Preconception indicators and associations with health outcomes reported in UK routine primary care data: a systematic review

Danielle Schoenaker, PhD
Senior Research Fellow
School of Human Development and Health, Faculty of Medicine, University of Southampton, Southampton, UK
MRC Lifecourse Epidemiology Centre, University of Southampton, Southampton, UK
NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK

Elizabeth M Lovegrove, BSc, BMBS, MRCGP
GP and NIHR In Practice Fellow
Primary Care Research Centre, Faculty of Medicine, University of Southampton, Southampton, UK

Emma H Cassinelli, BSc, MRes
PhD candidate
Centre for Public Health, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, UK

Jennifer Hall, PhD, FFPH, MBChB
Clinical Associate Professor
Institute for Women's Health, University College London, London, UK

Majel McGranahan, MBChB, MPH, MFPH
MRC Clinical Research Fellow
Warwick Medical School, University of Warwick, Coventry, UK

Laura McGowan, PhD
Lecturer in Nutrition and Behaviour Change
Centre for Public Health, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, UK

Helen Carr, MBBS, MRCGP, MSc
GP
NHS Surrey Heartlands, UK

Nisreen A Alwan, FFPH, PhD
Professor of Public Health
School of Primary Care, Population Sciences and Medical Education, Faculty of Medicine, University of Southampton, Southampton, UK
NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK
NIHR Applied Research Collaboration Wessex, Southampton, UK

Judith Stephenson, MD, FPH
Professor of Sexual and Reproductive Health
Institute for Women's Health, University College London, London, UK

Keith M Godfrey, FMedSci
Professor of Epidemiology and Human Development
School of Human Development and Health, Faculty of Medicine, University of Southampton, Southampton, UK
MRC Lifecourse Epidemiology Centre, University of Southampton, Southampton, UK
NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK

Correspondence to
Danielle Schoenaker
University of Southampton
MRC Lifecourse Epidemiology Centre
Tremona Road, Southampton SO16 6YD, UK
D.Schoenaker@soton.ac.uk
https://orcid.org/0000-0002-7652-990X

Word count: 2,514 words, 4 Tables, 1 Figure, 1 Box.

Abstract

Background: Routine primary care data may be a valuable resource for preconception health research and informing provision of preconception care.

Aim: To review how primary care data could provide information on the prevalence of preconception indicators and examine associations with maternal and offspring health outcomes.

Design and Setting: Systematic review of observational studies using UK routine primary care data.

Method: Literature searches were conducted in five databases (March 2023) to identify observational studies that used national primary care data from individuals aged 15-49 years. Preconception indicators were defined as medical, behavioural and social factors that may impact future pregnancies. Health outcomes included those that may occur during and after pregnancy. Screening, data extraction and quality assessment were conducted by two reviewers.

Results: From 5,259 records screened, 42 articles were included. The prevalence of 30 preconception indicators was described for female patients, ranging from 0.01% for sickle cell disease to >20% for each of advanced maternal age, previous caesarean section (among those with a recorded pregnancy), overweight, obesity, smoking, depression and anxiety (irrespective of pregnancy). Few studies reported indicators for male patients (n=3) or associations with outcomes (n=5). Most studies had low risk of bias, but missing data may limit generalisability.

Conclusion: Findings demonstrate that routinely collected UK primary care data can be used to identify patients' preconception care needs. Linking primary care data with health outcomes collected in other datasets is underutilised but could help quantify how optimising preconception health and care can reduce adverse outcomes for mothers and children.

Keywords: general practice; preconception care; pregnancy outcomes; pre-pregnancy care; primary care.

How this fits in:

- Provision of preconception care is not currently embedded into routine clinical practice but may be informed by routinely collected primary care data.
- This systematic review demonstrates that UK primary care data can provide information on the prevalence of a range of medical, behavioural and social factors among female patients of reproductive age, while limited research has examined male preconception health or associations with maternal and offspring health outcomes.
- Routinely recorded electronic patient record data can be used by primary healthcare professionals to search for preconception risk factors and thereby support individualised preconception care, while aggregate data can be used by public health agencies to promote population-level preconception health.
- Further data quality improvements and linkage of routine health datasets are needed to support the provision of preconception care and future research on its benefits for maternal and offspring health outcomes.

