POLYCYSTIC OVARY SYNDROME IN ADULTS:
A LITERATURE REVIEW AND CLINICAL PRACTICE GUIDELINE FOR THE PRIMARY CARE NURSE PRACTITIONER

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Abstract

Polycystic ovary syndrome (PCOS) is a complex, multifaceted syndrome with multiple health implications and long-term health risks (Fauser et al., 2012). Women with PCOS require management and guidance from their primary care NP in collaboration with multiple specialists. The heterogeneity of the syndrome makes diagnosis, symptomatic treatment, and long-term management complex and individualized (Fauser et al., 2012). Long-term complications of PCOS include increased risk for insulin resistance (IR), cardiovascular disease (CVD), endometrial cancer, obesity, depression and anxiety, infertility, and various dermatological manifestations (Fauser et al., 2012). Nurse Practitioners (NP) are in a unique position, as primary care providers, to co-manage these women with various specialists. Currently in Canada, however, there are no primary care guidelines for the diagnosis and management of PCOS. This literature review was developed for the purpose of finding supporting evidence for the creation of a clinical practice guideline to assist NPs in the diagnosis and long-term management of adult women with PCOS.

*Keywords:* Polycystic ovary syndrome, cardiovascular risk, insulin resistance, nurse practitioner, guideline, primary care
Introduction

Polycystic ovary syndrome (PCOS) is a multifaceted disease with a wide range of clinical presentations, varying diagnostic criteria, and multiple long-term metabolic and cardiovascular complications (Fauser et al., 2012). The complexity of symptoms and complications of PCOS require involvement of various different specialists; however, the primary care provider, such as a Nurse Practitioner (NP) or General Practitioner (GP), is involved in the overall long-term co-management.

With an advanced scope of practice, NPs are in a unique position to initiate investigations and rule out other possible causes of the presenting complaint thereby preventing unnecessary specialist referrals and cost to the health care system. NPs are also involved in long-term management of patients with PCOS when initiating screening to prevent chronic complications of the disease. Complications include increased risk of insulin resistance (IR), cardiovascular disease (CVD), endometrial cancer, obesity, depression and anxiety, infertility, and various dermatological manifestations (Legro et al., 2013).

Currently, in Canada, there are no primary care guidelines for the diagnosis and management of PCOS. Primary care providers have limited guidance regarding initial testing and long-term screening precautions, thus contributing to under or over ordering of diagnostic tests, increased cost to the healthcare system, and potential missed opportunities for early screening and prevention. This literature review will provide the evidence necessary to create a clinical practice guideline for use by NPs in primary care with the purpose of guiding clinical practice and removing uncertainty regarding initial diagnostic procedures, referrals, and long-term management for adult women with PCOS.
Current Guidelines

Five specific noteworthy guidelines were reviewed and frequently referenced for purposes of this paper. One of these is the Australian document from 2015 entitled *Evidenced-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome* by the Jean Hailes for Women’s Health organization in collaboration with the Centre for Research Excellence in Polycystic Ovary Syndrome (Jean Hailes for Women’s Health, 2015). This particular guideline provides an in-depth evidence based guide to the care of women with PCOS based on various aspects of the syndrome. Advice from this document can be very helpful in guiding care, but is not very concise or easily accessible for a quick reference by the primary care NP. The Jean Hailes for Women’s Health organization also created a tool entitled: *Polycystic Ovary Syndrome GP Tool*. This provides a quick reference for GPs regarding the initial workup and management of a woman presenting with PCOS. This tool is easily accessible and straightforward to use, however it is targeted towards GPs in Australia (Jean Hailes for Women’s Health, 2015a).

The Endocrine Society also has developed guidelines entitled: *Diagnosis and Treatment of Polycystic Ovary Syndrome: An Endocrine Society Clinical Practice Guideline* (Legro et al. 2013). This guideline is also a very extensive, comprehensive guideline that examines the most important aspects for diagnosis and management of PCOS. This guideline, similar to the Jean Hailes for Women’s Health guideline, is thorough, but neither succinct nor targeted for use in the primary care setting.

Also of note, three different consensus workshops have been held in Europe with members from the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) to establish guidelines for the
diagnosis and management of PCOS. The first of these workshops took place in Rotterdam, the Netherlands in 2003, and resulted in the creation of the most widely accepted diagnostic criteria to date: the Rotterdam Criteria for Diagnosis of PCOS (Rotterdam, 2004). The second took place in Thessaloniki, Greece in 2007 and focused on infertility treatments. This resulted in the document entitled: *Consensus on Infertility Treatment Related to Polycystic Ovary Syndrome* (Tarlatzis, 2008). The third workshop took place in Amsterdam, the Netherlands, in 2010 and resulted in the document entitled: *Consensus on Women’s Health Aspects of Polycystic Ovary Syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group* (Fauser et al., 2012). This most recent document summarizes the current knowledge regarding polycystic ovary syndrome.

**Gaps**

All five of these documents are highly cited and reputable evidence-based guidelines developed by experts in each of their respective fields. However, they are either very in-depth and lack tangible, easy to obtain information or are not targeted for direct patient care by the NP in BC. Nurse Practitioners in BC would benefit from a framework for making evidenced-based clinical decisions that is clear, succinct, and summarizes the current guideline recommendations.

**Purpose**

This literature review seeks to understand the current accepted diagnostic criteria, the controversies in diagnosis, and the gaps that exist in clinical practice knowledge. It will investigate potential complications of PCOS and evaluate the recommendations made in the recent meta-analyses, systematic reviews, and current guidelines regarding diagnosis,
workup and screening. It will focus on the NP scope of practice in BC and take into
consideration limitations regarding making diagnoses and ordering tests. Evaluating these
aspects of the diagnosis and management of PCOS will assist in the development of a tool to
assist NPs in the care of adult women with PCOS.

In Canada, there is currently no guideline or decision-making tool for the diagnosis
or management of PCOS in the primary care setting. This contributes to delayed diagnosis
due to uncertainty regarding initial diagnostic tests and referrals, insufficient supports for
lifestyle changes, and inadequate follow up and long-term management for the various
complications associated with PCOS. Also, there is a potential for increased burden on the
health care system due to either over ordering of diagnostics or under screening for the
long-term complications associated with PCOS. A guideline would outline initial
diagnostics, other conditions that need to be considered and ruled out, and the long-term
screening necessary for women with PCOS throughout their life.

Methods

In preparation for this literature review and creation of the clinical practice
guideline, multiple databases were accessed and various search terms were used. Limits
were set to include only articles published in the past 10 years, humans, and review articles.
The reference pages of articles were also analyzed in order to obtain more information
about specific journal articles or studies that were commonly sited. Databases searched
include the UBC Library search, Pubmed, Medline, and The Cochrane Database. Search
terms included a combination of polycystic ovar* syndrome AND cardiovascular disease;
cardiovascular disease risk; insulin resistance; metabolic abnormalities; obesity; endometrial cancer; cancer; infertility; depression; mental health.

Searches for current practice guidelines were performed via Google search engine with terms including polycystic ovary syndrome and polycystic ovary syndrome guidelines. Site-specific searches were also performed on the Society of Obstetricians and Gynaecologists of Canada (SOGC) website and the American Congress of Obstetricians and Gynecologists (ACOG).

**Pathophysiology**

The pathophysiology of PCOS is complex and multifactorial and, even after much investigation into the pathogenesis, the cause remains relatively unclear. In addition to the numerous genes that are identified with PCOS, there is growing evidence to suggest that particular environmental factors such as low socio-economic status, smoking, poor diet, and lack of exercise also contribute to the development of the syndrome (Barthelmess & Naz, 2015). Additionally, hypotheses exist suggesting high testosterone levels in-utero seem to contribute to the development of the disease later in life (Vito, 2006).

Although the exact cause is still largely unknown, central to this syndrome is the hormone imbalance created by elevated androgen and insulin levels (Teede, Deeks, & Moran, 2010). The complex interplay of genetic, environmental, and hormonal factors, contribute to the development of PCOS and directly correlate to an increase in metabolic complications, cardiovascular risk, endometrial cancer, obesity, depression, infertility, and various dermatological manifestations (Huang & Coviello, 2012).
Diagnosing PCOS

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders in women, affecting as many as 15% of females (Fauser et al., 2012). It is usually detected during the early reproductive years due to presenting complaints such as menstrual irregularity, clinical hyperandrogenism, or infertility (Fauser et al., 2012). The clinical presentation varies according to severity of the illness and the diagnostic criteria used. Three different criteria have been proposed and are outlined in Table 1. In 1990, the first diagnostic criteria were developed by the National Institutes of Health (Lujan, Chizen, & Pierson, 2008). These criteria required the presence of both menstrual disturbances (either oligovulation or anovulation) and clinical or biochemical signs of hyperandrogenism (Lujan et al., 2008). Since this time, research has shown that PCOS encompasses a much more varied clinical presentation, which led to the development of the Rotterdam criteria in 2003. These criteria encompass a broader expression of the syndrome and require two of the following three criteria: oligo- and/or anovulation, clinical and/or biochemical hyperandrogenism, or polycystic ovaries (Rotterdam, 2004). Initially experts had difficulty with the Rotterdam criteria, because these broader diagnostic criteria made it possible to diagnose PCOS in the absence of menstrual irregularity or hyperandrogenism – two components that were previously thought to be requirements of the syndrome (Lujan et al., 2008). In 2006, The Androgen Excess and Polycystic Ovary Syndrome Society proposed a revised set of criteria that recognized the broad clinical presentation of PCOS but required the presence of both hyperandrogenism and ovarian dysfunction; the latter being defined by oligo- and/or anovulation and/or polycystic ovaries (Lujan et al., 2008). However
currently, the most widely accepted diagnostic criteria still remain the Rotterdam criteria due to its broad and inclusive nature (Legro et al., 2013).

