



## Effective Health Care Polycystic Ovary Syndrome (PCOS) Nomination Summary Document

### Results of Topic Selection Process & Next Steps

- The focus of this nomination on medical maintenance therapies for women with PCOS not trying to conceive (i.e., Key Question 2) was found to be addressed by a number of evidence-based guidelines and systematic reviews. The most recent and comprehensive of these products are listed below. Given that the identified existing guidelines and reviews cover this aspect of the topic, no further activity will be undertaken on these portions.
  - 2013 guideline published by the Endocrine Society titled *Diagnosis and treatment of polycystic ovary syndrome* (Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab Dec 2013; 98(12):4565-4592)
  - 2014 guideline by the Royal College of Obstetricians and Gynecologists titled *Long-term consequences of polycystic ovary syndrome* (Long-term consequences of polycystic ovary syndrome. Green-top guideline no. 33. Royal College of Obstetricians and Gynecologists;2014)
- The focus of this nomination on fertility therapy for women with PCOS trying to conceive (i.e., Key Question 3) was found to be addressed by an in-process AHRQ systematic review *Management of Infertility*, which will include women with PCOS as a subgroup. To view a description and status of the research review: <http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/>. To sign up for notification when this and other EPC Program topics are posted, please go to: [https://subscriptions.ahrq.gov/service/multi\\_subscribe.html?code=USAHRQ](https://subscriptions.ahrq.gov/service/multi_subscribe.html?code=USAHRQ).
- The remaining areas of focus (i.e., Key Questions 4-6) of this nomination are not feasible for a full systematic review due to the limited data available review at this time. These aspects of the topic could potentially be considered for new research.

### Topic Description

- Nominator(s):** A research associate on behalf of the American College of Obstetricians and Gynecologists (ACOG) via the web
- Nomination Summary:** The nominator is interested in improving complications of polycystic ovary syndrome (PCOS) such as type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), anovulation, amenorrhea, infertility, and hirsutism. A systematic review on the long-term risks of PCOS and effective management and treatment strategies could help inform clinicians on the best evidence-based treatment options.
- Key Question 1:** This is a natural history question, not a comparative effectiveness question. A PICO statement is not applicable for this question. This Key Question was not included in our examination of the literature.

**Key Question 2:**

**Population(s):** Women diagnosed with PCOS who are not attempting to conceive

**Intervention(s):** Combination oral contraceptives, progestin, insulin-sensitizing agents

**Comparator(s):** Placebo, usual care, or other interventions

**Outcome(s):** Anovulation, amenorrhea, incidence of CVD, incidence of T2DM, medication harms

**Key Question 3:**

**Population(s):** Women diagnosed with PCOS who are attempting to conceive

**Intervention(s):** Clomiphene, gonadotropins, ovarian drilling, insulin-sensitizing agents, letrozole, in vitro fertilization

**Comparator(s):** Placebo, no intervention or the above interventions compared to each other

**Outcome(s):** Anovulation, amenorrhea, pregnancy, infertility, medication harms

**Key Question 4:**

**Population(s):** Women with PCOS who are overweight or obese

**Intervention(s):** Weight loss (achieved through behavior modification, weight loss medications, or bariatric surgery)

**Comparator(s):** No weight loss, no intervention

**Outcome(s):** Anovulation, amenorrhea, pregnancy, infertility, medication harms

**Key Question 5:**

**Population(s):** Women diagnosed with PCOS who are on medical maintenance therapy

**Intervention(s):** Medical maintenance therapy (pharmacotherapy for PCOS) with behavior modification (diet and exercise)

**Comparator(s):** Medical maintenance therapy without behavior modification

**Outcome(s):** Anovulation, amenorrhea, pregnancy, hirsutism, infertility, medication harms

**Key Question 6**

**Population(s):** Women diagnosed with PCOS and hirsutism

**Intervention(s):** Oral contraceptives, antiandrogens (spironolactone, flutamide, finasteride), insulin-sensitizing agents, eflornithine

**Comparator(s):** Placebo, other interventions

**Outcome(s):** Severity of hirsutism, medication harms

**Key Questions from Nominator:**

**Key Question 1:** Do women with PCOS have an increased risk of developing T2DM and/or CVD compared with women without PCOS?

**Key Question 2:** In women with PCOS who are not attempting to conceive, how do the following medical maintenance therapies compare in effectiveness of treating anovulation, amenorrhea, incidence of CVD, and incidence of T2DM?

**Key Question 3:** In women with PCOS who are attempting to conceive, how does the effectiveness of the following methods of ovulation induction/ conception compare?

**Key Question 4:** In women with PCOS who are overweight or obese, what is the comparative effectiveness of weight loss compared to no weight loss in improving

ovarian function?

**Key Question 5:** In women with PCOS, what is the comparative effectiveness of supplementing medical maintenance therapies to treat PCOS with behavior modification (diet and exercise) compared with medical maintenance therapies alone in improving outcomes?

**Key Question 6:** How does the effectiveness of the following medical agents compare in treating hirsutism in women with PCOS?

## Considerations

- Key Question 2 of this topic is adequately addressed by multiple evidence-based guidelines and systematic reviews. Some of these guidelines and systematic reviews include the following:
  - 2013 guideline published by the Endocrine Society titled *Diagnosis and treatment of polycystic ovary syndrome*
    - This guideline was based on a systematic review of the evidence from MEDLINE, Embase, the Cochrane Library, Web of Science, Scopus, PsycINFO, and CINAHL up to April 2011. It examined use of hormonal contraceptives, and metformin. Progestin was also discussed as it related to a component of a hormonal contraceptive.
    - Recommendations included the following: hormonal contraceptives should be first line therapy for menstrual abnormalities, hirsutism, and acne; metformin can improve menstrual irregularities, obesity, and cutaneous symptoms, but is not effective at treating hirsutism, acne, or infertility; hormonal contraceptives and metformin can be considered in adolescents; and thiazolidinediones were not recommended due to an unfavorable risk-benefit ratio for the treatment of PCOS.
  - 2014 guideline by the Royal College of Obstetricians and Gynecologists titled *Long-term consequences of polycystic ovary syndrome*
    - The guideline was based on a systematic review of the literature. Although the guideline did not specifically address women who are not trying to conceive with separate recommendations, it seemed to include this population in the recommendations. The guideline indicated that there is currently insufficient evidence to recommend insulin-sensitizing agents.
- Key Question 3 on fertility therapy for women with PCOS was addressed by an in-process AHRQ systematic review *Management of Infertility*, which will include women with PCOS as a subgroup.
  - The in-process review includes the following evidence question: What are the comparative safety and effectiveness of available treatment strategies for women with polycystic ovary syndrome (PCOS) who are subfertile/infertile and who wish to become pregnant? a) Does the optimal treatment strategy vary by patient characteristics such as age, ovarian reserve, race, body mass index, presence of other potential causes of female infertility, or presence of male factor infertility?
- For Key Questions 4-6, our search identified few studies to inform a new systematic review. While we did identify a number of studies on hirsutism, these studied a wide variety of interventions and comparators. The feasibility of a new systematic review was low based on these factors.