INPLASY PROTOCOL

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None declared.

Prospective risk of type 2 diabetes in normal weight women with polycystic ovary syndrome

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Review question / Objective: **To investigate the risk for type 2 diabetes (T2D) in normal weight women with PCOS. The following PECOs (Population, Exposure, Comparator and Outcome) were included: Population: Pre- and postmenopausal women. Exposure: PCOS Comparator: Healthy control or background population. Outcome: T2D.**
Condition being studied: **Polycystic ovary syndrome (PCOS) is a common endocrine disorder of reproductive-aged women with a prevalence of 15–20%. Polycystic ovary syndrome (PCOS) is most often defined according to the Rotterdam criteria, which include irregular ovulation, biochemical/clinical hyperandrogenism, and/or polycystic ovaries when other causes are excluded.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 June 2022 and was last updated on 16 June 2022 (registration number INPLASY202260070).

INTRODUCTION

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METHODS

Search strategy: We searched for published studies in PubMed and Embase until April 2022. The terms used in the search were polycystic ovary syndrome, polycystic ovarian syndrome, PCOS, diabetes, T2D, T2DM, NIDDM, and HbA1c. Furthermore, a lateral search was conducted based on reference lists of included articles. Recent meta-analyses regarding PCOS and T2D were hand-searched for potentially eligible articles. Controlled studies were defined as clinical studies with a comparison (control) group. The following PECOs (Population, Exposure, Comparator and Outcome) were included: Population: Pre- and postmenopausal women, Exposure: PCOS, Comparator: Healthy control or background population, Outcome: T2D. Criteria for study selection are further specified below. Inclusion criteria: Publications should include prospective studies on development of T2D in women with PCOS. The definitions of PCOS were by Rotterdam criteria or by National Institute of Health (NIH), according to diagnosis code (ICD-10) or could be self-reported. Study cohorts should include normal weight women with PCOS or cohorts of mixed BMI, where normal weight women with PCOS were investigated separately as a sub-cohort. Studies without a control cohort were allowed, but results of these studies were presented and discussed separately. Study outcome: The primary study outcome was diagnosis of T2D based on WHO criteria using HbA1c or oral glucose tolerance test (OGTT) or alternatively self-reported diagnosis of T2D or diagnosis code on T2D in register based studies. Exclusion criteria: Excluded publications were cross-sectional studies, intervention studies, studies in pregnant women, reviews, and editorials. Studies in cohorts of mixed BMI were excluded if they did not report results in normal weight women separately.

Participant or population: The definitions of PCOS were by Rotterdam criteria or by National Institute of Health (NIH), according to diagnosis code (ICD-10) or could be self-reported. Study cohorts should include normal weight women with PCOS or cohorts of mixed BMI, where normal weight women with PCOS were investigated separately as a sub-cohort.

Intervention: The exposure was PCOS.

Comparator: Healthy controls.

Study designs to be included: Prospective studies were allowed with or without a control group.

Eligibility criteria: Excluded publications were cross-sectional studies, intervention studies, studies in pregnant women, reviews, and editorials. Studies in cohorts of mixed BMI were excluded if they did not report results in normal weight women separately.

Information sources: We searched for published studies in PubMed and Embase until April 2022. Furthermore, a lateral search was conducted based on reference lists of included articles. Recent meta-analyses regarding PCOS and T2D were hand-searched for potentially eligible articles.

Main outcome(s): The primary study outcome was diagnosis of T2D based on WHO criteria using HbA1c or oral glucose tolerance test (OGTT) or alternatively self-reported diagnosis of T2D or diagnosis code on T2D in register based studies.

Additional outcome(s): We applied BMI categories according to WHO, where underweight is defined as BMI ≤ 18.4 kg/m2, normal weight 18.5-24.9 kg/m2, overweight 25-29.9 kg/m2 and obesity ≥ 30 kg/m2. In Asian populations, normal weight was defined as BMI < 23 kg/m2.

Data management: We used Pubmed and Excell for data management.

Quality assessment / Risk of bias analysis: We retrieved information regarding first author, publication year, country of origin, study design, study population (age, ethnicity), PCOS definition, follow up and study results. The method for definition of PCOS was described as clinical evaluation, self reported, diagnosis code. We evaluated method for diagnosis of T2D, based on OGTT, or fasting blood glucose,, ICD-10 diagnosis code, or self-reported.

Strategy of data synthesis: We present a table including first author, publication year, country of origin, study design, study population (age, ethnicity), number of normal weight participants, PCOS definition, follow up duration and main study results.

Subgroup analysis: We investigate predisposing factors for T2D in PCOS including hyperandrogenism, ethnicity, and menstrual cycle.

Sensitivity analysis: In some cases we present data for the full study cohort and for the lean subgroup of participants separately.

Language: English language publications.

Country(ies) involved: Denmark.

Keywords: polycystic ovary syndrome; type 2 diabetes; prospective; review.

Dissemination plans: Systematic review in peer reviewed journal.

Contributions of each author:
Author 1 - Dorte Glintborg - The author contributed to the development of the selection criteria, drafted and finalized manuscript.
Email: d.glintborg@gmail.com
Author 2 - Naja Due Kolster - Litterature search, tables, preliminary draft.
Author 3 - Pernille Ravn - The author contributed to the development of the selection criteria, helped writing of manuscript.
Author 4 - Marianne Skovsager Andersen - The author contributed to the development of the selection criteria, helped writing of manuscript.