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<td>Both needed for diagnosis:</td>
<td>Two of three needed for diagnosis:</td>
<td>Both needed for diagnosis:</td>
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<tr>
<td>1. Oligo-ovulation or chronic anovulation</td>
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<td>1. Ovarian dysfunction (oligo/anovulation and/or polycystic ovarian morphology)</td>
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<td>2. Clinical and/or biochemical signs of hyperandrogenism</td>
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<td>3. Polycystic ovaries</td>
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*note: all three diagnostic criteria require exclusion of other etiologies of androgen excess and anovulatory infertility prior to diagnosis of PCOS

Adapted from Lujan, Chizen, and Pierson (2008)

**Phenotypes**

Due to the expansion of the diagnostic conditions within the Rotterdam criteria, four different subgroups, or phenotypes, have been recognized based on their clinical presentation (Table 2). The breakdown of the four different phenotypes, A, B, C, and D, is based on presence or absence of oligo- or amenorrhea, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovarian morphology. The most prevalent and also most associated with long-term health risks, is phenotype A, which includes all three clinical characteristics (Rotterdam, 2004).
Table 2

<table>
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<th>Phenotype classification based on Rotterdam (2003) diagnostic criteria for PCOS</th>
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<tr>
<td><strong>Phenotype</strong></td>
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<tr>
<td>Oligo-anovulation</td>
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<td>Hyperandrogenemia</td>
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<td>Polycystic morphology</td>
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Diagnosis

Although it is not within the NP scope in BC to diagnose PCOS independently (College of Registered Nurses of British Columbia, 2015), NPs must be aware of the diagnostic criteria when ordering tests and hypothesizing on potential differential diagnoses. The heterogeneity of the signs and symptoms of PCOS make the syndrome difficult to diagnose; however, with appropriate resources, NPs can be well educated regarding the diagnostic criteria for PCOS and other disorders that can present with similar symptoms, resulting in appropriate use of diagnostic tests and prompt referrals.

Understanding the definition of the term syndrome will help explain how the heterogeneity of the clinical presentation of PCOS contributes to the complexity of diagnosis. According to Azziz, et al., a syndrome is, “a collection of signs and features, in which no single test is diagnostic. In essence, the whole (or global assessment) is greater than the sum of the individual features” (Azziz et al., 2009, p. 4237). This definition fits well with PCOS as the heterogeneity of the syndrome is broad with varied clinical presentations, and there is no single diagnostic test to detect the presence of PCOS. Along with the clinical features and manifestations required for diagnosis of PCOS, the syndrome is associated with a number of additional signs and symptoms, which will be explored within the context...
One of the three diagnostic features of PCOS, according to the Rotterdam criteria, is irregular menses (see Table 1). Women with PCOS can present with various different menstrual symptoms including amenorrhea: the absence of menstruation for greater than three cycles in a previously menstruating woman, or the absence of menstruation greater than six months in woman with previously abnormal menstruation (Andreeff, 2014); oligomenorrhea: persistent menstrual cycles ≥45 days (Villarroel, et al., 2015); or regular menses: average 28 days, ranges from 24-35 days (Jean Hailes for Women’s Health, 2015). According to the Rotterdam criteria, it is possible for a woman to continue to have regular menstruation and still be diagnosed with PCOS; however, the presence of amenorrhea or oligomenorrhea, assist in making the diagnosis of PCOS (Rotterdam, 2004).

Hyperandrogenism is another one of the three diagnostic features of PCOS (see Table 1). Although present in approximately 60-80% of cases, hyperandrogenism can sometimes be difficult to establish (Jean Hailes for Women’s Health, 2015). It can either be determined by physical characteristics of hyperandrogenemia, such as hirsutism, acne, and androgenic alopecia, or by monitoring laboratory values of serum androgen levels (Rotterdam, 2004). Although hirsutism remains the most reliable indicator of clinical hyperandrogenism, it is still difficult to use as a diagnostic measure due to normal variations in race with South Asian and Mediterranean populations having a greater degree and Asian populations having a lesser degree of non-pathological hirsutism. It is also a highly subjective measure and even with the use of grading tools such as the Ferriman-Galleyway Hirsutism Scale (Bode, Seehusen, & Baird, 2012), to objectify the symptoms,
accuracy remains difficult (Rotterdam, 2004). Acne and androgenic alopecia can also develop in women with PCOS as a result of hyperandrogenemia; however, these measures are less well studied and the existing literature is somewhat conflicting so therefore should not be used as a measure of hyperandrogenism (Rotterdam, 2004).

Serum androgens are a better indicator of hyperandrogenemia, however diagnosis is still challenging based on available laboratory technology and tests used. Testosterone measurements are often designed for use in males, resulting in decreased accuracy when assessing for female levels. Also, if a woman is taking an oral contraceptive pill, or has not been off of it for at least 3 months, results may be inaccurate (Jean Hailes for Women’s Health, 2015). Regardless of these controversies, serum androgens can still give an indication of the presence and degree of hyperandrogenemia and can be ordered to rule in a diagnosis of PCOS based on patient presentation of clinical hyperandrogenism, amenorrhea, or infertility. First line laboratory tests that should be considered by the NP include total and free testosterone (Jean Hailes for Women’s Health, 2015). The specialist may consider additional testing once referral is made.

If the above two diagnostic criteria are positive, identification of polycystic ovaries by ultrasound is not necessary for a diagnosis of PCOS (see Table 1). However, performing a pelvic ultrasound can be beneficial in confirming the presence of polycystic ovaries as well as assessing for endometrial hyperplasia and potential risk of endometrial cancer (Rotterdam, 2004). Polycystic ovaries are detected by ultrasound, either transvaginally or transabdominally. Transvaginal ultrasound provides more accurate detection of the presence of polycystic ovaries, but should not be performed in adolescents who have not yet become sexually active (Jean Hailes for Women’s Health, 2015). As described by the
various different phenotypes of PCOS, polycystic ovaries are often, but not always present in women with PCOS. The physical appearance of an ovary affected by PCOS is described as multiple cyst-like structures. These ‘cysts’ are immature follicles that have not had the chance to fully develop. Detection of immature follicles on ultrasound can be a normal finding in many women; however, is considered pathological based on the number of cysts that present (Dewailly et al., 2014). The current accepted diagnostic criteria for PCOS defines polycystic ovaries as the presence of ≥12 follicles in a single ovary, measuring 2-9mm; and/or, ovarian volume >10ml (Rotterdam, 2004). Since the Rotterdam criteria were established, controversy has arisen regarding the use of ≥12 follicles as a cut off due to advancements in technology and greater ease at identifying follicles on ultrasound, subsequently leading to over diagnosis of PCOS. In 2014, the Androgen Excess and Polycystic Ovary Syndrome Society published a task force report, which analyzed the current literature and made a recommendation that the diagnostic criteria for the number of follicles present should be increased to ≥25 follicles. If using ovarian volume to diagnose PCOS in cases of poor image quality and inability to identify individual follicles, the volume of ≥10ml is still recommended (Dewailly et al., 2014).

Diagnostic controversy.

Controversy exists regarding the diagnosis and management of PCOS, primarily due to the discrepancies in the three different versions of the diagnostic criteria. In 2012, a National Institutes of Health workshop on PCOS took place and the experts proposed many recommendations in order to clarify the syndrome (National Institutes of Health, 2012). Included in these recommendations was the universal adoption of the Rotterdam criteria for diagnosis due to its broad, inclusionary conditions. By adopting a widely accepted
definition of PCOS, diagnosis becomes less complicated and treatment is more easily managed (National Institutes of Health, 2012). Experts also believe that the name PCOS is distracting because it focuses on the presence of polycystic ovaries, which are not necessary, nor sufficient on their own, to diagnose the syndrome (National Institutes of Health, 2012).

**PCOS and Insulin Resistance**

**What is Insulin and Insulin Resistance?**

Insulin is a hormone secreted by the pancreas that assists in regulating the production, absorption, and utilization of glucose, thus, ensuring maintenance of steady glucose levels (Moller & Flier, 1991). Insulin resistance (IR) can be defined as a subnormal biological response to normal levels of insulin and can occur in various target areas of the body such as the muscles, liver, and brain. When left unmanaged, it can quickly develop into more severe disorders such as metabolic syndrome or diabetes mellitus type 2 (DM2) (Mantzoros, 2015).

**Insulin Resistance and PCOS**

Polycystic ovary syndrome has numerous impacts on the metabolic functioning of women with this disorder, particularly with an increased prevalence of IR, metabolic syndrome, and DM2. Though not all women with PCOS suffer from IR, studies estimate between 65%-80% of women with PCOS are resistant to insulin, depending on the diagnostic criteria used (Jean Hailes for Women’s Health Foundation, 2015). Although IR is commonly associated with obesity in individuals without PCOS, IR in PCOS seems to be
prevalent regardless of level of obesity. Obese woman with PCOS are seen to have a 3 to 4 fold increase in DM2 and lean women with PCOS are seen to have a 2 to 3 fold increase in the prevalence of DM2 (Wang et al., 2011). Another multi-site, longitudinal study evaluated 2543 women with the phenotypic presentation of androgen excess coupled with menstrual irregularity: phenotype A and B (Table 2), and found that these women were at higher risk for metabolic syndrome compared to the control group (Polotsky, et al., 2012). Results of these studies suggest that PCOS is an independent risk factor for the development of IR and the subsequent development of DM2 should be closely monitored.

Recommendations within these studies are congruent with the suggestions made by Fauser et al., (2012), who advise biochemical screening for IR in women with PCOS who fit the following criteria: “hyperandrogenism with anovulation, acanthosis nigricans, obesity (BMI> 30 kg/m2, or >25 in Asian populations), in women with a family history of T2D [diabetes mellitus type 2] or GDM [gestational diabetes]” (Fauser et al., 2012, p. 34).

Throughout the literature reviewed, it is evident that the most useful test for screening and monitoring IR is with an oral glucose tolerance test (OGTT) since approximately 80% of cases of prediabetes can be missed with other tests such as a fasting blood sugar level (Jean Hailes for Women’s Health, 2015). The OGTT involves fasting blood work and hourly interval testing of blood glucose levels for 2 hours following a challenge of 75-gram oral glucose ingestion (Stovall, Bailey, & Pastore, 2011). This should be done at onset of initial diagnosis for PCOS and continue every two years for the duration of the woman’s life (Jean Hailes for Women’s Health, 2015).

