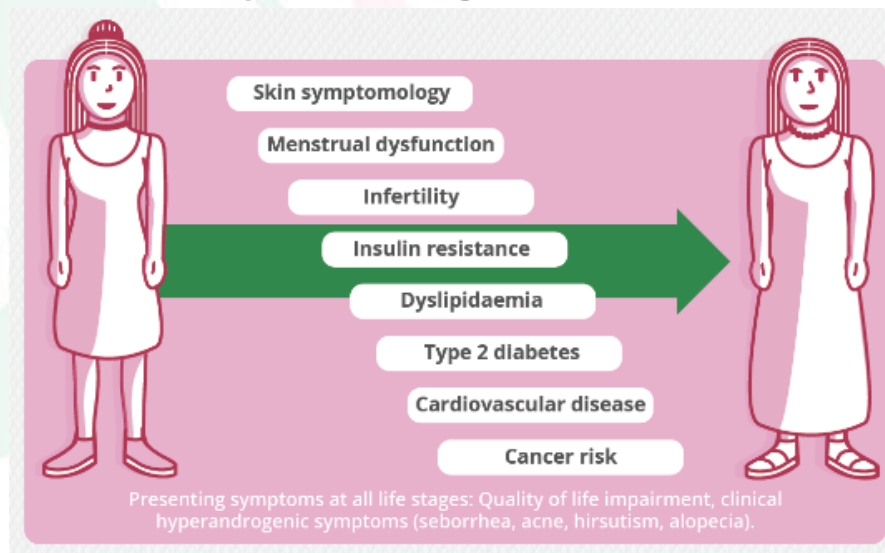
A large, stylized green graphic on the left side of the slide. It depicts the profile of a person's head and neck, facing right. The shape is composed of smooth, flowing curves, with a prominent ear and a defined jawline. The color is a solid, medium green.

## Rationale for early diagnosis and treatment

# Why is early recognition and treatment of androgen excess important?



- Hyperandrogenic skin symptoms cause significant **quality of life** and **psychological** impairment<sup>1-4</sup>
- Androgen excess due to biochemical hyperandrogenism may have a **long-term impact** on general health<sup>5</sup>



Androgen excess therefore represents a significant health **economic burden**<sup>6</sup>



A diagnostic pathway –  
Ask, Assess, Consider Test



# Four key steps in the recognition and diagnosis of androgen excess



**1. ASK**



**2. ASSESS**



**3. CONSIDER**



**4. TEST**



# 1. ASK



## What to ask<sup>1,2</sup>

- ☐ Previous or ongoing treatment and/or self care (e.g. use of make-up, shaving, waxing)
- ☐ Detailed history of menstrual pattern<sup>1</sup>
- ☐ Menstrual irregularity<sup>1</sup>
- ☐ Ovulatory dysfunction
- ☐ Detailed family history of similar disorders<sup>2</sup>



## Why?

Make-up or regular waxing or shaving can disguise the **symptom severity**

Hyperandrogenic skin symptoms and menstrual or ovulatory dysfunction could indicate **polycystic ovary syndrome (PCOS)**



## 2. ASSESS<sup>1</sup>



**S**eborrhea



**A**lopecia



**H**irsutism

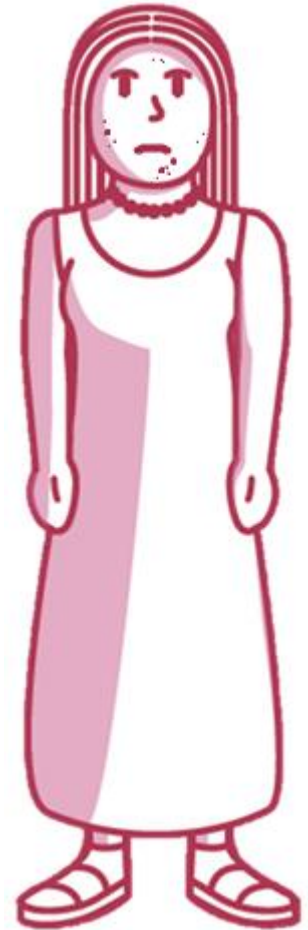


**A**cne

Body mass  
index (BMI)

