

APPENDIX

TABLE V: Evaluation of Generated Answers for PCOS-Related Questions

Question	Generated Answer	Reference Answer	B2S	RS	FS	BS	CS	H
What is Polycystic Ovary Syndrome (PCOS)?	The Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder characterized by multiple cysts in the ovaries, elevated levels of androgens, and insulin resistance. It affects approximately 1% of women worldwide and is more common in women of African descent. The exact cause	Polycystic Ovary Syndrome (PCOS) is a hormonal and metabolic disorder that affects women of reproductive age and is diagnosed using the Rotterdam Criteria (2003), which require the presence of at least two out of the following three features: hyperandrogenism (or clinical signs such as hirsutism and androgenic alopecia), ovulatory dysfunction (irregular or absent menstruation), and polycystic ovaries seen on ultrasound (with at least 12 follicles or ovary volume >10 cm ³). PCOS is associated with a range of systemic manifestations, including insulin resistance, obesity, and increased risk of type 2 diabetes, indicating that ovarian dysfunction is often a consequence of broader metabolic disturbances.	0.082	0.221	0.317	0.403	0.903	G
How is PCOS diagnosed in adults?	PCOS is a syndrome characterized by the presence of multiple clinical manifestations, including menstrual irregularities, acne, hirsutism, and weight gain. These symptoms are thought to result from abnormalities in the hypothalamic-pituitary-gonadal axis, which leads to elevated levels of androgens (testosterone, estradiol, and progesterone) in women. The diagnosis of PCOS requires the identification of at least two of these symptoms, along with other relevant clinical and laboratory findings. The Rotterdam criteria are the most widely accepted criteria for managing PCOS, but they are not widely available in Canadian laboratories. The AES defines PCOS as a syndrome characterized by the presence of multiple clinical manifestations, including menstrual irregularities, acne, hirsutism, and weight gain, resulting from abnormalities in the hypothalamic-pituitary-gonadal axis.	The diagnosis of PCOS in adults is based on the Rotterdam criteria, which requires at least two of the following three features to be present, after excluding other conditions: Oligo- and/or anovulation (meaning infrequent or absent ovulation, leading to irregular periods); Clinical and/or biochemical signs of hyperandrogenism; Polycystic ovaries as seen on an ultrasound.	0.115	0.157	0.333	0.301	0.838	G

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What is the connection between insulin resistance and PCOS?	The connection between insulin resistance and polycystic ovary syndrome (PCOS) is similar to that observed in non-insulin-dependent diabetes mellitus (NIDDM). Insulin resistance is associated with an increased prevalence of obesity, and women with upper, rather than lower, body obesity have an increased frequency of hyperandrogenism. In PCOS, muscle mass is increased, and potential androgen-mediated changes in lean body mass must also be controlled for in order to explain the association of insulin resistance and PCOS. Studies in which body composition, assessed by hydrostatic weighing, has been matched to normal control women, and in which lean PCOS women, who had body composition and waist to hip girth ratios similar to controls, were studied, have confirmed that PCOS women are insulin resistant, independent of those potentially confounding parameters. Hyperandrogenism is implicated in insulin resistance in PCOS, and studies in cultured cells have confirmed the impression from these in vivo studies that an intrinsic defect in insulin action is present in PCOS. However, studies in PCOS have shown that obesity and PCOS are not synonymous, and that the ED value of insulin for suppression of hepatic glucose production is significantly increased only in obese PCOS women. This synergistic negative effect of obesity and PCOS on hepatic glucose production is an important factor in the pathogenesis of glucose intolerance. Sequential multiple-insulin-dose euglycemic clamp studies have indicated that the ED insulin for glucose uptake is significantly increased, and that maximal rates of glucose disposal are significantly decreased in lean and in obese PCOS women. It appears that body fat has a more pronounced negative effect on insulin sensitivity in women with PCOS, although adipocytes have failed to confirm earlier reports in blood cells of decreases in insulin receptor number and/or receptor affinity in PCOS.	Insulin resistance plays a central role in the pathophysiology of PCOS by disrupting glucose metabolism, increasing androgen production, and contributing to fat accumulation, particularly in visceral areas. Women with PCOS frequently exhibit reduced insulin sensitivity, which not only exacerbates metabolic symptoms such as obesity and dyslipidemia but also increases the risk of developing type 2 diabetes. This metabolic dysfunction is closely linked to menstrual irregularities, anovulation, and infertility, making insulin resistance a core target in PCOS management through dietary, pharmacological, and lifestyle interventions.	0.075	0.127	0.224	0.351	0.811	G
Why is a low glycaemic index (GI) diet often recommended for PCOS?	A low glycaemic index (GI) diet often recommended for PCOS is a high protein, moderate carbohydrate, moderate fat diet.	A low glycaemic index (GI) diet is recommended for women with PCOS because it reduces postprandial blood glucose spikes and insulin demand, which helps to manage insulin resistance—a central feature of PCOS. The study showed that such a diet, rich in whole grains, vegetables, legumes, and lean proteins, led to improved metabolic and hormonal profiles. Additionally, it was effective in increasing the dietary intake and bioavailability of essential water-soluble vitamins that are often deficient in PCOS.	0.035	0.227	0.353	0.407	0.823	G

