**PICO Search Assignment Worksheet Name\_\_\_JUN\_\_MA\_\_\_\_**

A 57 year old female with history of polycystic ovary syndrome was diagnosed with breast cancer. I know that PCOS possibly increases risk of cancer. I was wondering if PCOS can increase the risk of breast cancer of women.

**Search Question:**

Clinical question: Is PCOS a risk factor of breast cancer?

PICO question: Are women with PCOS are at increased risk of breast cancer, compared to those without PCOS?

**Question Type:** What kind of question is this?

**Prevalence** Screening Diagnosis

Prognosis Treatment Harms

I got three systematic review articles and one nationwide population-based retrospective cohort study. If there are not enough systematic review articles, high-quality and large-size-sample cohort and case control studies will be fine since RCT studies are not realistic for this research.

**PICO search terms:**

|  |  |  |  |
| --- | --- | --- | --- |
| **P** | **I** | **C** | **O** |
| women | PCOS | without PCOS | breast cancer |
| females | polycystic ovary syndrome |  | mammary malignancy |
|  |  |  | mammary neoplasm |

**Search tools and strategy used:**

I used PubMed to search for “PCOS + breast cancer” in “systematic review”, and found 62 articles.

I also used Cochrane to search for “PCOS + breast cancer” in “review”, and found 9 article.

I also used ScienceDirect to search for “PCOS + breast cancer” in review articles with open access, and found 132 articles within three years.

Then, I read the titles and abstracts of these articles from the most recent article until I found three most related review articles with full text.

**Results found:**

**Polycystic ovary syndrome and risk of endometrial, ovarian, and breast cancer: a systematic review.**

**Harris HR, Terry KL.**

**Fertil Res Pract. 2016 Dec 5;2:14. doi: 10.1186/s40738-016-0029-2. eCollection 2016. Review.**

**PMID: 28620541**

Abstract:

BACKGROUND:

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder with an estimated prevalence of 4-21% in reproductive aged women. The altered metabolic and hormonal environment among women with PCOS may increase their risk of some types of cancer.

METHODS:

We performed a comprehensive review of the literature using numerous search terms for all studies examining the associations between polycystic ovary syndrome and related characteristics and cancer published in English through October 2016. This review summarizes the epidemiological findings on the associations between PCOS and endometrial, ovarian, and breast cancers and discusses the methodological issues, complexities, and underlying mechanisms of these associations.

RESULTS:

We identified 11 individual studies and 3 meta-analyses on the associations between PCOS and endometrial cancer, 8 studies and 1 meta-analysis for ovarian cancer, and 10 studies and 1 meta-analysis for breast cancer. Multiple studies reported that women with PCOS were at a higher risk for endometrial cancer; however, many did not take into account body mass index (BMI), a strong and well-established risk factor for endometrial cancer. The association with ovarian cancer was less clear, but a potentially increased risk of the borderline serous subtype was reported by two studies. No consistent association between PCOS risk and breast cancer was observed.

CONCLUSION:

The associations between PCOS and endometrial, ovarian, and breast cancer are complex, with the need to consider many methodological issues in future analyses. Larger well-designed studies, or pooled analyses, may help clarify these complex associations.

Key points:

* No consistent association between PCOS risk and breast cancer was observed.

I chose it because it is not old (2016) and it exactly answered my question to show there is no consistent association between PCOS risk and breast cancer. It is a systematic review article, including 2 Registry Cohort studies, 5 Cohort studies, 3 Case-control studies and 1 meta-analysis with sample size from 12 to 4730 on the associations between PCOS and breast cancer.

Link: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5424400/>

**Risk of endometrial, ovarian and breast cancer in women with polycystic ovary syndrome: a systematic review and meta-analysis.**

**Barry JA, Azizia MM, Hardiman PJ.**

**Hum Reprod Update. 2014 Sep-Oct;20(5):748-58. doi: 10.1093/humupd/dmu012. Epub 2014 Mar 30. Review.**

**PMID: 24688118**

Abstract:

BACKGROUND:

Polycystic ovary syndrome (PCOS) is a common condition affecting ∼8% of women. The objective of the present study was to quantify separately the risk of endometrial cancer, ovarian cancer and breast cancer in women with PCOS compared with non-PCOS controls, and quantify separately the risk to women of all ages as well as the risk to premenopausal women.