Waist/height  
ratio (WHR)

Blood pressure  
(BP)





## 2. ASSESS<sup>1-2</sup>



Clinical signs of acne include greasy skin, altered keratinisation inflammation and bacterial colonisation by *P Acnes* <sup>1,2</sup>

**Comedonal acne**



**Papulo-pustular  
acne**



**Nodular acne**



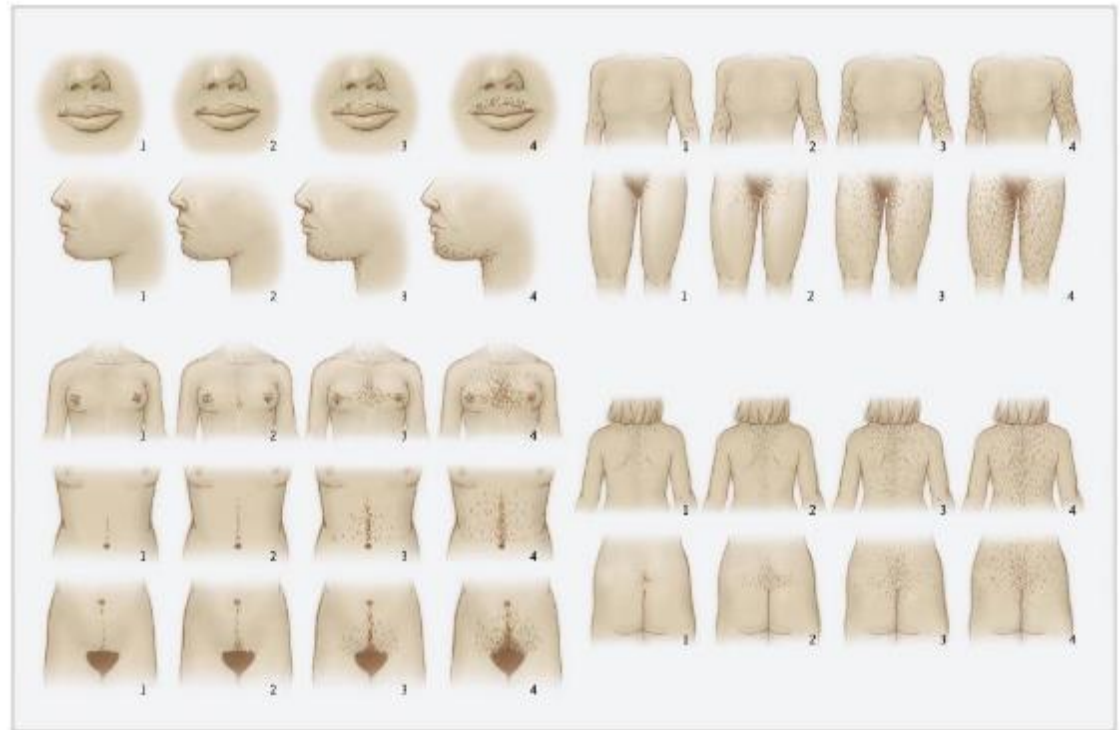
\*For assistance with the identification of acne due to androgen excess, please see the AWARE 'Educational manual: Female acne for non-dermatologists'



## 2. ASSESS<sup>1-4</sup>



Hirsutism is  
evaluated and  
quantified by  
the modified  
Ferriman-  
Gallwey score<sup>1-4</sup>





# 3. CONSIDER<sup>1-5</sup>



**Emotional wellbeing**

**Quality of life**

**Long-term health**







## 4. TEST<sup>1</sup>



- A number of conditions can cause androgen excess
  - Polycystic ovary syndrome (PCOS)
  - Thyroid dysfunction
  - Androgen-secreting tumours
  - Non-classic congenital adrenal hyperplasia (NCAH)
- Other potential causes of skin symptoms of androgen excess
  - Androgenic medications
  - Skin irritants
  - Genetic predisposition





# 4. TEST<sup>1</sup>



## Confirming the cause of androgen excess<sup>1-3</sup>

### Laboratory tests to exclude other disorders:

- Serum thyroid stimulating hormone (TSH)
- Serum prolactin
- Serum 17-hydroxyprogesterone (OHP)