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Question	Generated Answer	Reference Answer	B2S	RS	FS	BS	CS	H
What is the role of Metformin in managing PCOS?	The role of Metformin in managing PCOS is discussed in the context of the CONTEXT above. Metformin is a low cost, readily available medication that has been extensively used as an insulin sensitizer for over seven decades in DM2 and for several decades in PCOS. Insulin resistance is documented on clamp studies in 75% of lean women and 95% of overweight women, and addressing this has underpinned the use of metformin in PCOS. Metformin is currently widely used by women with PCOS, yet there is variability in recommendations across health professional specialties, with endocrinologists familiar with metformin and more likely to prescribe this therapy. Also the efficacy of metformin in terms of improving clinical outcomes remains uncertain. Mild side effects do cause some concern, and metformin use in PCOS is generally off label. However, metformin is a low cost, readily available medication and off label use in PCOS is allowed in many countries. A multitude of studies have been completed in PCOS for a range of clinical outcomes and synthesis of the literature and recommendations on metformin use was prioritized. Summary of systematic review evidence Metformin versus placebo Twenty RCTs that address outcomes for this comparison were identified, of which 19 RCTs were in adults, and 1 was in adolescents. Weight: When 5 RCTs were combined in meta-analysis, there was no statistically significant difference between metformin and placebo . When three of the studies in those with BMI > 25kg/m2 were subgrouped , metformin was better than placebo. BMI: When 15 RCTs were combined in meta-analysis, and when 11 of the RCTs in those with BMI > 25kg/m2 was subgrouped	Metformin is an insulin-sensitizing medication. In PCOS, it is recommended primarily for the management of metabolic features, such as insulin resistance, and to reduce the risk of type 2 diabetes. It may offer some benefit in improving menstrual regularity but is less effective for this than birth control pills.	0.041	0.118	0.209	0.260	0.801	G
Can inositol supplements help with PCOS symptoms?	Inositol supplements can be helpful for PCOS symptoms, but they should not be used alone. They may improve insulin sensitivity and reduce inflammation, but they do not address the underlying causes of PCOS. Inositol supplements may also interfere with other medications used to treat PCOS, such as antidepressants and antihypertensives. Therefore, it's essential to discuss the potential benefits and risks of inositol supplements with your healthcare provider before starting any new treatment regimen.	Yes, inositol, particularly myo-inositol, is an effective treatment for PCOS. The study confirmed that inositol improves insulin sensitivity, restores ovulatory function, and regulates the menstrual cycle. It also reduces the risk of cardiovascular complications and does so without the gastrointestinal side effects associated with metformin. When combined with folate, inositol has shown even greater benefits in metabolic and reproductive outcomes.	0.110	0.207	0.270	0.416	0.803	G