Conclusions from analyzing the literature support monitoring for and treating insulin resistance in the long-term management of women with PCOS. Understanding the
prevalence of IR among women with PCOS can assist in decisions about the necessity of
universal screenings and can also help target women at high risk for IR and prevent long-
term complications.

**Recommendations**

Recommendations regarding screening and monitoring were ascertained
throughout review of the current literature. Screening for IR includes a 2hr 75g OGTT at
onset of initial diagnosis of PCOS and every two years for the duration of the woman's life.
Women should be screened annually if they possess risk factors for the development of
DM2, such as: hyperandrogenism with anovulation, acanthosis nigricans, obesity (BMI> 25
kg/m2), ethnicity (Aboriginal, Hispanic, South Asian, Asian, or African descent), parental
history of diabetes, history of high blood glucose levels, or physical inactivity (Jean Hailes
for Women's Health, 2015).

First line treatment for diabetes is metformin. When starting women with PCOS on
metformin, it is important to note that additional benefits include the reduction of
androgen levels as well as regulation of menstruation (Barthelmess & Naz, 2015).
Prescribing of metformin can be considered by the primary care NP, either alone, or in
collaboration with the endocrinologist, for regulating sugar levels as well as reducing other
symptoms of PCOS.

**Management Guidelines**

1. Screening for IR with a 2-hr 75g OGTT is recommended in women with PCOS at
onset of diagnosis and every two years thereafter.
2. Screening with a 2-hr 75g OGTT should be performed every year if the patient possesses the following risk factors (Ekoé, Punthakee, Ransom, Prebtani, & Goldenberg, 2013; Jean Hailes for Women’s Health, 2015):

- PCOS presentation: hyperandrogenism with anovulation
- Acanthosis nigricans
- Obesity (BMI> 25 kg/m²)
- Ethnicity: Aboriginal, Hispanic, South Asian, Asian, or African descent
- Parental history of diabetes
- History of high blood glucose levels
- Physical inactivity

3. Treatment of elevated blood sugar levels should start with metformin 250-500mg PO BID (BC Guidelines, 2015b).

4. If not being followed by endocrinology already, the patient should be referred to endocrinology at onset of diagnosis of diabetes.

**PCOS and Cardiovascular Disease**

It is evident throughout the literature that PCOS is associated with many known cardiovascular disease (CVD) risk factors; however, controversy exists regarding a direct cause and effect relationship between the presence of PCOS and the ultimate development of CVD (Bates & Legro, 2013). Literature suggests the cause of higher prevalence of CVD in women with PCOS is related to life-long metabolic disturbances, IR, dyslipidemia, hypertension, abdominal obesity, depression, and sleep apnea (Bates & Legro, 2013), (Chang & Wild, 2009). Challenges exist however, in quantifying CVD risk directly from
PCOS or from the common accompanied manifestations because PCOS is predominantly a pre-menopausal syndrome (Chang & Wild, 2009). Diagnosis of PCOS typically does not occur after menopause (Legro et al. 2013) because androgen excess diminishes and polycystic ovaries regress after menopause. Conversely, cardiovascular events are much more common in postmenopausal women (Chang & Wild, 2009).

Some studies have used markers of cardiovascular risk in order to predict potential for CVD risk in women with PCOS. These markers include coronary artery calcification, peripheral endothelial reactivity, and carotid intima-media wall thickness. Chang and Wild (2009), provide a review of the studies which have used the previously mentioned cardiac risk markers; however, results presented by Chang and Wild (2009) remain inconclusive regarding when and how to screen women with PCOS for cardiovascular disease. The recommendations made by Fauser et al. (2012), state that coronary artery calcification and carotid intima media wall thickness are increased in PCOS compared to control groups, independent of obesity or age risk factors. Fauser et al. (2012) also state that the relationship between PCOS and cardiovascular mortality is yet to be determined and further research is needed to make a recommendation on timing and frequency of screening (Fauser et al., 2012). In summarizing recommendations from these articles, both recognize a correlation between PCOS and cardiovascular risk, but are unable to determine a direct cause and effect relationship between PCOS and CVD development and CVD mortality.

The Jean Hailes for Women’s Health guideline (2015), on the other hand, recognizes the increased prevalence of cardiac risk markers in women with PCOS and subsequently suggests recommended screening. Similarly however, they also struggled to find evidence
to prove the most effective screening tool or method of assessing CVD risk. They suggest that women with the following risk factors should be screened regularly for CVD: “obesity, cigarette smoking, dyslipidemia, hypertension, impaired glucose tolerance, lack of physical activity, and those with metabolic syndrome and/or type 2 diabetes” (Jean Hailes for Women’s Health, 2015, p.14). Recommended screening intervals should be based on the presence of any of the above risk factors.

In summary, although there is insufficient evidence regarding a direct correlation between PCOS and the development of cardiovascular disease, it is clear that by reducing risk factors, women can reduce their overall CVD risk.

**Recommendations**

Recommendations for reducing the risk of developing CVD in women with PCOS include screening for the following CVD risk factors at every visit: “obesity, cigarette smoking, dyslipidemia, hypertension, impaired glucose tolerance, lack of physical activity, and those with metabolic syndrome and/or type 2 diabetes” (Jean Hailes for Women’s Health, 2015, p.14). This would include monitoring waist circumference and BMI, current smoking and exercise habits, monitoring blood pressure, and monitoring lab work for lipid profiles and oral glucose tolerance testing (OGTT), at least every 2 years or annually if risk factors present.

**Management Guidelines**

1. Screening for CVD should be performed every 2 years (Jean Hailes for Women’s Health, 2015).
2. If risk factors present, screening should be performed every 1 year (Jean Hailes for Women’s Health, 2015).

3. Screening includes monitoring for the presence of CVD risk factors and entails assessing:
   - Waist circumference: target <88cm (Goldenberg & Punthakee, 2013)
   - BMI: target <25 kg/m² (Jean Hailes for Women’s Health, 2015)
   - Smoking status: goal is reduction or quitting smoking (BC Guidelines, 2014)
   - Exercise habits: goal is 30 min of moderate to vigorous activity 5-7 days a week (BC Guidelines, 2014)
   - Blood pressure: target <140/90 or <130/90 if diabetic (BC Guidelines, 2015a)
   - Lipid profiles: aim is LDL <3.5 (BC Guidelines, 2014)
   - OGTT: target <11.0 (Ekoé, et al., 2013)

4. Women with high blood pressure or hyperlipidemia should be treated appropriately by the NP according to BC Guideline recommendations (BC Guidelines, 2014).

5. Counselling for smoking cessation strategies should be provided for women who smoke. Resources to offer include www.quitnow.ca (BC Guidelines, 2014).

6. Referral to a cardiologist should be considered to optimize patient care (Jean Hailes for Women’s Health, 2015).

**PCOS and Cancer Risk**

The strength of the association between endometrial cancer risk and PCOS remains controversial; however, many studies and review articles do recognize a relationship between these two factors. One meta-analysis by Chittenden, Fullerton, Maheshwari, and
Bhattacharya, (2009), suggest that women with PCOS are three times more likely to develop endometrial carcinoma than women who do not have PCOS. Women with PCOS are at higher risk for developing endometrial cancer due to chronic oligoovulation or anovulation, which results in endometrial hyperplasia and progression to endometrial cancer (Chittenden et al., 2009). Additionally, many of the clinical features of PCOS are also shared risk factors for endometrial cancer such as, “obesity, hypertension, type II diabetes, unopposed oestrogen, and nulliparity” (Chittenden et al., 2009, p. 398). Since the time the Chittenden et al., article was written in 2009, Haoula, (2012), performed a meta-analysis, which critiqued many of the studies done on PCOS and endometrial cancer risk based on limitations of size as well as the diagnostic inclusion criteria. However, despite this critique, Haoula still discovered a 3-fold increase in the risk of developing endometrial cancer in women who have PCOS (Haoula, 2012).

It has been suggested by some researchers that women with PCOS are also at higher risk of developing other estrogen dependent cancers such as breast and ovarian cancer. However, a meta-analysis by Barry, Azizia, and Hardiman, (2014), did not find sufficient evidence to prove a link. Similar to determining CVD risk, defining a direct cause and effect relationship between PCOS and breast and ovarian cancer risk is complicated by other clinical features of PCOS, most notably obesity (Barry, Azizia, & Hardiman, 2014). Also the review articles that Barry, Azizia, and Hardiman, (2014), analyzed have shown insufficient evidence to prove an increased risk of other cancers based on the numbers of studies reviewed for the article and the diagnostic criteria used. Therefore, based on the literature reviewed for this paper, a conclusion cannot be drawn regarding the correlation between PCOS and either breast or ovarian cancer risk and recommendations for screening
guidelines cannot be made.

**Recommendation**

Evidence in the literature reveals a link between PCOS and endometrial cancer with an almost 3-fold increase in risk compared to women without PCOS. Since there are no screening recommendations for monitoring the presence of endometrial cancer, clinical guidelines should recommend ordering diagnostics, such as ultrasound and endometrial biopsy, based on clinical presentation (Fauser et al., 2012). This would include length of time of amenorrhea and any abnormal uterine bleeding (Fauser et al., 2012), coupled with the presence of risk factors such as: “obesity, hypertension, type II diabetes, unopposed oestrogen, and nulliparity” (Chittenden et al., 2009, p. 398).

Treatment recommendations include both non-pharmacological and pharmacological therapies. Non-pharmacological management to reduce endometrial cancer risk includes diet and exercise regimens. Studies report regulation of ovulation and menstruation in women who have lost as little as 5% of their total body weight (Tarlatzis et al., 2008). Goal for diet and exercise management should be directed at losing approximately 5-10% body weight (Jean Hailes for Women’s Health, 2015). Pharmacologic treatments to regulate menstruation and reduce cancer risk involve initiation of combination oral contraceptives (COC). Unless imminent desire for pregnancy is involved, the initiation of COC can help balance the unopposed estrogen seen in PCOS and regulate menstruation (Legro et al., 2013). Low-dose COCs are proven to be more effective than higher dose COCs in managing the other associated manifestations of PCOS (Jean Hailes for Women’s Health, 2015).
**Management Guidelines**

Management goals are based upon reducing risk factors for the development of cancer.

