INPLASY PROTOCOL

To cite: Wang et al. Increased risk for subsequent primary lung cancer among female hormone-related cancer patients: a meta-analysis based on over four million cases. Inplasy protocol 202270044. doi: 10.37766/inplasy2022.7.0044

Received: 08 July 2022

Published: 08 July 2022

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Support: **2022nsfsc1464.**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None declared.

Increased risk for subsequent primary lung cancer among female hormone-related cancer patients: a meta-analysis based on over four million cases

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Review question / Objective: **To identify the risk of lung cancer in FHRC patients compared to the general population.**
Condition being studied: **The incidence rate of lung cancer in women is obviously increasing over the past decade and previous evidence have indicated the significant relationship between disturbances in hormone levels and the risk of lung cancer. Therefore, we hypothesized female hormone-related cancer (FHRC), including the breast, endometrial, cervix, and ovary cancer, patients may experience a higher risk of developing subsequent lung cancer.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 July 2022 and was last updated on 08 July 2022 (registration number INPLASY202270044).

INTRODUCTION

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METHODS

Search strategy: The PubMed, EMBASE, Web of Science, and Cochrane Library electronic databases will be searched from the inception to July 10, 2022. “neoplasm”, “carcinoma”, “breast”, “lung”, “pulmonary”, “second primary” and “subsequent primary", "breast carcinoma", "cervical cancer", "cervical carcinoma", "endometrial carcinoma", "endometrial cancer", "ovarian cancer", "ovarian carcinoma", "ovary cancer".

Participant or population: 1) Cohort studies enrolled female patients who were diagnosed with the first primary breast, endometrial,cervix or ovary cancer and examined the risk of subsequent primary lung cancer comparing to the generalfemale population; 2) the standardized incidence ratios (SIRs), defining as the observed number of secondprimary lung cancer in the cohort relative to the expected number of subsequent primary lung cancer cases, together with corresponding 95% confidence interval (CI) were reported; 3) full-text articles were available; 4)in the articles in which the tata were duplicated or significantly overlapped, only the most recent orinformative studies were includedCohort studies enrolled female patients who were diagnosed with the first primary breast, endometrial,cervix or ovary cancer and examined the risk of subsequent primary lung cancer comparing to the generalfemale population; 2) the standardized incidence ratios (SIRs), defining as the observed number of secondprimary lung cancer in the cohort relative to the expected number of subsequent primary lung cancer cases,together with corresponding 95% confidence interval (CI) were reported; 3) full-text articles were available; 4)in the articles in which the tata were duplicated or significantly overlapped, only the most recent orinformative studies were included.

Intervention: Cohort studies enrolled female patients who were diagnosed with the first primary breast, endometrial, cervixor ovary cancer and examined the risk of subsequent primary lung cancer comparing to the general femalepopulation; 2) the standardized incidence ratios (SIRs), defining as the observed number of second primarylung cancer in the cohort relative to the expected number of subsequent primary lung cancer cases, togetherwith corresponding 95% confidence interval (CI) were reported; 3) full-text articles were available; 4) in thearticles in which the tata were duplicated or significantly overlapped, only the most recent or informativestudies were included.

Comparator: General female population.

Study designs to be included: Cohort studies.

Eligibility criteria: (1) female patients were pathologically diagnosed with primary breast, endometrial, cervix or ovary cancer; (2) the incidence rate of lung cancer between FHRC patients and the general population were compared, presenting as the standardized incidence ratio (SIR) and 95% confidence interval (CI); (3) lung cancer was diagnosed pathologically; (4) the SIRs with 95% CIs were reported in articles or enough data were provided to calculate them; (5) the lung cancer incidence rates of whole population in the research area or healthy people were used as controls and at least the age was matched during the calculation of SIRs and 95% CIs; (6) full-texts were available.

Information sources: electronic databases.

Main outcome(s): Standardized incidence ratios (SIRs).

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa scale (NOS) will be applied for the quality assessment and studies with a NOS score of six or higher are defined as high-quality studies. All the literature search, selection, data extraction, and quality assessment will be performed by two authors independently and any disagreement will be resolved by team discussion. Begg’s funnel plot and test will be conducted to detect publication bias. A

P value <0.05 are regarded as statistical difference.

Strategy of data synthesis: All the statistical analyses will be performed by STATA (version 15.0) software. The SIRs and 95% CIs will be combined to determine the risk for subsequent primary lung cancer among FHRC patients compared to the general population. The heterogeneity among included studies will be assessed by I2 statistics and Q tests. If significant heterogeneity are detected presenting as I2 >50% or P<0.1, the random-effects model will be applied; otherwise, the fixed-effects model will be used. Besides, subgroup analysis based on the tumor type, follow-up period, treatment, age, and source of SIR and sensitivity analysis for breast, endometrial, cervix, ovary, and all FHRC patients will be conducted to identify the source of heterogeneity and stability of pooled results in this meta-analysis.

Subgroup analysis: Subgroup analyses will be stratified by the follow-up time, tumor type, and some other parameters will be performed.

Sensitivity analysis: We will address the influence of each study by testing whether, deleting each in turn, will have changed significantly the pooled results of the meta-analysis.

Country(ies) involved: China.

Keywords: female hormone-related cancer; risk; subsequent primary lung cancer; meta-analysis.

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