METHODS:

We conducted a systematic review and meta-analysis of observational studies. Studies were eligible for inclusion if they compared women with PCOS to non-PCOS groups for fatal or non-fatal gynaecological cancers. Studies listed in MEDLINE and EMBASE published up to 7 October 2013 in any language were identified, and relevant papers were also searched by hand. Relevant data (for example, study design, source of control data, diagnostic criteria) were extracted and tabulated.

RESULTS:

From 698 references, 11 studies (5 of endometrial cancer and 3 each of ovarian and breast cancer) met the inclusion criteria for the meta-analysis (919 women with PCOS and 72054 non-PCOS controls). Using the Mantel-Haenszel method, with fixed or random effects model as appropriate, women with PCOS were at a significantly increased risk of endometrial cancer (odds ratio (OR), 2.79; 95% confidence interval (CI), 1.31-5.95, P < 0.008), but the risk of ovarian and breast cancers was not significantly increased (OR, 1.41; 95% CI, 0.93-2.15, P < 0.11 and OR, 0.95; 95% CI, 0.64-1.39, P < 0.78, respectively). However when studies which included women aged over 54 years were excluded from the analysis, the risk for women with PCOS increased further for endometrial cancer (OR, 4.05; 95% CI, 2.42-6.76, P < 0.00001), became significantly increased for ovarian cancer (OR, 2.52; 95% CI, 1.08-5.89, P < 0.03), but remained non-significant for breast cancer (OR, 0.78; 95% CI, 0.46-1.32, P < 0.35).

CONCLUSIONS:

This is the first meta-analysis to examine gynaecological cancers in women with PCOS younger than 54 years of age compared with controls of similar age. Current data suggest that women of all ages with PCOS are at an increased risk of endometrial cancer but the risk of ovarian and breast cancer was not significantly increased overall. These results highlight the potential risk of gynaecological cancer morbidities associated with PCOS. However, the available evidence is far from robust and variation in diagnostic criteria for PCOS, associated risk factors (particularly obesity), and selection bias in the studies may have resulted in an exaggeration of the increased risk. Furthermore, women who have PCOS should also be made aware that any increased risk for endometrial cancer must be judged in the context of its relatively low incidence in the general population. A large well-controlled prospective study is required in order to gain a more accurate estimate of the risk of gynaecological cancers in women with PCOS.

Key points:

* The risk of breast cancers was not significantly increased in women with PCOS (OR, 0.95; 95% CI, 0.64-1.39, P < 0.78)

I chose it because it is not very old (2014) and it demonstrated that the risk of breast cancers was not significantly increased in women with PCOS most relevant that perfectly answered my question. It is the first meta-analysis to examine gynaecological cancers in women with PCOS younger than 54 years of age compared with controls of similar age. It is a systematic review and meta-analysis article, including 1 Cohort studies and 2 Case-control studies with sample size from 332 to 34835.

Link: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4326303/>

**The association between polycystic ovary syndrome and breast cancer: a meta-analysis.**

**Shobeiri F, Jenabi E.**

**Obstet Gynecol Sci. 2016 Sep;59(5):367-72. doi: 10.5468/ogs.2016.59.5.367. Epub 2016 Sep 13.**

**PMID: 27668199**

Abstract:

OBJECTIVE:

The results of epidemiological studies investigated the association between polycystic ovary syndrome (PCOS) and the breast cancer are inconsistent. This meta-analysis was conducted to estimate the association between PCOS and the breast cancer risk. We searched PubMed, Web of Science, and Scopus for observational studies until June 2015. Data were independently extracted and analyzed using 95% odds ratio, and confidence intervals (CIs) based on the random-effects models.

METHODS:

We identified 970 references and conducted eight studies with 45,470 participants and 243,064 person- year.

RESULTS:

The association between PCOS and the breast cancer risk in case-control studies 0.87 (95% CI, 0.44 to 1.31) and that of cohort studies was estimated 1.18 (95% CI, 0.93 to 1.43).

CONCLUSION:

This meta-analysis demonstrated that PCOS no does increase the risk of breast cancer. Further prospective cohort studies are needed to provide convincing evidence in order to PCOS can increase or not effect on the risk of the breast cancer.

Key points:

* The association between PCOS and the breast cancer risk in case-control studies was 0.87.
* The association between PCOS and the breast cancer risk in cohort studies was 1.18.
* PCOS no does increase the risk of breast cancer.

I chose it because it is not old (2016) and it exactly answered my question to show that PCOS no does increase the risk of breast cancer. It is a systematic review and meta-analysis article, including 5 Cohort studies and 3 Case-control studies with sample size from 332 to 228554.