**Also important to assess:**  
Quality of life

**When PCOS is suspected, additional tests are used**

### Confirm PCOS

- Serum testosterone
- Ultrasound ovarian morphology

### Confirm severity of dysfunction

- Anti-Mullerian hormone (AMH)
- Sex hormone binding globulin (SHBG)
- Metabolic tests



# Essentials for the identification of androgen excess in women of reproductive age



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## Essentials for the identification of androgen excess in women of reproductive age

Androgen excess affects approximately 10–20% of women of reproductive age.<sup>1</sup>  
Women with androgen excess may have accompanying anovulation and/or polycystic ovary syndrome (PCOS), both of which have reproductive and metabolic implications if left untreated.<sup>2,3,4</sup>

The global AWARE group is an independent panel of physicians with expert interest in the treatment of androgen excess in women.  
Formation of the AWARE group and its ongoing work is supported by Bayer AG.

### ? 1. ASK<sup>5</sup>

#### What to ask?

- Previous treatment and/or self care (e.g. use of make-up, shaving, waxing)
- Menstrual irregularity (intervals <21 days or >35 days; prolonged or heavy menstrual bleeding)
- Ovulatory dysfunction (irregular intervals, intervals of <21 or >35 days; or delayed ovulation)

#### Why?

- Make-up or regular waxing or shaving can disguise the symptom severity
- Hyperandrogenic skin symptoms and menstrual or ovulatory dysfunction could be **PCOS**

### 2. ASSESS<sup>5</sup>

#### What to assess?

- Clinical presence of skin symptoms such as acne<sup>\*</sup>, hirsutism, seborrhea and alopecia

\*For assistance with the identification of acne due to androgen excess, please see the 'Educational manual: Female acne for non-dermatologists'

- Biochemical evidence of elevated androgens
- Body mass index (BMI)
- Waist/height ratio (WHR)
- Blood pressure (BP)

#### Why?

Androgen excess can present as:

- **clinical hyperandrogenism** - the pilosebaceous unit has increased sensitivity to normal serum androgen levels
- **biochemical hyperandrogenism** - excessive production and/or secretion of androgens which may be of ovarian or adrenal origin and a symptom of **PCOS**
- Central obesity and preventable diseases associated with metabolic syndrome may indicate **PCOS** as the cause of androgen excess

#### SUSPECT PCOS?

Please use 'The effective management and monitoring of PCOS checklist'

### 3. CONSIDER<sup>6-10</sup>

#### What to consider? Why?

- Emotional wellbeing
- Quality of life
- Long term health
- Hyperandrogenic skin symptoms are associated with significant quality of life and psychological impairment
- Androgen excess may lead to increased risk of metabolic syndrome and endometrial hyperplasia or malignancy if left untreated, particularly if there is accompanying anovulation or **PCOS**<sup>2,3,4</sup>

### 4. TEST<sup>5</sup>

#### What to test?

- Thyroid stimulating hormone (TSH)
- Prolactin
- Quality of life

#### Why?

- Thyroid dysfunction, pituitary tumours and non-classic congenital adrenal hyperplasia (NCAH) are all potential causes of androgen excess

1. Redmond GP. Int J Fertil Womens Med. 1998;43(2):91-7. 2. Fowler BC. J Am Soc Reprod Med. 2012;97(1):28-38. e25. 3. Berry J et al. Hum Reprod Update. 2014;20(5):748-758. 4. Chivandani BG et al. Reprod Biomed Online. 2009;19:398-405. 5. Simmens S and Pate KA. Clin Epidemiol 2014;6:1-13. 6. Ekback MP et al. Dermatol. 2013;227:278-284. 7. Altan et al. Int J Dermatol 2000;39:354-357. 8. Koo JYM and Smith LL. Pediatr Dermatol 1991;8:185-188. 9. Stern RS. Dermatol 2000;43:1042-1048. 10. Kallit SC and Givildroger DJ. Br J Dermatol. 1999;140(2):273-82.