1. Women with PCOS should have a menstrual bleed at least 4 times every year (Chittenden et al., 2009).

2. First line treatment for amenorrhea in order to reduce the risk of endometrial cancer includes lifestyle management such as diet and exercise with a goal weight loss of 5-10% body weight (Klein & Poth, 2013).

3. Pharmacologic treatments include initiation of low-dose combination oral contraceptives to regulate hormone levels (Jean Hailes for Women’s Health, 2015).

4. Referral to gynecology should be considered in women with persistent oligomenorrhea or amenorrhea who are not menstruating at least 4 times per year.

**PCOS and Obesity**

It is estimated that 38-88% of women with PCOS are overweight or obese (Barber, McCarthy, Wass, & Franks, 2006); however, exact numbers are difficult to obtain due to a lack of representative data on this measure (Lim, Norman, Davies, & Moran, 2013). A review article by Barber, et al. (2006), evaluates studies that show a strong correlation between obesity and the severity of PCOS symptoms, such as menstrual irregularities, hirsutism, and infertility. This was demonstrated by noting the reduction in severity of PCOS symptoms as a result of weight reduction. Many studies indicate that even a 5% reduction in weight can result in return of menstruation and improvement of symptoms of hyperandrogenemia (Barber et al., 2006).
It is possible for lean women to also suffer from PCOS, so even though obesity and PCOS are strongly correlated, obesity is not always necessary for the development of the syndrome (Barber et al., 2006). Therefore, it would be incorrect to assume that obesity causes PCOS; yet, there is evidence in the literature to suggest that obesity worsens the androgenic, reproductive, and metabolic symptoms (Barber et al, 2006).

Conversely, an in depth meta-analysis by Lim et al., (2013) state that obesity only had significant detrimental effects on reproductive and metabolic aspects of PCOS and made no difference to total testosterone, hirsutism, or cholesterol levels. This meta-analysis was performed after researchers noticed conflicting information in the current literature regarding the impact of obesity on PCOS (Lim et al., 2013). It is known that being overweight has negative impacts on many aspects of the overall health of a woman with PCOS, and being obese or morbidly obese increases these impacts. Further research is required to determine exact cut-off ranges for the degree of obesity that causes detrimental effects, as well as the ability to quantify psychological factors that contribute to obesity (Lim et al., 2013).

**Recommendations**

Further research is needed to pinpoint specifics; however, for the overall health of the woman, lifestyle changes are recommended for overweight or obese women, aiming for 5-10% loss of current body weight (Lim et al., 2013). Jean Hailes for Women’s Health guidelines recommend lifestyle modifications to lessen the severity of PCOS symptoms in women who are overweight or obese (see Table 3) (Jean Hailes for Women’s Health, 2015). Weight loss is also known to have positive impacts on mood, quality of life, fertility,
cardiovascular health, and metabolic consequences of PCOS (Jean Hailes for Women’s Health, 2015).

According to the BC Guideline document entitled *Overweight and Obese Adults: Diagnosis and Management* lifestyle management is recommended for women in obesity class 1; however, for women in obesity class 2 or 3, lifestyle management may be an adjunct to more aggressive treatments such as pharmacologic or surgical interventions (BC Guidelines, 2011). Also, women with comorbidities such as type 2 diabetes, hypertension, CVD, osteoarthritis, dyslipidemia, and sleep apnea, require more intensive interventions since these other conditions will also get better as a result of weight loss (BC Guidelines, 2011).

**Management Guidelines**

1. Weight, height, BMI calculation, and waist circumference should be obtained at each annual or biennial visit.

2. Target waste circumference is <88cm and target BMI is <25 kg/m², see table 3 (BC Guidelines, 2011).

3. In the overweight or obese population, the NP should provide adequate diet and exercise counselling regarding lifestyle measures to reduce obesity and increase exercise habits. The NP should stress that even a 5% reduction in weight assists in return of menstruation and improvement of symptoms of hyperandrogenemia (Barber et al., 2006).

4. Obesity class 1: Lifestyle management is recommended (BC Guidelines, 2011).

5. Obesity class 2 or 3, or women with comorbidities such as type 2 diabetes, hypertension, CVD, osteoarthritis, dyslipidemia, and sleep apnea: more intensive
interventions such as lifestyle management in combination with pharmacologic or surgical interventions is recommended (BC Guidelines, 2011).

   a. Caloric restriction of 500-1000kcal/day
   b. Physical activity: 30+ minutes of moderate to vigorous physical activity 5-7 times per week
   c. No more than 0.5-1kg/week weight loss
   d. Establishing initial weight loss goal of 5-10% of body weight
   e. Referral to weight loss program and support groups

7. Pharmacologic therapy for obesity class 2 and 3 after diet, exercise, and behavioural programs have failed: orlistat (Xenical) (BC Guidelines, 2011).

8. Referral to surgeon for gastric bypass surgery if unable to obtain or maintain weight reduction strategies

<table>
<thead>
<tr>
<th>Table 3: BMI Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight Classification</strong></td>
</tr>
<tr>
<td>Underweight</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Overweight</td>
</tr>
<tr>
<td>Obese: Class 1</td>
</tr>
<tr>
<td>Obese: Class 2</td>
</tr>
<tr>
<td>Obese: Class 3</td>
</tr>
</tbody>
</table>

(adapted from BC Guidelines, 2011)

**PCOS and Mental Health**

Depression and anxiety are two conditions that women with PCOS often face. The largest meta-analysis done to date was performed by Veltman-Verhulst, Boivin, Eijkemans, & Fauser in 2012. This analysis reviewed 28 studies that evaluated women’s reported
experiences in three different domains: depression, anxiety, or emotional-subscases of quality of life (emoQoL). Results of this study show that women with PCOS experience significantly greater emotional distress than control women within all three domains (Veltman-Verhulst et al., 2012). The studies do not give explicit explanations regarding the cause of this emotional distress; however, they propose that stigmatizing factors such as infertility, hirsutism, and obesity contribute. Interestingly, subgroup analysis results indicate that emotional distress was seen in lean, fertile women with PCOS, as well as in obese, infertile women with PCOS, suggesting that the cause of emotional distress in PCOS is multifactorial and not solely due to the physical manifestations of the syndrome (Veltman-Verhulst et al., 2012). Authors of this meta-analysis suggest that further studies are required to determine the cause of emotional distress and investigate the correlation between these two conditions (Veltman-Verhulst et al., 2012).

The consensus document written by Fauser et al. (2012), supports the information gathered by Veltman-Verhulst et al., (2012). Fauser et al. (2012) specifically comment that women with PCOS are in a high-risk group for reduced quality of life due to psychological and behavioral disorders. Some of the studies evaluated in this article used a screening tool called the QOL Questionnaire for Women with PCOS (PCOSQ), which is the only validated disease-specific screening tool for PCOS. Results of studies that use this tool show that PCOS has substantial unfavorable effects on quality of life, most often due to weight management issues (Fauser et al., 2012).

Evidenced based guidelines by the Jean Hailes for Women’s Health organization (2015), also comment on the correlation between emotional distress and PCOS. They state, that the prevalence of depression in women with PCOS is 28%-64% compared to 7.1%-8%.
in the general population and prevalence of anxiety in PCOS is 34%-57%, compared to 18% in the general population. Also, when experienced, depression and anxiety were more severe in women with PCOS compared to the general population. Similarly, they state that the cause is likely multi-factorial, ranging from physical and biochemical factors to the chronic and complex nature of the syndrome (Jean Hailes for Women’s Health, 2011).

**Recommendations**

All three of the meta-analyses and consensus documents reviewed above, offer similar recommendations in regards to screening for emotional distress and decreased quality of life. Early and regular screening is important to monitor for risk and progression of psychological disorders related to PCOS.

Veltman-Verhulst et al., (2012), recommends that instead of using a specific screening tool, practitioners should have a discussion with their patients regarding their current moods and state of emotional distress. Discussions with patients provide an opportunity to investigate current emotional states as well as a chance to offer education regarding potential emotional impacts in the future. By administering a screening tool at a single point in time, some women who are at risk for developing depression or anxiety in the future can be missed (Veltman-Verhulst et al., 2012).

The Jean Hailes for Women’s Health guideline section on depression and anxiety recommends three screening questions that can be asked at every visit. If any of these screening questions indicate the presence or potential for depression or anxiety, disease specific screening questionnaires can then be administered, including either one or more of the following: Kessler Psychological Distress Scale 10 (K-10), Depression Anxiety Stress Scale (DASS-21), Patient Health Questionnaire (PHQ9), or Generalized Anxiety Disorder 7
item scale (GAD7). Referral to a psychiatrist is also recommended for further assessment and management as felt appropriate by the primary care provider (Jean Hailes for Women’s Health, 2015). Similarly, the BC Guidelines recommend two open-ended questions to screen for and detect the presence of emotional distress. Answering yes to either one of these questions prompts further investigation into type and degree of emotional distress. The BC Guidelines questions include: “Have you lost interest or pleasure in things you usually like to do? Have you felt sad, low, down, depressed or hopeless?” (BC Guidelines, 2013, p. 1).

Management Guidelines

1. NPs should have discussions with their patients regarding moods and quality of life and screen for the presence of emotional distress with every annual or biennial visit.

