

Supplementary Information

TITLE:

Risk of breast cancer among women with polycystic ovary syndrome: a nationwide population-based cohort study

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1. Description of the Danish national registers and Statistics Denmark

The Danish Cancer Institute possesses a project database with current versions of the Danish national registers with pseudo-anonymized data. The database is maintained and hosted at Statistics Denmark. The data used in this study was extracted by our data manager from the following registers:

a. Danish Civil Registration System

Since 1968, all Danish citizens are assigned a unique personal identification number (CPR-number) at birth or immigration and has been registered in the Danish Civil Registration System [1]. The CPR-number from this register allows us to accurately link individual level information from other national registers. The Danish Civil Registration System includes high quality data, which is regularly validated and checked for errors. From this register, we extracted date of birth and death, sex and migrations. Thus, we identified all women born between 1 January 1940 and 31 December 1993, women who died and women who migrated in and out of Denmark in the study period.

b. Danish National Patient Register

This register includes all inpatient records since 1977 and all outpatient records since 1995 [2, 3]. Records include admission dates, discharge dates and outpatient visit dates, and diagnostic and procedural codes. Diagnoses are registered using the International Classification of Diseases, 8th edition (ICD-8 codes) up to 1994, and 10th edition (ICD-10 codes), from 1994 onwards. For this study, PCOS diagnoses were obtained from this register (please see section 2, Table S1 for specific codes used).

c. Danish National Prescription Register

Complete information on type (according to the Anatomical Therapeutic Chemical [ATC] Classification System), quantity and date of dispensing of all prescription drugs dispensed at pharmacies in Denmark since 1995 are recorded in this register [4]. For this study we extracted information on prescriptions for drugs for infertility treatment from this register (please see section 2, Table S2 for specific codes).

d. Danish Cancer Register

The Danish Cancer Register, established in 1943, is a research register and reporting of incident cancer cases is mandatory. [5]. All incident cases of cancer in Denmark are registered using modified ICD-7 codes, until 1978, and ICD-10 codes, from 1978 onwards. Further, since 1987, cancer morphology and topography have also been registered using the International Classification of Diseases for Oncology, third edition (ICD-O-3). This register is regularly checked for consistency and validity. Here we identified all incident cases of breast cancer (please see section 2, Table S3 for specific codes).

e. Statistics Denmark

Statistics Denmark is a central institution which hosts and administers numerous population-based registers. The Integrated Database for Labor Market Research, which holds information on socioeconomic indicators, was used identified the highest achieved level of education for all women in our study [6]. The registers hosted at Statistics Denmark have a high degree of validity and coverage for the population of Denmark and are updated annually.

f. Danish Medical Birth Register

The Danish Medical Birth Register contains information on all livebirths (since 1968) and stillbirths (since 1972) [7]. Parity status of the women in the study population was determined based on this register.

g. In-Vitro Fertilization (IVF) Register

Recording of all IVF treatments carried out at public and private fertility clinics in Denmark is mandatory. The IVF Register contains information on all treatments with IVF, intra-cytoplasmic sperm injection, frozen embryo replacements and egg donations, since 1994. All intra-uterine inseminations have also been recorded since 2006 [8]. Women with a record in this register were identified as women treated for infertility in our study.

2. Codes used in the study to extract information from the Danish national registers.

Table S1. Codes used for diagnoses from the Danish National Patient Register, 1977–2018.

Diagnoses	Codes
<i>ICD-8 codes (1977–1993)</i>	
Polycystic ovarian syndrome	25690
Obesity	27799
Diabetes mellitus type II	250*
<i>ICD-10 codes (from 1994)</i>	
Polycystic ovarian syndrome	E282A, E282C
Obesity	E65*, E66*
Diabetes mellitus type II	E11*, E13*, E14*

Abbreviations: ICD-8, International Classification of Diseases, 8th edition; ICD-10, International Classification of Diseases, 10th edition

*Includes all subcodes

Table S2. Codes used for cancer diagnoses in The Danish Cancer Register, 1977–2018.

<i>Type of cancer</i>	<i>Codes</i>
<i>ICD-7 codes</i>	
Breast cancer	1700-1705
<i>ICD-10 codes</i>	
Breast cancer	C50*
<i>ICD-O-3 codes</i>	
Ductal breast cancer	85003, 80223, 85013, 85213, 85413, 85403, 85103, 82113, 80103, 80123, 80133, 80203, 80213, 80323, 80463, 80503, 81403, 81413, 82303, 82463
Lobular breast cancer	85203, 84903, 80373
Mucinous breast cancer	84803, 84813
Other/unspecified breast cancer	All other codes†

Abbreviations: ICD-7, International Classification of Diseases, 7th edition; ICD-10, International Classification of Diseases, 10th edition, ICD-O-3, International Classification of Diseases for Oncology, 3rd edition

*Includes all subcodes

†Only invasive cancers (ie, with “3” as the last digit)

Table S3. Codes used for drugs in the Danish National Prescription Register, 1995–2018.

<i>Type of drug</i>	<i>ATC codes</i>
Hormonal contraceptives	G02BA03, G02BB01, G03AA01, G03AA03, G03AA05, G03AA0, G03AA09, G03AA10, G03AA11, G03AA12, G03AA13, G03AA14, G03AB03, G03AB04, G03AB05, G03AB06, G03AB08, G03AC01, G03AC02, G03AC03, G03AC06, G03AC08, G03AC09, G03HB01
IVF/ICSI drugs	H01CA*, H01CC*, G03G*, G03XA, L02AE*, N04BC01

Abbreviations: ATC, Anatomical Therapeutic Chemical; ICSI, intracytoplasmic sperm injection, IVF, in-vitro fertilization

*Includes all subcodes

3. References

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