Link: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5028643/>

**A nationwide population-based retrospective cohort study of the risk of uterine, ovarian and breast cancer in women with polycystic ovary syndrome.**

**Shen CC, Yang AC, Hung JH, Hu LY, Tsai SJ.**

**Oncologist. 2015 Jan;20(1):45-9. doi: 10.1634/theoncologist.2014-0311. Epub 2014 Nov 19.**

**PMID: 25410097**

Abstract:

BACKGROUND:

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age. We used a nationwide population-based retrospective cohort study to explore the relationship between PCOS and the subsequent development of gynecological cancers including uterine, breast, or ovarian cancer.

METHODS:

We identified subjects who were diagnosed with PCOS between January 1, 2000, and December 31, 2004, in the Taiwan National Health Insurance (NHI) Research Database. A comparison cohort was constructed for patients without known PCOS who were also matched according to age. All PCOS and control patients were observed until diagnosed with breast cancer, ovarian cancer, or uterine cancer or until death, withdrawal from the NHI system, or December 31, 2009.

RESULTS:

The PCOS cohort consisted of 3,566 patients, and the comparison cohort consisted of 14,264 matched control patients without PCOS. The adjusted hazard ratio (HR) of uterine cancer and breast cancer in subjects with PCOS were higher (HR: 8.42 [95% confidence interval: 1.62-43.89] and HR: 1.99 [95% confidence interval: 1.05-3.77], respectively) than that of the controls during the follow-up. With the Monte Carlo method, only the mean adjusted HR of 1,000 comparisons for developing uterine cancer during the follow-up period was greater for the PCOS group than for the control groups (HR: 4.71, 95% confidence interval: 1.57-14.11).

CONCLUSION:

PCOS might increase the risk of subsequent newly diagnosed uterine cancer. It is critical that further large-scale, well-designed studies be conducted to confirm the association between PCOS and gynecological cancer risk.

Key points:

* The adjusted hazard ratio (HR) of breast cancer in subjects with PCOS were higher (HR: 1.99 [95% confidence interval: 1.05-3.77]) than that of the controls during the follow-up.
* With the Monte Carlo method, the mean adjusted HRs for the development of breast cancer were not higher than that of the control patients (mean adjusted HR: 1.61, 95% CI: 0.91–2.84).

I chose it because it is not old (2015) and it showed that the risk of the development of breast cancer were not higher than that of the control patients that exactly answered my question. It is a nationwide population-based retrospective cohort study with 3,566 patients with PCOS and 14,264 matched control patients without PCOS.

Link: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4294614/>

**What is the clinical “bottom line” and conclusion derived from these articles in answer to your question?**

Question: Are women with PCOS are at increased risk of breast cancer, compared to those without PCOS?

Answer:  The first study showed no consistent association between PCOS risk and breast cancer was observed.

          The second study demonstrated that the risk of breast cancers was not significantly increased in women with PCOS (OR, 0.95; 95% CI, 0.64-1.39, P < 0.78).

          The third study demonstrated that PCOS no does increase the risk of breast cancer. The association between PCOS and the breast cancer risk in case-control studies 0.87 (95% CI, 0.44 to 1.31) and that of cohort studies was estimated 1.18 (95% CI, 0.93 to 1.43).

The fourth study showed the mean adjusted HRs for the development of breast cancer were not higher than that of the control patients (mean adjusted HR: 1.61, 95% CI: 0.91–2.84).

Conclusion: women with PCOS are not at increased risk of breast cancer, compared to those without PCOS.

I weighed the third study highest because it is not old (2016) systematic review and meta-analysis article, including the large size of sample (5 Cohort studies and 3 Case-control studies with sample size from 332 to 228554). Of course, it has limitations, including the limited number of eligible studies and the effects of confounding variables such as hormone therapy, menopausal status and family history of breast cancer, an issue which may lead to selection bias.

I weighed the first study second because it is not old (2016) systematic review article, including many relevant studies (2 Registry Cohort studies, 5 Cohort studies, 3 Case-control studies and 1 meta-analysis with sample size from 12 to 4730). Limitations include variation of PCOS diagnostic criteria, etiologic heterogeneity of cancer subtypes, confounding and mediating factors, menopausal status, and co-morbid conditions.

Third is the second study because it is a not new (2014) systematic review and meta-analysis article, including 1 Cohort studies and 2 Case-control studies with sample size from 332 to 34835. Certain limitations include the heterogeneity due to variation in PCOS phenotypes in different ethnicities, diagnostic criteria for PCOS and cohort sizes. Additionally it was limited by the small number of studies suitable for inclusion and their overall quality.