2. Women with PCOS should be screened for emotional distress with the following two questions (BC Guidelines, 2013):

   In the past month:

   I. Have you lost interest or pleasure in things you usually like to do?

   II. Have you felt sad, low, down, depressed or hopeless?

3. If a woman answers yes to either question, further screening is recommended with the PHQ-9 (Appendix A) or the GAD-7 questionnaire (Appendix B)

4. NPs should refer to the BC Guideline for full management guidelines:

   http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/depression_full_guideline.pdf
PCOS and Infertility

The American Academy of Family Practice defines infertility as, “the inability to achieve pregnancy after one year of regular, unprotected intercourse” (Lindsay & Vitrikas, 2015, p. 308), however, women who are older than 35 years of age are considered infertile after 6 months of unprotected intercourse (Lindsay & Vitrikas, 2015). Many women with PCOS experience infertility secondary to ovulatory dysfunction and endometrial receptivity (Ecklund & Usadi, 2015). Infertility is further exacerbated by the presence of obesity and insulin resistance, which has effects on the granulosa cells in the ovaries causing premature lutenization and subsequent disruption of normal oocyte maturation (Ecklund & Usadi, 2015).

Although the NP cannot treat or manage infertility, preconception counselling and initial investigations can take place in the primary care setting. Preconception counselling should include discussions regarding limitation or avoidance of factors that can contribute to infertility, such as, smoking and excessive alcohol consumption, as well as discussion and education regarding frequency of intercourse. Recommendations include having unprotected intercourse every 1-2 days around the time of ovulation (Lindsay & Vitrikas, 2015).

Weight loss remains first-line therapy for treatment of infertility in women with PCOS (Tarlatzis et al., 2008). The NP can initiate counselling and monitoring of lifestyle management and assist in goal setting for weight loss. According to Tarlatzis et al., (2008), women who have lost as little as 5% of their total body weight often report spontaneous return of ovulation and subsequent successful pregnancies (Tarlatzis et al., 2008).
Weight loss counselling should include both diet and exercise regimens (Jean Hailes for Women’s Health, 2015). Diet considerations include a calorie-restricted diet with reduced glycemic load. This will not only assist with infertility due to weight loss, but also has a positive impact on reducing hyperinsulinemia and its metabolic consequences, one of which being infertility (Tarlatzis et al., 2008). With the exception of the above recommendations, very few studies have been done to evaluate which diet in particular is most beneficial and within those, no consensus has been drawn regarding the optimal diet for women with PCOS (Tarlatzis et al., 2008). Nutrition counseling by the primary care provider and referral to dietitian can assist patients in optimizing initial weight loss and strategies on maintaining this throughout life (BC Guidelines, 2011).

Exercise is also recommended for obese women with PCOS to assist in weight loss; noting that individual considerations must be made for many women in regards to cardiovascular and musculoskeletal health when initiating any exercise regimen. Studies have not shown exercise alone to be overly beneficial in providing significant weight loss; however, when coupled with diet, better initial and long-term weight loss management is obtained (Tarlatzis et al., 2008).

The Jean Hailes for Women’s Health guideline (2015) recommends not offering pharmacologic therapy for ovulation induction in women who have a BMI ≥35 until 3-6 months of lifestyle interventions of diet and exercise have been trialed or the patient has undergone bariatric surgery (Jean Hailes for Women’s Health, 2015). NPs can assist in this aspect of care by initiating discussion about weight loss management, reviewing the benefits of weight loss when trying to conceive, and initiating referrals to dieticians, exercise therapists, or surgeons.
Recommendations

Preconception counselling is one of the main areas of focus in which NPs can assist with infertility in women with PCOS (Tarlatzis et al., 2008). Initiation of lifestyle management with a goal weight loss target of 5-10% body weight should occur prior to discussion and consideration of ovulation induction (Jean Hailes for Women’s Health, 2015). Nurse Practitioners can also initiate diagnostic evaluation prior to referral to an infertility specialist. Workup includes laboratory blood tests such as FSH, LH, progesterone, estradiol, prolactin, and TSH (Lindsay & Vitrikas, 2015).

Referral to an infertility clinic should take place for continuation of investigations, if necessary, and exploration of management options. Multiple pharmacologic options are available to assist women in obtaining a successful pregnancy; however, prescribing these medications is outside the NP scope in British Columbia (College of Registered Nurses of British Columbia, 2016).

Women with PCOS who do become pregnant require close monitoring for pregnancy related complications as they are at higher risk for gestational diabetes and hypertensive disorders (Ecklund & Usadi, 2015). It is outside the scope of the NP in BC to deliver babies, therefore referral to a GP or to an obstetrician for delivery needs to take place prior to 28 weeks gestation (College of Registered Nurses of British Columbia, 2015).

Management Guidelines

1. Lifestyle management for weight loss is first line treatment for infertility in obese women with PCOS and should be trialed for 3-6 months prior to discussions and interventions for ovulation induction (Jean Hailes for Women’s Health, 2015).
2. Counselling should include discussion regarding avoiding factors that may contribute to infertility such as: smoking, excessive alcohol use, and ensuring the couple is engaging in intercourse at least every 1-2 days around the time of ovulation.

3. Diagnostic laboratory workup for infertility by the NP includes: FSH, LH, progesterone, estradiol, prolactin, and TSH (Lindsay & Vitrikas, 2015).

4. Referral to an infertility specialist should occur after lifestyle interventions for weight loss have been attempted for 3-6 months and pregnancy has not been successful (Jean Hailes for Women’s Health, 2015).

**PCOS and Dermatology**

Androgens play an important role in the disease process of PCOS as well as in the clinical manifestations including: hirsutism, acne, and alopecia. Another dermatologic manifestation of PCOS is acanthosis nigricans which can develop as a result of insulin resistance (Housman & Reynolds, 2014).

Clinical signs of hyperandrogenemia are very common in PCOS and are one of the hallmark diagnostic features of the syndrome. Up to 60% of women with PCOS experience hirsutism, defined as excessive male pattern terminal body hair seen in women (Bode et al., 2012). Although hirsutism can differ between ethnicities, it remains a valid physical indicator of hyperandrogemia (Housman & Reynolds, 2014). Most commonly, this is seen on the upper lip, chin, areola, chest, back, and lower abdomen. Acne is another common manifestation of hyperandrogenism; usually seen on the lower face, neck, chest, and upper back. Varying presentations of both hirsutism and acne can be attributed to the activity of
isoenzymes and the sensitivity of androgen receptors and is not always directly attributed to levels of serum androgens (Housman & Reynolds, 2014). Androgenic alopecia can also be seen in PCOS; however, is much less common than hirsutism and acne. Careful history and physical examination assist in directing the diagnosis of alopecia towards androgenic alopecia or other causes of alopecia. Laboratory investigations can be helpful in confirming diagnosis and correlation to hyperandrogenism (Thiedke, 2003).

Due to cultural differences of hirsutism in women with and without PCOS, monitoring for hirsutism and use as a diagnostic feature can be challenging (Housman & Reynolds, 2014). The Ferriman-Gallwey scale of hirsutism is a tool that attempts to objectify this very subjective symptom by grading the amount of hair present on nine different body parts using graphics. These body parts include the upper lip, chin, chest, abdomen, pubic area, arms, legs, back, and buttocks (Bode et al., 2012). Critics of this tool discuss the limitation of not allowing for scoring of hair in other body parts (eg. side burns). However, despite its limitations, this scale remains the most commonly used tool to score hirsutism (Bode et al., 2012).

Recommendations

Current guidelines by Fauser et al. (2012) recognize that hirsutism is an adequate marker for hyperandrogenism; however, biochemical hyperandrogenemia should also be evaluated in women that are suspected to have PCOS. Conversely, they state that acne and alopecia are not good indicators of hyperandrogenemia so should not be used as a marker of clinical hyperandrogenism when diagnosing PCOS (Fauser et al., 2012).

Treatment regimens should be based on clinical presentation and patient preference for ridding excess body hair or treating acne. Treatment for hirsutism is focused
on reducing androgen production, decreasing circulating free testosterone, and limiting androgen bioactivity to target hair follicles. Interventions for hyperandrogenemia focus on reducing steroid production from the ovaries, thus reducing bioavailability. Oral contraceptive pills (OCP) are commonly used for this purpose, either alone, or in combination with an antiandrogen such as spironolactone (Fauser et al., 2012). Due to the life cycle of terminal hair, at least 6 months of treatment is necessary to see clinical results (Bode et al., 2012). Laser therapy may be recommended but is expensive and time-consuming. It is an effective measure for elimination of unwanted body hair, so can be recommended to patients if cost is not a factor (Bode et al., 2012).

Acne can be treated with various topical or systemic acne therapies based on clinical presentation and patient preference (Fauser et al., 2012). Topical retinoids remain first line mono-therapy for treatment of non-inflammatory acne, and can be used in combination with a topical antibiotic for inflammatory acne (Titus & Hodge, 2012). Combination oral contraceptives in women who are not wishing to become pregnant can also be very effective in the treatment of both inflammatory and non-inflammatory acne (Titus & Hodge, 2012).

Management Guidelines

1. Interventions for clinical hyperandrogenemia focus on reducing steroid production from the ovaries, thus reducing bioavailability.

2. Oral contraceptive pills are commonly used for clinical hyperandrogenemism, either alone, or in combination with an antiandrogen such as spironolactone (Fauser et al., 2012).
3. Laser therapy is an effective measure for elimination of unwanted body hair but is expensive and time-consuming. It can be recommended to patients if cost is not a factor (Bode et al., 2012).

4. Acne management includes assessment and determination of type and severity of acne. First line treatment options include combination estrogen and progesterone oral contraceptive pills, or topical retinoid, either alone, or in combination with a topical antibiotic (Titus & Hodge, 2012).

**Diagnostic workup**

Initial diagnostic workup for the woman presenting with symptoms suggestive of PCOS is somewhat dependent on clinical presentation. According to the Rotterdam criteria, in order to make a diagnosis of PCOS, certain clinical features need to be present and other diseases or syndromes need to be ruled out. Therefore, it is critical that, before making the diagnosis of PCOS, other conditions are considered and a thorough diagnostic workup is performed (Rotterdam, 2004).

**Other Conditions to Rule In or Rule Out**

The NP can assist in narrowing down the diagnosis by ordering particular diagnostic tests based on the patient’s presenting complaint and clinical picture. Other conditions that have similar clinical manifestations of PCOS include: hyperthyroidism, hyperprolactinemia, 21-hydroxylase-deficient congenital adrenal hyperplasia, Cushing’s syndrome, androgen secreting neoplasms, and idiopathic hirsutism (Azziz et al., 2009).