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Does having PCOS automatically mean I will be infertile?	Yes, women with PCOS are at an increased risk of GDM, preterm birth, pre-eclampsia, miscarriage, still birth, longer time to conception, poor embryo development, reduced embryo implantation rates, ovarian hyper stimulation syndrome (OHSS) and ectopic pregnancy. International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2018 101 CONTENTS Chapter Five	No, a diagnosis of PCOS does not automatically mean you will be infertile, but it is a leading cause of infertility in women. The hormonal imbalances in PCOS disrupt regular ovulation, making it difficult to conceive naturally. However, many women with PCOS are able to get pregnant, either on their own or with the help of lifestyle changes and fertility treatments.	0.098	0.121	0.192	0.257	0.674	PG
How does myo-inositol help with fertility in PCOS?	Myo-inositol helps with fertility in PCOS by improving insulin sensitivity, which can lead to better glucose control and improved ovulation. It also helps to reduce inflammation and oxidative stress, which can improve fertility outcomes. Additionally, myo-inositol may have anti-inflammatory effects that could help reduce symptoms of PCOS such as acne and hair loss. However, more research is needed to fully understand the potential benefits and risks of myo-inositol in PCOS.	Myo-inositol is emerging as an effective and well-tolerated alternative to metformin in the treatment of PCOS. It improves insulin sensitivity, restores ovulation, and helps regulate the menstrual cycle without the gastrointestinal side effects often associated with metformin. When combined with folate, myo-inositol also supports homocysteine regulation and improves reproductive and metabolic outcomes. Its use has shown significant promise in clinical studies, making it a preferred supplement for women seeking natural management options for PCOS.	0.183	0.199	0.336	0.500	0.780	G
How does PCOS affect a person's mental and emotional well-being?	The article discusses the impact of PCOS on a person's mental and emotional well-being. It highlights the negative effects of social stigma, cultural norms, and individual experiences on the personality of individuals living with PCOS. The article suggests that exploring the socio-cultural perspective on PCOS involves understanding the intricate interplay between cultural norms, societal expectations, and individual experiences.	Women with PCOS are more likely to experience mental health concerns including anxiety, depression, low self-esteem, and poor body image. These symptoms are believed to result from both the physical symptoms of PCOS and the hormonal imbalances that can influence mood and cognition. Psychological support and interventions should be considered as part of PCOS management.	0.115	0.154	0.202	0.357	0.635	PG
Why are body image issues common in women with PCOS?	The most effective tool/method to assess body image distress in women with PCOS is the Multidimensional Body-Self Relations Questionnaire (MBSRQ). This questionnaire assesses body dissatisfaction, disordered eating, body size estimation, and weight. It is easy to use and widely applicable.	Body image issues are common in PCOS due to visible symptoms like acne, hirsutism, obesity, and hair loss. These features can negatively impact self-confidence and social functioning. Coupled with societal expectations, women with PCOS may be more prone to emotional distress. Addressing these issues through counseling and patient education is important.	0.142	0.170	0.289	0.334	0.725	PG

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Should women with PCOS be checked for depression and anxiety?	Yes, women with PCOS should be checked for depression and anxiety. Women with PCOS are at increased risk of depression and anxiety, and these clinical questions were prioritized due to their high prevalence and severity. The evidence suggests that depression and anxiety symptoms are more common in PCOS and increase with increasing BMI, duration of menstrual cycle, and hormone levels. Depression: Depressive symptoms and depression are more common in PCOS, with daily fatigue, sleep disturbances, and diminished interest prominent . A meta-analysis of 10 studies reported increased depressive symptom scores in 44% with PCOS versus 17% in controls (OR: 4.03, 95% CI: 2.96-5.5, p<0.01) . A meta-analysis of 910 women with PCOS and 1347 controls reported higher depressive symptom scores in PCOS , although these may not have been clinically significant. A meta-analysis of 26 studies including 4716 participants from 14 countries , noted scores were not in a clinically significant range in half of studies, and others were consistent with mild depression. A meta-analysis of 91 studies with PCOS and 13	Yes, routine screening for depression and anxiety is recommended in women with PCOS, given their higher prevalence in this population. Psychological comorbidities significantly affect quality of life and treatment adherence. Mental health assessments should be incorporated into routine care.	0.068	0.120	0.245	0.324	0.876	G
What are the common metabolic issues associated with PCOS?	The prevalence of impaired glucose tolerance (IGT) and DM2 is further increased in women with PCOS with excess weight, especially in high-risk ethnic groups.	Women with PCOS often present with metabolic abnormalities including insulin resistance, disordered carbohydrate metabolism, and increased fat accumulation, particularly around internal organs. These disturbances contribute to the development of obesity and are linked with conditions such as non-alcoholic fatty liver disease (NAFLD) and dyslipidemia. Additionally, the metabolic dysfunction in PCOS increases the risk for type 2 diabetes and cardiovascular complications, further complicating its management and making metabolic correction a key therapeutic goal.	0.034	0.122	0.286	0.357	0.743	PG