Last is the fourth study because it is a not new (2015) and it is not a systematic review and meta-analysis article. Certain limitations include no detailed information of potentially confounding factors, such as tobacco use, alcohol consumption, and family history of malignancy diseases, short follow-up period, possible underestimated prevalence due to use of the ICD-9 codes from the database for diagnosis of PCOS, and the diagnoses in NHI claims without verification for scientific purposes.

**Summary of Evidence**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author (Date) | | Level of Evidence | | Sample/Setting  (# of subjects/ studies, cohort definition etc. ) | | Outcome(s) studied | | Key Findings | | Limitations and Biases | |
| Harris HR, Terry KL.  (2016) | | systematic review | | 2 Registry Cohort studies, 5 Cohort studies, 3 Case-control studies and 1 meta-analysis with sample size from 12 to 4730 on the associations between PCOS and breast cancer. | | Breast cancer | | No consistent association between PCOS risk and breast cancer was observed. | | Since high BMI is a common characteristic of PCOS, one cannot exclude the possibility that reported associations may be attributable to a higher BMI in women with PCOS, on average.  Beyond BMI, the adjustment for cancer risk factors varied widely between studies and may also explain differences between studies as some characteristics of PCOS, such as infertility, are risk factors for these cancers. | |
| Barry JA, Azizia MM, Hardiman PJ.  (2014) | | systematic review and meta-analysis | | 1 Cohort studies and 2 Case-control studies with sample size from 332 to 34835. | | Breast cancer | | The risk of breast cancers was not significantly increased in women with PCOS (OR, 0.95; 95% CI, 0.64-1.39, P < 0.78) | | It is possible that variations in diagnostic criteria for PCOS could have introduced selection bias into analysis, and concerns regarding the reliability of PCOS diagnosis are further raised by the prevalence of the syndrome in some of the included studies.  The heterogeneity evident can be summarized as being due to variation in PCOS phenotypes in different ethnicities, diagnostic criteria for PCOS and cohort sizes. | |
| Shobeiri F, Jenabi E.  (2016) | | systematic review and meta-analysis | | 5 Cohort studies and 3 Case-control studies with sample size from 332 to 228554 | | Breast cancer | | The association between PCOS and the breast cancer risk in case-control studies was 0.87.  The association between PCOS and the breast cancer risk in cohort studies was 1.18.  PCOS no does increase the risk of breast cancer. | | Certain limitations to the finding should be considered, the most important of which was the limited number of eligible studies. Second, they attempted to use an adjusted form of OR estimate, while some studies did not report adjusted forms of effect measure, an issue which may result in information bias. Third, they could not assess the effect of confounding variables such as hormone therapy, menopausal status and family history of breast cancer, an issue which may lead to selection bias. Finally, they found 'ONE' study that seemed potentially eligible to be included in this meta-analysis, but they could not access the full text of this study. This issue may raise the possibility of selection bias. | |
| Shen CC, Yang AC, Hung JH, Hu LY, Tsai SJ.  (2015) | | a nationwide population-based retrospective cohort study | | a nationwide population-based retrospective cohort study with 3,566 patients with PCOS and 14,264 matched control patients without PCOS. | | Breast cancer | | The adjusted hazard ratio (HR) of breast cancer in subjects with PCOS were higher (HR: 1.99 [95% confidence interval: 1.05-3.77]) than that of the controls during the follow-up.  With the Monte Carlo method, the mean adjusted HRs for the development of breast cancer were not higher than that of the control patients (mean adjusted HR: 1.61, 95% CI: 0.91–2.84). | | Certain limitations include no detailed information of potentially confounding factors, such as tobacco use, alcohol consumption, and family history of malignancy diseases, short follow-up period, possible underestimated prevalence due to use of the ICD-9 codes from the database for diagnosis of PCOS, and the diagnoses in NHI claims without verification for scientific purposes. | |

Magnitude of any effects:

No associated between PCOS and risk of breast cancer.

Clinical significance:

The current studies do not support that women with PCOS are at increased risk of breast cancer, compared to those without PCOS. So the clinical recommendation is for women with PCOS, the breast cancer screening and prevention should be same as for those without PCOS.

Any other considerations important in weighing this evidence to guide practice?

Further high-quality studies are needed to provide convincing evidence in order to PCOS can increase or not effect on the risk of the breast cancer.