For women presenting with amenorrhea or oligomenorrhea, diagnostics would be indicated to rule out other causes such as pregnancy, hyperandrogenemia,
hyperthyroidism, hyperprolactinemia, or ovarian insufficiency (Barbieri & Ehrmann, 2015). Table 4 provides reference ranges for normal values and expected results to rule in the following diseases. Testing to rule out pregnancy would include a urine or serum beta hCG; for hyperthyroidism a thyroid stimulating hormone (TSH) level and, if indicated from the TSH, a Free T4 level; for hyperprolactinemia, a serum prolactin level; and for ovarian insufficiency, a follicle stimulating hormone (FSH) level (Barbieri & Ehrmann, 2015).

For a patient presenting with clinical signs of hyperandrogenism, it would be necessary to rule out non-classic congenital adrenal hyperplasia (NCCAH), Cushing’s syndrome, adrenal tumors, androgen-secreting tumors, or ovarian hyperthecosis (Barbieri & Ehrmann, 2015). NCCAH is due to a deficiency in 21-hydroxylase and can be ruled out by measuring a morning level of 17-hydroxyprogesterone (17-OHP) in the early follicular phase. It is more prevalent and should be considered more seriously in certain populations such as women of Eastern European Jewish, Hispanic, Slavic, or Italian decent (Nieman & Merke, 2016). Cushing’s syndrome may have many of the same symptoms as PCOS such as hirsutism, oligomenorrhea, and obesity; however, it would include other clinical features (such as: hypertension, supraclavicular fat pads, purple abdominal striae, or proximal muscle weakness) that are not present in PCOS (Nieman, 2015). Since the index of suspicion for Cushing’s syndrome is low based on the absence of Cushing’s specific symptoms, only first line tests are indicated in ruling out the diagnosis. This would include monitoring 24-hour urinary free cortisol (UFC) excretion (Nieman, 2015). An adrenal tumor should be ruled out by checking dehydroepiandrosterone sulfate (DHEA-S) levels. These levels would be markedly elevated in the presence of an adrenal tumor, much higher than what is seen in a woman with PCOS (Nieman, 2016). A woman with an androgen
secreting ovarian tumor or ovarian hyperthecosis would present with more severe signs of hyperandrogenism. The first test to rule this out would be a total testosterone level. If this is significantly higher than the expected range for PCOS, these diagnoses could be considered and further testing can be done to confirm (Barbieri & Ehrmann, 2015).

In addition to the laboratory tests listed above, a pelvic ultrasound would be indicated to rule in PCOS if diagnosis cannot be made based on the presence of menstrual irregularity and hyperandrogenism (Fauser et al. 2012). Transvaginal ultrasound provides more accurate detection of the presence of polycystic ovaries, but should not be performed in adolescents who have not yet become sexually active; in this case, transabdominal ultrasound is recommended (Jean Hailes for Women’s Health, 2015).

<table>
<thead>
<tr>
<th>Presenting Complaint</th>
<th>Diagnosis to Consider</th>
<th>Laboratory test</th>
<th>Expected abnormal result if condition present</th>
<th>Normal range* (adult female)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amenorrhea/Oligomenorrhea</td>
<td>Pregnancy</td>
<td>serum beta-hCG</td>
<td>&gt;5 IU/L</td>
<td>&lt;5 IU/L</td>
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<tr>
<td></td>
<td>Hyperthyroidism</td>
<td>TSH (then if indicated, free T4)</td>
<td>&lt;0.27 mU/L</td>
<td>0.27-4.2 mU/L</td>
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<tr>
<td></td>
<td>Hyperprolactinemia</td>
<td>Prolactin</td>
<td>&gt;20.0 mU/L</td>
<td>10.5-20.0 mU/L</td>
</tr>
<tr>
<td></td>
<td>Ovarian insufficiency</td>
<td>FSH (would be in post menopausal range)</td>
<td>&gt;25.0 ug/L</td>
<td>&lt;25.0 ug/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; 20.0 IU/L</td>
<td>20.0-135 IU/L</td>
</tr>
<tr>
<td>Hirsutism</td>
<td>Nonclassic congenital adrenal hyperplasia (NCCAH)</td>
<td>follicular phase 17 OHP</td>
<td>&gt;6 nmol/L</td>
<td>0.3-4.0 nmol/L</td>
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<tr>
<td></td>
<td>Cushing's syndrome</td>
<td>24 hour urine cortisol</td>
<td>&gt;660 nmol/d</td>
<td>30-220 nmol/d</td>
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<tr>
<td></td>
<td>Adrenal tumor</td>
<td>dehydroepiandrosterone sulfate (DHEA-S)</td>
<td>&gt;13.6 umol/L</td>
<td>&lt;10.8 umol/L</td>
</tr>
<tr>
<td></td>
<td>Androgen-secreting tumor</td>
<td>total testosterone</td>
<td>&gt;5.2 nmol/L</td>
<td>&lt;1.8 nmol/L</td>
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<tr>
<td></td>
<td>Ovarian hyperthecosis</td>
<td>total testosterone</td>
<td>&gt;5.2 nmol/L</td>
<td>&lt;1.8 nmol/L</td>
</tr>
</tbody>
</table>

*Normal ranges obtained from: (Lifelabs Clinical Laboratories, 2015)
Nurse Practitioners

Nurse Practitioners are registered nurses (RN) who have nursing experience and advanced level education and scope of practice. Educational philosophies for RNs and NPs focus on a holistic approach to care, taking into account many different aspects of a patient's physical and mental health, as well as their social situation, family, and quality of life (CNA, 2014). Responsibilities of the NP include diagnosing and treating illnesses, prescribing medications, ordering tests, and referring to specialists based upon the Scope of Practice outlined by the regulating body for NPs: the College of Registered Nurses of British Columbia (CRNBC) (College of Registered Nurses of British Columbia, 2016).

The level of education required in each province differs according to provincial regulations (MacDonald, Schreiber, & Davis, 2005). In British Columbia (BC), to become an NP, first a baccalaureate RN preparation is required, followed by practical experience as an RN. The NP education is a combined Masters of Nursing and NP program, followed by a national written exam and a provincially regulated practical exam (Spence, Agnew, & Fahey-Walsh, 2015).

Scope of Practice

Nurse practitioners are key members of the health care team and are likely to see women presenting with signs and symptoms of PCOS in a primary care setting. NPs need to be able to recognize all the possible manifestations and clinical presentations that are possible when women first present to a care provider. It is also imperative that NPs understand the scope and limitations surrounding their role in PCOS, the necessary workup prior to referral, and appropriate practitioners to collaborate with in order to optimize care for the individual.
According to the CRNBC scope of practice document entitled *Applying the Competencies Required for Nurse Practitioners in British Columbia* (2015), PCOS is regarded as a category ‘C’ diagnosis; meaning that a diagnosis needs to be made in collaboration with a physician or specialist. The definition of this category ‘C’ reads: “The nurse practitioner establishes or strongly suspects the diagnosis and consults with a physician for the management plan or consults with a physician to confirm the diagnosis” (College of Registered Nurses of British Columbia, 2015, pg. 32). This referral can result in long term follow up and management by the specialist physician or a short term, one time, consultation in which the care is placed back in the hands of the NP. In the case of PCOS, the NP will be referring to an endocrinologist and potentially other specialist such as a cardiologist, dermatologist, or fertility specialist for collaborative care. In BC, NPs have certain restriction on prescribing authority for medications. Some of these include the medications that are used in the treatment and management of PCOS; therefore, collaboration with specialists is essential.

**What is a Guideline?**

A clinical practice guideline is a tool for practitioners to use to assist them in making appropriate clinical decisions regarding patient diagnosis, treatment, screening, health promotion, and follow-up or referrals (Brouwers, et al., 2013). They are usually composed by a team of experts who have a wide breadth of clinical knowledge as well as experience in research and clinical trials. The combination of evidence-based literature with the clinical expertise of the authors make the information provided in guidelines vital to
optimizing patient care by the primary care practitioner (Misso, Boyle, Norman, & Teede, 2014).

In BC, clinical practice guidelines are overseen and published by the Guidelines and Protocols Advisory Committee (GPAC) which is a collaborative group of individuals from Doctors of BC and the Ministry of Health (BC Guidelines, nd). GPAC has published over 50 guidelines, flow sheets, summaries, and tools for patient education.

**PCOS Guideline**

The clinical practice guideline that will accompany this literature review was developed for the successful completion of NURS 596 Culminating Project for the Masters of Nursing/Nurse Practitioner program at the University of British Columbia. It was developed for use by NPs in BC in order to outline the diagnostic criteria of PCOS and assist in understanding the diagnostic workup and long-term management of adult women with PCOS. It is intended for use in a clinical practice setting when working with adult women presenting to their primary care NP with symptoms such as amenorrhea, hirsutism, or infertility. It provides NPs with guidance to make decisions regarding the care and work-up for women with PCOS. It focuses on appropriate diagnostic workup, timing for referrals, and the long-term screening and management necessary to optimize the care of women after their diagnosis of PCOS. Upon completion, this guideline will be submitted to GPAC for potential implementation into the BC Guidelines for use by all primary care providers.

**Discussion**

PCOS is a complex, multifaceted syndrome with multiple health implications and long-term health risks (Fauser et al., 2012). Women with PCOS require management and
guidance from their primary care NP as well as multiple specialists. Due to the heterogeneity of the syndrome, diagnosis, symptomatic treatment, and long term management is very complex and individualized (Fauser et al., 2012). Long-term complications of PCOS include increased risk for IR, CVD, endometrial cancer, obesity, depression and anxiety, infertility, and various dermatological manifestations (Fauser et al., 2012).

Diagnosis of PCOS is complicated by various different diagnostic criteria. Research for this literature review reveals that the most widely accepted diagnostic criteria to date is the Rotterdam criteria, which was developed in 2003. These criteria encompass a broader expression of the syndrome and require two of the following three criteria: oligo- and/or anovulation, clinical and/or biochemical hyperandrogenism, or polycystic ovaries (Rotterdam, 2004). It is outside the scope of practice for NPs in BC to diagnose PCOS, however, NPs are highly involved in the co-management with various specialists and play a vital role in the health of women with PCOS.