# Risk factors prompting further investigation

**The Global Aware Group**  
Appropriate Care For Women With Androgen Excess

## Essentials for safe practice and prescribing in the management of androgen excess

### 5. EXPLAIN

**What to explain?**

- The pathophysiology of symptoms in simple, patient-focused language
- How the treatments work
- The need for a follow-up plan

**Why?**

- Increasing patient knowledge helps to empower patients<sup>11</sup>
- To help patients understand the importance of correct and consistent treatment, especially in long-term conditions<sup>12</sup>
- Skin symptoms such as acne and hirsutism often require long-term treatment<sup>13</sup>

### 6. TREAT

**What to treat?**

- Bothersome symptoms of clinical hyperandrogenism i.e. acne, hirsutism, seborrhea and alopecia
- Symptoms of biochemical hyperandrogenism such as endometrial or metabolic complications

• Use established treatment combinations for androgen excess and follow clinical guidelines and relevant criteria for use

• Patients must be carefully screened before using any estrogen/progestogen combinations, and pregnancy must be excluded

• Further guidance on contraindications is available in the "WHO MEC for contraceptive use"<sup>14</sup>

**Why?**

- To help to improve the symptom-related quality of life and psychological impairment<sup>14,15</sup>
- To help reduce the risk of both reproductive and metabolic/cardiovascular consequences associated with long-term androgen excess disorders<sup>2,19</sup>

• EE in combination with progestogens with antiandrogenic potential (CPA, CMA, DNG or DRSP) are preferred treatment options<sup>14,17</sup>

• CPA combined with EE is indicated for the treatment of moderate to severe acne related to androgen-sensitivity (with or without seborrhea) and/or hirsutism, in women of reproductive age<sup>14,18</sup>

### 7. REFER IF

**When to refer?**

- Suspicion of androgen-secreting tumour
- Undiagnosed bleeding
- Severe psychological morbidity for example, severe anxiety and/or depression
- Scarring acne
- Fertility problems

**Why?**

- An androgen-secreting tumour requires urgent confirmation of diagnosis and treatment
- Menstrual dysfunction and irregular bleeding can have multiple, different etiologies; the possibility of endometrial abnormality should be excluded with use of ultrasound (if available)
- For effective treatment of depression, anxiety or other symptom of psychological morbidity due to symptoms of androgen excess
- Severe, scarring acne requires specialist treatment from a dermatologist
- Referral for assisted reproduction techniques and counselling may be needed for women who still have difficulty conceiving due to androgen excess

EE: ethinylestradiol; CPA: cyproterone acetate; CMA: chlormadinone acetate; DNG: dienogest  
11. Chen J et al. Health Educ Behav. 2016;43(1):25-34. 12. Brown HT and Bissell MJ. Mayo Clin Proc. 2011;86(4):394-514. 13. Storrer M et al. Fertil Steril. 2000;75(4):718-21.  
14. Ching JF et al. J Pediatr Adolesc Gynecol. 2016;27(3):160-71. 15. World Health Organization (WHO). Available at: [http://www.who.int/reproductive-health/publications/who\\_mq\\_gh\\_testing/MQC-5rev](http://www.who.int/reproductive-health/publications/who_mq_gh_testing/MQC-5rev).  
17. Yildiz BO. Semin Reprod Med. 2008;28(1):11-20. 18. Diane-35® Summary of Product Characteristics. 19. Legro RS et al. J Clin Endocrinol Metab. 2015;96(12):4368-4392.



## 7. REFER IF

- Suspicion of androgen-secreting tumour
- Undiagnosed bleeding
- Severe psychological morbidity for example, severe anxiety and/or depression
- Scarring acne
- Fertility problems



## Some practical reminders

# Remember...



- The cause of androgen excess is not always detectable using biochemical tests
- In some cases, clinical symptoms result from the hypersensitivity of skin tissue to normal androgen levels.
  - However, the clinical symptoms causing psychological distress or impaired quality of life should still be addressed
- Menstrual irregularity can be a good indicator of PCOS, particularly in combination with clinical hyperandrogenic skin symptoms