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Why is niacinamide recommended in PCOS?	Niacinamide is recommended in PCOS due to its efficacy in reducing symptoms such as acne, hair loss, and infertility. It is also effective in improving insulin resistance, reducing inflammation, and promoting healthy cholesterol levels. However, niacinamide is not recommended for long-term use due to potential side effects such as skin irritation, headaches, and gastrointestinal distress.	Niacinamide, a form of vitamin B3, is recommended in PCOS due to its role in lipid metabolism, antioxidant defense, and reduction of cardiovascular risk. The study found that supplementation with niacinamide can help lower the activity of LpPLA2, reduce triglycerides, and improve HDL cholesterol, all of which are commonly disrupted in PCOS. Additionally, niacinamide and its metabolites support ovarian function and help reduce hyperandrogenism by modulating pathways affected by oxidative stress and inflammation.	0.177	0.233	0.255	0.483	0.758	G
How does PCOS change after menopause?	The post-menopausal phenotype of PCOS includes oligo- and/or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovaries by ultrasound. However, these three criteria for diagnosis change naturally with age impacting on phenotype and presenting challenges in diagnosis. Overall, it is acknowledged that there is inadequate evidence of the natural history of PCOS and the concept of whether PCOS resolves and/or persists remains unclear pending better longitudinal studies. Postmenopausal phenotypes of PCOS are poorly defined, with limited longitudinal natural history studies. Uncertainty in assessment and diagnosis at this life stage leads to confusion for health professionals and women on long term health risks and screening recommendations.	PCOS is considered a lifelong condition. Even after menopause, women who had PCOS may continue to have elevated androgen levels. A diagnosis of PCOS can be considered in postmenopausal women if there is a documented long-term history of irregular cycles and hyperandrogenism from their reproductive years.	0.068	0.130	0.235	0.363	0.816	G
Is In-Vitro Fertilization (IVF) a common treatment for PCOS?	Yes, In-vitro Fertilization (IVF) is a common treatment for PCOS.	IVF is generally considered a third-line treatment for anovulatory infertility in women with PCOS. It is usually recommended only after lifestyle interventions and several cycles of ovulation induction have failed, or if there is another reason for infertility, such as blocked fallopian tubes or a male partner's low sperm count.	0.016	0.190	0.262	0.314	0.840	G
Can practicing yoga help with PCOS?	No, practicing yoga does not help with PCOS. Yoga is a complete prescription for PCOS, but it does not cure PCOS. Practicing yoga can help improve overall health and well-being, but it cannot cure PCOS.	Yes, studies suggest that yoga can be a beneficial part of a PCOS management plan. It can help reduce stress and may lead to improvements in weight, hormonal balance, and other PCOS symptoms. Regular practice contributes to an overall healthy lifestyle.	0.148	0.237	0.323	0.453	0.883	G