**Implications for Practice**

The purpose of this literature review was to find supporting evidence to create a clinical practice guideline for use by the NP in BC. Throughout the development of this literature review, many other guidelines and review articles were evaluated and a Nurse Practitioner Clinical Practice Guideline was developed based on the evidence. This guideline is shown in Appendix C and is specific to adult patients with PCOS and has incorporated BC Guidelines as well as PCOS specific guidelines from other countries.

This literature review and clinical practice guideline will support NPs in the evaluation and management of adult women with PCOS. It also assists NPs in confidently
assessing women presenting with the various clinical manifestations of PCOS and allow them to rule in and rule out other causes of the symptoms.

**Further Research and Projects**

Despite the comprehensive nature of this literature review and clinical practice guideline it is solely developed for management of the adult women with PCOS. Future research and guideline development could be directed towards the care and management of women with PCOS in special populations such as adolescents or postmenopausal women. It could also cover special considerations in the health of the woman with PCOS during pregnancy.

**Conclusion**

Polycystic ovary syndrome is a complex disease with varying clinical presentations, diagnostic criteria, and long-term metabolic and cardiovascular complications (Fauser et al., 2012). The complexity of symptoms and complications of PCOS require involvement of various different specialists; however, the primary care provider, such as the NP, is involved in the overall long-term management. This literature review evaluates the current literature recommendations regarding diagnosis, workup, and management of women with PCOS. It also highlights the disorders that can possibly mimic PCOS and provides the resources necessary for the NP to rule out these disorders and narrow down a diagnosis of PCOS. Due to the advanced level of education and scope of practice of the NP, they are in a unique position to provide care to women with PCOS. With the assistance of the information presented in this literature review and accompanying primary care
guideline, the NP will have the tools necessary provide comprehensive, holistic care to women with PCOS.
References


doi:10.1016/j.mce.2012.10.029


doi:10.1097/OGX.0b013e3182227fc94
Appendix A

Patient Health Questionnaire (PHQ-9)

Patient name: ______________________________ Date: ______________

1. Over the last 2 weeks, how often have you been bothered by any of the following problems?

<table>
<thead>
<tr>
<th>Problem</th>
<th>Not at all (0)</th>
<th>Several days (1)</th>
<th>More than half the days (2)</th>
<th>Nearly every day (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Little interest or pleasure in doing things.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>b. Feeling down, depressed, or hopeless.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>c. Trouble falling/staying asleep, sleeping too much.</td>
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<td>☐</td>
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<td>d. Feeling tired or having little energy.</td>
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<td>☐</td>
<td>☐</td>
<td>☐</td>
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<td>e. Poor appetite or overeating.</td>
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<td>f. Feeling bad about yourself, or that you are a failure, or have let yourself or your family down.</td>
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<td>☐</td>
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<td>g. Trouble concentrating on things, such as reading the newspaper or watching TV.</td>
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<td>h. Moving or speaking so slowly that other people could have noticed. Or the opposite; being so fidgety or restless that you have been moving around more than usual.</td>
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<td>☐</td>
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<td>☐</td>
<td>☐</td>
</tr>
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</table>

2. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not difficult at all  ☐ Somewhat difficult  ☐ Very difficult  ☐ Extremely difficult

TOTAL SCORE ____________
Instructions – How to Score the PHQ-9

Major depressive disorder is suggested if:

- Of the 9 items, 5 or more are checked as at least ‘more than half the days’
- Either item a. or b. is positive, that is, at least ‘more than half the days’

Other depressive syndrome is suggested if:

- Of the 9 items, a., b. or c. is checked as at least ‘more than half the days’
- Either item a. or b. is positive, that is, at least ‘more than half the days’

Also, PHQ-9 scores can be used to plan and monitor treatment. To score the instrument, tally each response by the number value under the answer headings, (not at all=0, several days=1, more than half the days=2, and nearly every day=3). Add the numbers together to total the score on the bottom of the questionnaire. Interpret the score by using the guide listed below.

Guide for Interpreting PHQ-9 Scores

<table>
<thead>
<tr>
<th>Score</th>
<th>Recommended Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>Normal range or full remission. The score suggests the patient may not need depression treatment.</td>
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<tr>
<td>5-9</td>
<td>Minimal depressive symptoms. Support, educate, call if worse, return in 1 month.</td>
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<tr>
<td>10-14</td>
<td>Major depression, mild severity. Use clinical judgment about treatment, based on patient’s duration of symptoms and functional impairment. Treat with antidepressant or psychotherapy.</td>
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<td>15-19</td>
<td>Major depression, moderate severity. Warrants treatment for depression, using antidepressant, psychotherapy or a combination of treatment.</td>
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<td>Major depression, severe severity. Warrants treatment with antidepressant and psychotherapy, especially if not improved on monotherapy; follow frequently.</td>
</tr>
</tbody>
</table>

(UBC Mood, n.d.)
Appendix B

Generalized Anxiety Disorder (GAD-7)

GAD-7 stands for "generalized anxiety disorder" and the 7 questions in the tool. Choose one answer for each of the 7 questions below:

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Feeling nervous, anxious or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Worrying too much about different things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Trouble relaxing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Being so restless that it’s hard to sit still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Becoming easily annoyed or irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Feeling afraid, as if something awful might happen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Add up your results for each column

Total score (add column totals together)

What your total score means

- Your total score is a guide to how severe your anxiety disorder may be:
  - 0 to 4 = mild anxiety
  - 5 to 9 = moderate anxiety
  - 10 to 14 = moderately severe anxiety
  - 15 to 21 = severe anxiety

If your score is 10 or higher, or if you feel that anxiety is affecting your daily life, call your doctor.

(Healthlink BC, 2015)
Appendix C

British Columbia Nurse Practitioner Guidelines

Polycystic Ovary Syndrome:
Diagnosis and Management in the Adult Patient

Effective Date: April 2016

Scope
This guideline provides recommendations for the primary care Nurse Practitioner to assist in diagnosis and long-term management of Polycystic Ovary Syndrome (PCOS) in adult women ≥ 19 years of age.

Key Recommendations
• PCOS is a multifaceted disease with multiple long-term cardiovascular and metabolic risk factors. Management guidelines focus on decreasing risk factors and screening for presence of associated comorbidities.
• Diagnosis of PCOS is based on the Rotterdam criteria.
• Multidisciplinary management between specialists and the primary care NP will optimize care of women with PCOS.
• Women with PCOS should be encouraged to see their primary care provider every 2 years or every 1 year if at high risk for cardiovascular or metabolic disease

Definition
Polycystic ovary syndrome is a multifaceted disease with a wide range of clinical presentations, various different diagnostic criteria, and multiple long-term metabolic and cardiovascular complications (Fauser et al., 2012).

Pathophysiology
The cause of PCOS is complex and multifactorial and even after much investigation into the pathogenesis, the cause is still relatively unclear. In addition to the numerous genes that are identified to be correlated with PCOS, there is growing evidence to suggest that particular environmental factors such as low socio-economic status, smoking, poor diet, and lack of exercise also contribute to the development of the syndrome (Barthelmess & Naz, 2015).

Detection
Clinical investigations for the presence of polycystic ovary syndrome would begin after a patient presents with symptoms such as clinical hyperandrogenism, oligomenorrhea or amenorrhea, or infertility.
**Diagnosis**

Polycystic ovary syndrome is usually detected during the early reproductive years due to presenting complaints such as menstrual irregularity, clinical hyperandrogenism, or infertility (Fauser et al., 2012). It is not within the NP scope in BC to diagnose PCOS, however, NPs can assist in the initial diagnostic workup to help rule in, or rule out other causes of the presenting complaint.

Diagnosis is based on the Rotterdam criteria:
- Patient must have 2 of the 3 following (and exclusion of other etiologies):
  1. Oligo-ovulation or chronic anovulation
  2. Clinical and/or biochemical signs of hyperandrogenism
  3. Polycystic ovaries

**Initial Diagnostic Workup**

Ruling out other etiologies that could be producing PCOS-like symptoms, is essential prior to diagnosis of PCOS. Table 2 outlines other etiologies and diagnostic workup to rule in or rule out these potential diagnoses.

In addition to the laboratory tests in Table 2, a pelvic ultrasound would be indicated to rule in PCOS if diagnosis cannot be made based on the presence of menstrual irregularity and hyperandrogenism (Fauser et al. 2012).
- Transvaginal ultrasound is preferred
- Transabdominal ultrasound is recommended for adolescents who have not yet become sexually active

### Table 1

<table>
<thead>
<tr>
<th>Presenting Complaint</th>
<th>Diagnosis to Consider</th>
<th>Laboratory test</th>
<th>Expected abnormal result if condition present</th>
<th>Normal range* (adult female)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amenorrhea/Oligomenorrhea</td>
<td>Pregnancy</td>
<td>serum beta-hCG</td>
<td>&gt;5 IU/L</td>
<td>&lt;5 IU/L</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>TSH</td>
<td>&lt;0.27 mU/L</td>
<td>&lt;0.27-4.2 mU/L</td>
<td></td>
</tr>
<tr>
<td>Hyperprolactinemia Ovarian insufficiency</td>
<td>(then if indicated, free T4)</td>
<td>&gt;20.0 mU/L</td>
<td>10.5-20.0 mU/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prolactin</td>
<td>&gt;25.0 ug/L</td>
<td>&lt;25.0 ug/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FSH (would be in post menopausal range)</td>
<td>&gt;20.0 IU/L</td>
<td>20.0-135 IU/L</td>
<td></td>
</tr>
<tr>
<td>Hirsutism</td>
<td>Nonclassic congenital adrenal hyperplasia (NCAH)</td>
<td>follicular phase 17 OHP</td>
<td>&gt;6 nmol/L</td>
<td>0.3-4.0 nmol/L</td>
</tr>
<tr>
<td></td>
<td>Cushing’s syndrome Adrenal tumor</td>
<td>24 hour urine cortisol dehydroepiandrosterone sulfate (DHEA-S)</td>
<td>&gt;660 nmol/d</td>
<td>30-220 nmol/d</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;13.6 umol/L</td>
<td>&lt;10.8 umol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Androgen-secreting tumor Ovarian hyperthecosis</td>
<td>total testosterone</td>
<td>&gt;5.2 nmol/L</td>
<td>&lt;1.8 nmol/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total testosterone</td>
<td>&gt;5.2 nmol/L</td>
<td>&lt;1.8 nmol/L</td>
</tr>
</tbody>
</table>

*Normal ranges obtained from: (Lifelabs Clinical Laboratories, 2015)
Management Guidelines for Initial Workup and Long-Term Screening

Metabolic Risk: PCOS is associated with increase risk for insulin resistance, metabolic syndrome, and Type 2 diabetes mellitus.