# Conclusions



- There are a number of **challenges in the recognition** of androgen excess, including:
  - Global and ethnic differences in prevalence and primary presentation<sup>1,2</sup>
  - Presentation of a combination of non-specific symptoms<sup>3,4</sup>
  - Difficulty assessing skin symptoms<sup>2,5</sup>
- **Early recognition and diagnosis** of androgen excess is important
  - It allows prompt treatment of hyperandrogenic skin symptoms and can lead to improvements in quality of life and psychological wellbeing<sup>6-10</sup>
- Despite the challenges, there are **tools and resources available** to help aid awareness and aid diagnosis



## Resources

## Checklists



**The Global  
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Appropriate Care For Women  
With Anorexia Excess

## Female acne for non-dermatologists

- Acne affects between 50% and 95% of adolescents<sup>1</sup>
- Up to 40% of women are still affected in their mid-twenties<sup>2</sup>
- The development of acne is influenced by both hormonal and non-hormonal factors; in approximately 15% of women, it is caused by androgen excess<sup>3</sup>
- Acne has a significant impact on quality of life<sup>4\*</sup>

### Aims of this manual

This manual aims to increase awareness of the role androgen excess plays in female acne, as well as enhance understanding and facilitate appropriate use of hormonal antiandrogens as an effective treatment. The global ANVARE group is a panel of experts working to ensure that women with androgen excess receive appropriate care.

**Find more** 

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# Testing your knowledge



1. Which of the following could be a non-hormonal cause of acne?
- A. Genetic predisposition
  - B. Medication use
  - C. Cosmetics
  - ☒ D. All of the above<sup>1</sup>



# Testing your knowledge



## 2. What is SAHA syndrome?

- A. SAHA – Skin, Acne, Hyperandrogenism, Alopecia
- ☒ B. Simultaneous presentation of seborrhea, acne, hirsutism and alopecia<sup>1,2</sup>
- C. SAHA - Serum, Androgens, Hair loss, Acne
- D. Simultaneous presentation of specifically distributed acne and hirsutism in androgen excess

# Testing your knowledge



3. In addition to androgen-secreting tumours which of the following conditions can also cause androgen excess
- A. Polycystic ovary syndrome (PCOS)
  - B. Thyroid dysfunction
  - C. Non-classic congenital adrenal hyperplasia (NCAH)
  - D.

 All of the above<sup>1</sup>

# Testing your knowledge



4. Why is early recognition and treatment of androgen excess important?
- A. Hyperandrogenic skin symptoms cause significant quality of life and psychological impairment
  - B. Androgen excess due to biochemical hyperandrogenism may have a long-term impact on general health
  - C. Androgen excess represents a significant health economic burden
  - D.

 All of the above<sup>1-6</sup>

# Find The Global AWARE Group educational materials on the European Menopause & Andropause Society website



<https://www.emas-online.org/nonemaseducationalmaterials/>

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- Non EMAS educational materials

### The Global AWARE Group Educational Materials

 **The Global AWARE Group**  
Appropriate Care For Women With Androgen Excess

The global AWARE (Appropriate care for Women with AndRogen Excess) group is a panel of independent physicians with an expert interest in androgen excess. Their mission is to address the unmet need in androgen excess to ensure that women receive appropriate care. Since its formation in 2015, the AWARE group and its ongoing work is supported by Bayer. The group have created a number of useful resources that are available to download below. These resources aim to support healthcare professionals in the recognition, diagnosis and appropriate treatment of androgen excess. You may want to use these materials to support discussions with colleagues, for example, in a workshop setting.

**Your patient, Camila**

- 19 years old
- Presents with moderate acne that has failed to improve with topical antibiotic treatment
- She tells you that her acne became much worse a year ago
- She also tells you that she is too embarrassed to go out with her friends because she feels miserable about her skin
- She is taking a combined oral contraceptive (COC)

**Female acne for non-dermatologists**  
A practical educational manual

**Polycystic ovary syndrome**  
affects up to 1 in 6 women of reproductive age

**Women with hirsutism caused by androgen excess experience high levels of psychological distress**

**Androgen excess is linked to long-term medical problems, particularly in women with polycystic ovary syndrome**

**What are the signs and symptoms of androgen excess?**

**Assessment and Diagnosis of Polycystic Ovary Syndrome (PCOS)**

The AWARE group is a panel of independent physicians with an expert interest in androgen excess in women. Formation of the AWARE group and its ongoing work is supported and funded by Bayer AG.