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Can yoga and meditation help manage PCOS symptoms?	Yes, mindfulness meditation has been shown to improve sleep quality and duration in individuals with PCOS. This is supported by several randomized controlled trials (RCTs) that have evaluated the effectiveness of mindfulness meditation in improving sleep quality and duration in women with PCOS. One RCT conducted by Cawthron Institute (New Zealand) found that mindfulness meditation improved sleep quality	Yes, yoga and meditation can play a supportive role in managing PCOS by reducing stress levels, which in turn can help regulate the hypothalamic-pituitary-adrenal axis. Regular practice has been associated with reduced androgen levels, improved menstrual regularity, better mood, and overall improvement in quality of life.	0.096	0.189	0.337	0.256	0.624	PG
What role does niacinamide play in the cardiovascular health of PCOS patients?	The author suggests that niacinamide plays a role in the cardiovascular health of PCOS patients.	Niacinamide improves lipid metabolism by: Raising HDL. Lowering triglycerides and LDL. Reducing Lp-PLA2 activity, a marker of atherosclerosis. These effects are especially beneficial in PCOS patients, who are at increased risk of cardiovascular disease due to metabolic abnormalities.	0.030	0.185	0.296	0.373	0.781	G
What are the observed benefits of myo-inositol and folic acid supplementation in PCOS?	Yes, the observed benefits of myo-inositol and folic acid supplementation in PCOS are related to improved androgen profiles, including decreased testosterone levels and increased luteinizing hormone (LH) and follicle-stimulating hormone (FSH) concentrations. Additionally, myo-inositol has been shown to improve insulin sensitivity and reduce inflammation, both of which can contribute to PCOS symptoms.	Supplementation with myo-inositol and folic acid has been shown to: Restore menstrual regularity and ovulation. Improve insulin sensitivity. Reduce androgen levels. Lower cardiovascular risks. These benefits are especially pronounced in women over 30 with PCOS.	0.216	0.308	0.488	0.492	0.876	G
What were the main challenges in ensuring dietary compliance in the PCOS-II group?	The main challenge in ensuring dietary compliance in the PCOS-II group was self-reported dietary patterns, particularly a Mediterranean diet pattern.	Only 18 out of 40 PCOS patients proceeded to the post-intervention phase (PCOS-II), selected based on: Verified adherence to dietary recommendations. A minimum weight reduction of 2 kg over 3 months. This highlights the challenge of long-term dietary compliance in clinical populations.	0.064	0.149	0.295	0.369	0.773	G
What is the relationship between homocysteine levels and SHBG in PCOS?	Homocysteine levels are increased in polycystic ovary syndrome, which may be related to insulin resistance, inflammation, and oxidative stress. This can lead to an increase in plasma lipids, including low-density lipoproteins (LDL) and triglycerides, and an increase in lipoprotein subfractions such as apoprotein(a) and immunoreactive relationship to metabolic and endocrine parameters. Metformin has been shown to decrease plasma homocysteine levels in women with PCOS.	Elevated homocysteine levels in women with PCOS are inversely correlated with SHBG (sex hormone-binding globulin) levels. Low SHBG is associated with increased free androgens, exacerbating PCOS symptoms such as hirsutism and infertility.	0.132	0.162	0.353	0.392	0.709	PG

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What are the implications of elevated eicosanoids after dietary intervention in PCOS?	The implications of elevated eicosanoids after dietary intervention in PCOS are that it may lead to improvements in insulin sensitivity, lipid profile, and inflammation markers, which could potentially reduce the risk of cardiovascular disease and type 2 diabetes in women with PCOS. However, further research is needed to confirm these findings and to understand the underlying mechanisms involved.	Increased levels of certain eicosanoids (e.g., prostaglandins) after a reduction diet in PCOS patients were interpreted as markers of amplified repair processes. This indicates that the diet may activate endogenous pathways involved in tissue regeneration and inflammation resolution.	0.092	0.206	0.315	0.372	0.790	G
What was the statistical significance of waist-to-hip ratio differences between PCOS and controls?	The statistical significance of waist-to-hip ratio differences between PCOS and controls was due to muscle being the major site of insulin-mediated glucose use. Resistance in PCOS. PCOS women have an increased prevalence of obesity, and women with upper, as opposed to lower body, obesity have an increased frequency of hyperandrogenism. Since muscle is the major site of insulin-mediated glucose use and androgens can increase muscle	The waist-to-hip ratio (WHR) was significantly higher in PCOS patients (0.92 ± 0.08) compared to controls (0.78 ± 0.03), with a p-value of 1×10^{-6} . This supports the link between abdominal obesity and metabolic disturbances in PCOS.	0.104	0.216	0.366	0.266	0.784	G
How does niacinamide affect ovarian function in PCOS?	The OCP has long been used in PCOS to induce regular cycles, protect the endometrium and treat hyperandrogenism. Mechanisms of action include a significant first-pass hepatic effect, increasing production of hepatic proteins, including sex hormone binding globulin. This reduces free circulating androgen levels, even with low-dose OCPs. This important mechanism of antiandrogenic action does not occur with progestin alone or non-oral oestrogen-containing contraceptive preparations. The OCP also reduces ovarian androgen production. There has been concerning data that the OCP can increase insulin resistance and worsen glucose tolerance. Studies are inadequate and data conflicting, with more research needed; however, consideration should be given to the use of low-dose OCPs in the management of PCOS.	Niacinamide and its metabolite MNAM improve ovarian function by: Enhancing AMPK activity. Reducing hyperandrogenism. Modulating ROS through AOX1. In PCOS rat models, these changes led to better hormonal balance and metabolic health.	0.038	0.067	0.129	0.301	0.642	PG
What was the average daily intake of vitamin C in the PCOS-II group?	The average daily intake of vitamin C in the PCOS-II group was 3 of 10 data collected from the diaries and interviews included the following: quantity, way of Nutrients 2021,13,746 3of10 Themenusweret	After dietary intervention, the PCOS-II group consumed an average of 234.61 mg/day of vitamin C, significantly higher than both the PCOS-I group (68.53 mg/day) and the control group (101.37 mg/day), indicating strong adherence to the antioxidant-rich diet.	0.156	0.247	0.290	0.230	0.871	G
What was the average daily intake of folates in the PCOS-II group?	The average daily intake of folates in the PCOS-II group was 3 of 10 data collected from the diaries and interviews included the following: quantity, way of Nutrients 2021,13,746 3of10 Themenusweretakenon	The PCOS-II group consumed an average of 321.3 µg/day of folates after dietary intervention, which was significantly higher than the PCOS-I group (221.2 µg/day) and slightly higher than the control group (262.8 µg/day), indicating improved dietary adherence.	0.132	0.228	0.305	0.238	0.886	G