5. Screening for IR with a 2-hr 75g OGTT is recommended in women with PCOS at onset of diagnosis and every two years thereafter.

6. Screening with a 2-hr 75g OGTT should be performed every year if the patient possesses the following risk factors (Ekoé, Punthakee, Ransom, Prebtani, & Goldenberg, 2013; Jean Hailes for Women’s Health, 2015):
   - PCOS presentation: hyperandrogenism with anovulation
   - Acanthosis nigricans
   - Obesity (BMI > 25 kg/m²)
   - Ethnicity: Aboriginal, Hispanic, South Asian, Asian, or African descent
   - Parental history of diabetes
   - History of high blood glucose levels
   - Physical inactivity


8. If not being followed by endocrinology already, the patient should be referred to endocrinology at onset of diagnosis of diabetes.

Cardiovascular Disease Risk: PCOS is associated with higher cardiovascular disease risk

7. Screening for CVD should be performed every 2 years (Jean Hailes for Women’s Health, 2015).

8. If risk factors present, screening should be performed every 1 year (Jean Hailes for Women’s Health, 2015).

9. Screening includes monitoring for the presence of CVD risk factors and entails assessing:
   - Waist circumference: target < 88cm (Goldenberg & Punthakee, 2013)
   - BMI: target < 25 kg/m² (BC Guidelines, 2014)
   - Smoking status: goal is reduction or quitting smoking (BC Guidelines, 2014)
   - Exercise habits: goal is 30 min of moderate to vigorous activity 5-7 days a week (BC Guidelines, 2014)
   - Blood pressure: target < 140/90 or < 130/90 if diabetic (BC Guidelines, 2015a)
   - Lipid profiles: aim is LDL < 3.5 (BC Guidelines, 2014)
   - OGTT: target < 11.0 (Ekoé, et al., 2013)

10. Women with high blood pressure or hyperlipidemia should be treated appropriately by the NP according to BC Guideline recommendations.

11. Counselling for smoking cessation strategies should be provided for women who smoke. Resources to offer include www.quitnow.ca (BC Guidelines, 2014).

12. Referral to a cardiologist should be considered to optimize patient care (Jean Hailes for Women’s Health, 2015).
**Endometrial Cancer Risk:** Management goals are based upon reducing risk factors and preventing the development of endometrial cancer.

5. Women with PCOS should have a menstrual bleed at least 4 times every year (Chittenden, 2009).
6. First line treatment for amenorrhea in order to reduce the risk of endometrial cancer includes lifestyle management such as diet and exercise with goal weight loss of 5-10% body weight (Klein, 2013).
7. Pharmacologic treatments include initiation of low-dose combination oral contraceptives to regulate hormone levels (Jean Hailes for Women’s Health, 2015).
8. Referral to gynecology should be considered in women with persistent oligomenorrhea or amenorrhea who are not menstruating at least 4 times per year.

**Obesity:** Severity of PCOS symptoms is strongly correlated with increasing levels of obesity. Higher rates of obesity are seen in women with PCOS compared to control groups.

9. Weight, height, BMI calculation, and waist circumference should be obtained at each annual or biennial visit.
10. Target waist circumference is <88cm and target BMI is <25 kg/m², see Table 2 (BC Guidelines, 2011).
11. In the overweight or obese population, the NP should provide adequate diet and exercise counselling regarding lifestyle measures to reduce obesity and increase exercise habits. The NP should stress that even a 5% reduction in weight assists in return of menstruation and an improvement of symptoms of hyperandrogenemia.
12. Obesity class 1: Lifestyle management is recommended
13. Obesity class 2 or 3, or women with comorbidities such as type 2 diabetes, hypertension, CVD, osteoarthritis, dyslipidemia, and sleep apnea: more intensive interventions such as lifestyle management in combination with pharmacologic or surgical interventions is recommended.
14. Strategies for non-pharmacologic weight reduction include:
   a. Caloric restriction of 500-1000kcal/day
   b. Physical activity: 30+ minutes of moderate to vigorous physical activity 5-7 times per week
   c. No more than 0.5-1kg/week weight loss
   d. Establishing initial weight loss goal of 5-10% of body weight
   e. Referral to weight loss program and support groups
15. Pharmacologic therapy for obesity class 2 and 3 after diet, exercise, and behavioural programs have failed: orlistat (Xenical)
16. Referral to surgeon for gastric bypass surgery if unable to obtain or maintain weight reduction strategies
Table 2: BMI Ranges

<table>
<thead>
<tr>
<th>Weight Classification</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5-24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25-29.9</td>
</tr>
<tr>
<td>Obese: Class 1</td>
<td>30-34.9</td>
</tr>
<tr>
<td>Obese: Class 2</td>
<td>35-39.9</td>
</tr>
<tr>
<td>Obese: Class 3</td>
<td>≥ 40</td>
</tr>
</tbody>
</table>

(adapted from BC Guidelines, 2011)

**Mental Health:** Women with PCOS experience higher rates of anxiety, depression, and emotional distress compared to control groups.

5. NPs should have discussions with their patients regarding moods and quality of life and screen for the presence of emotional distress with every annual or biennial visit.

6. Women with PCOS should be screened for emotional distress with the following two questions (BC Guidelines, 2013):
   - In the past month:
     - III. Have you lost interest or pleasure in things you usually like to do?
     - IV. Have you felt sad, low, down, depressed or hopeless?

7. If a woman answers yes to either question, further screening is recommended with the PHQ-9 (Appendix A) or the GAD-7 questionnaire (Appendix B).

8. NPs should refer to the BC Guideline for full management guidelines: http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/depression_full_guideline.pdf

**Infertility:** Many women with PCOS experience infertility; however, infertility rates decrease with weight loss and lifestyle management.

5. Lifestyle management for weight loss is first line treatment for infertility in obese women with PCOS and should be trialed for 3-6 months prior to discussions and interventions for ovulation induction (Jean Hailes for Women’s Health, 2015).

6. Counselling should include discussion regarding avoiding factors that may contribute to infertility such as: smoking, excessive alcohol use, and ensuring the couple is engaging in intercourse at least 1-2 days around the time of ovulation.

7. Diagnostic laboratory workup for infertility by the NP includes: FSH, LH, progesterone, estradiol, prolactin, and TSH (Lindsay & Vitrikas, 2015).

8. Referral to an infertility specialist should occur after lifestyle interventions for weight loss have been attempted for 3-6 months and pregnancy has not been successful (Jean Hailes for Women’s Health, 2015).

**Dermatology:** PCOS is associated with multiple dermatological manifestations including hirsutism, acne, and alopecia.

5. Interventions for clinical hyperandrogenemia focus on reducing steroid production from the ovaries, thus reducing bioavailability.
6. Oral contraceptive pills are commonly used for clinical hyperandrogynism, either alone, or in combination with an antiandrogen such as spironolactone (Fauser et al., 2012).

7. Laser therapy is an effective measure for elimination of unwanted body hair but is expensive and time-consuming. It can be recommended to patients if cost is not a factor (Bode, Seehusen, & Baird, 2012).

8. Acne management includes assessment and determination of type and severity of acne. First line treatment options include combination estrogen and progesterone oral contraceptive pills, or topical retinoid, either alone, or in combination with a topical antibiotic (Titus & Hodge, 2012).
References


# Appendix A

## Patient Health Questionnaire (PHQ-9)

Patient name: _______________________________ Date: __________________

1. Over the last 2 weeks, how often have you been bothered by any of the following problems?

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<tr>
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<td>☐</td>
<td>☐</td>
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</tr>
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2. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not difficult at all  ☐ Somewhat difficult  ☐ Very difficult  ☐ Extremely difficult

**TOTAL SCORE ____________________**
Instructions – How to Score the PHQ-9

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- Of the 9 items, 5 or more are checked as at least ‘more than half the days’
- Either item a. or b. is positive, that is, at least ‘more than half the days’

Other depressive syndrome is suggested if:

- Of the 9 items, a., b. or c. is checked as at least ‘more than half the days’
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<td>Major depression, mild severity. Use clinical judgment about treatment, based on patient’s duration of symptoms and functional impairment. Treat with antidepressant or psychotherapy.</td>
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<td>Major depression, moderate severity. Warrants treatment for depression, using antidepressant, psychotherapy or a combination of treatment.</td>
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</tr>
</tbody>
</table>

(UBC Mood, n.d.)
Appendix B

Generalized Anxiety Disorder (GAD-7)

GAD-7 stands for "generalized anxiety disorder" and the 7 questions in the tool. Choose one answer for each of the 7 questions below:

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Feeling nervous, anxious or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Worrying too much about different things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Trouble relaxing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Being so restless that it's hard to sit still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Becoming easily annoyed or irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Feeling afraid, as if something awful might happen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Add up your results for each column

Total score (add column totals together)

What your total score means

- Your total score is a guide to how severe your anxiety disorder may be:
- 0 to 4 = mild anxiety
- 5 to 9 = moderate anxiety
- 10 to 14 = moderately severe anxiety
- 15 to 21 = severe anxiety

If your score is 10 or higher, or if you feel that anxiety is affecting your daily life, call your doctor.

(Healthlink BC, 2015)