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Question	Generated Answer	Reference Answer	B2S	RS	FS	BS	CS	H
What was the vitamin B6 intake in the PCOS-II group compared to controls?	Vitamin B6 intake in the PCOS-II group compared to controls is lower than that in the PCOS-I group and CG group.	Women in the PCOS-II group consumed 2.64 ± 0.78 mg/day of vitamin B6, significantly higher than the control group, which consumed 2.16 ± 0.91 mg/day, showing effective dietary adjustment post-intervention.	0.171	0.271	0.356	0.378	0.818	G
What is the significance of SHBG in PCOS?	The significance of SHBG in PCOS is that it plays a role in regulating hormone levels in women with PCOS. It is believed that SHBG helps maintain normal levels of estrogen and progesterone, which are necessary for normal ovulation and menstruation. Without adequate SHBG levels, estrogen levels can become too high, leading to symptoms such as irregular periods, heavy menstrual bleeding, and weight gain. By reducing SHBG levels, hormonal imbalances caused by PCOS can be addressed, potentially improving overall health outcomes.	SHBG (sex hormone-binding globulin) binds androgens in circulation. In PCOS, low SHBG results in increased free androgens, contributing to symptoms like hirsutism, acne, and menstrual irregularities. High homocysteine is inversely correlated with SHBG levels.	0.103	0.172	0.274	0.475	0.842	G
What are the three most important physiological systems affected by PCOS?	Hyperandrogenism and ultrasound features are the most common symptoms associated with PCOS.	PCOS primarily affects: Reproductive system (irregular cycles, infertility) Metabolic system (insulin resistance, dyslipidemia, NAFLD) Endocrine system (hyperandrogenism, thyroid and pituitary disruptions) These dysfunctions are inter-related, making PCOS a systemic disorder.	0.006	0.190	0.222	0.311	0.660	PG
How do Vitamin B6 and B12 interact in the homocysteine pathway?	Vitamin B6 and B12 interact in the homocysteine pathway by reducing homocysteine levels through the reduction of homocysteine to methionine. This can lead to an increase in folate levels, which can help reduce homocysteine levels further. Additionally, vitamin B6 and B12 can also help regulate homocysteine levels by reducing the production of homocysteine from methionine. However, there is limited evidence to support the use of these supplements for treating polycystic ovary syndrome.	Vitamin B6 assists in transsulfuration, while B12 is needed for remethylation of homocysteine to methionine. Both are essential in maintaining normal homocysteine levels, preventing vascular and reproductive complications in PCOS.	0.143	0.216	0.364	0.511	0.798	G

¹ B2S: BLEU-2 Score, RS: ROUGE-L Score, FS: F1 Score, BS: BERT Score, CS: Cosine Similarity Score, G: Grounded, PG: Partially Grounded, H: Hallucination