Introduction

Preconception care is the provision of biomedical, behavioural and social interventions to people of reproductive age (15-49 years) before conception may occur with the aim of improving short- and longer-term parental and child health outcomes.[1] Primary care teams have a key role in providing preconception care as identified by patients and healthcare professionals.[2, 3] Preconception care delivered in primary care improves knowledge and preconception health behaviours in female patients, but there is currently less evidence about male patients or the impact on pregnancy and longer-term health outcomes.[4, 5] In line with the National Institute for Health and Care Excellence (NICE) Clinical Knowledge Summary on preconception advice and management, primary care teams are encouraged to consider discussions about preconception health when appropriate, and to assess, manage and potentially optimise a range of physical and mental health conditions, health behaviours, and social needs prior to potential pregnancy.[6] However, routine provision of preconception care is not currently widespread in UK clinical practice.[7]

To build the case for implementation of strategies and guidelines that optimise the population's preconception health, the UK Preconception Partnership proposed an annual report card to describe and monitor preconception health.[8] Our scoping review to inform national surveillance identified 65 preconception indicators (medical, behavioural and social risk factors that may impact potential future pregnancies among individuals of reproductive age) that are recorded in existing UK routine health data.[9] A first report card was produced based on 23 indicators recorded in the national Maternity Service Data Set (MSDS), demonstrating that nine in 10 women in England enter pregnancy with at least one potentially modifiable risk factor for adverse pregnancy and birth outcomes.[10, 11] Similarly, an analysis of primary care data from the Royal College of General Practitioners Research and Surveillance Centre found that 91% of women of reproductive age have a behavioural or medical risk factor for adverse pregnancy outcomes.[12] These studies have to date focussed on preconception health of women (not men), and have not examined trends and trajectories in medical, behavioural and social indicators during the years leading up to pregnancy. Doing so would improve our ability to identify the population's preconception care needs throughout their reproductive years. Routinely collected primary care data is potentially a unique resource to describe and monitor preconception health, and to examine the impact of (changes in) preconception indicators on improving outcomes such as gestational diabetes and preterm birth.

To inform future research and surveillance, and develop policy and clinical practice recommendations, we aimed to systematically review the literature to explore how UK routine primary care data could provide information on the prevalence of preconception indicators and examine associations with maternal and offspring health outcomes.

Methods

Search strategy and selection criteria

The protocol for this review was registered with PROSPERO,[13] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA 2020) guideline used to ensure transparent reporting.[14] A search strategy was developed, and searches conducted on 27 March 2023 (from inception date) in five databases: MEDLINE (Ovid), EMBASE (Ovid), Scopus, CINAHL, Web of Science (Supplementary Table 1). Supplementary searches using 'preconception' and 'prepregnancy' terms were conducted using databases from the British Journal of General Practice, and UK primary care datasets.[13] Reference lists of included articles were screened for additional studies.

Articles were selected if they included findings from an observational study among individuals of reproductive age (15-49 years), used national patient-level routine primary care data collected in England, Wales, Scotland and/or Northern Ireland, and reported on the prevalence of at least one preconception indicator identified from our previous scoping review (Table 1).[9] Articles not including new/original peer-reviewed results, and conference abstracts, were excluded.

Selection process

Search results were collated in EndNote and duplicates removed, before uploading to Covidence software. Titles and abstracts, followed by full text articles, were screened independently by two reviewers for inclusion. Disagreements or uncertainties were resolved through discussion.

Data extraction and synthesis

A standardised data extraction form was developed and piloted. Data were extracted by one reviewer and checked by a second reviewer. Disagreements were resolved between the two reviewers. All extracted data on study characteristics (grouped by primary care database), prevalence of preconception indicators, and measures of association between preconception indicators and outcomes (grouped by preconception indicator), were presented in tables. Meta-analysis was not conducted due to heterogeneity in preconception indicator definitions and inclusion and exclusion criteria of study populations.

Risk of bias assessment

Risk of bias was assessed for study findings on the prevalence of preconception indicators using the 10-item scale developed by Hoy et al rating internal and external validity.[15] The Newcastle-Ottawa Scale (NOS) was used to rate risk of bias of study findings on associations between preconception indicators and health outcomes based on seven items related to selection, comparability, and exposure/outcome.[16] Risk of bias was assessed by one reviewer, and checked by a second reviewer. Disagreements were resolved between the two reviewers. Studies were classified as low, moderate or high risk of bias (findings on prevalence),[15] and good, fair or poor data quality (findings on associations)[16] (scoring guides in Supplementary Tables 2, 3A-3B).

Results

From 9,401 identified records, 4,142 duplicates were removed and after title and abstract screening (n=5,259), 117 full-text articles were evaluated for eligibility (Figure 1). 42 articles were included, reporting findings from 11 primary care databases such as the Clinical Practice Research Datalink (CPRD) and The Health Improvement Network (THIN).

Most articles reported findings from primary care databases that included patients from three (n=1) or all four UK nations (n=30), or from England (n=6), Scotland (n=3) or Northern Ireland only (n=2) (Table 2, Supplementary Table 4). In 11 studies, a primary care dataset was linked with at least one other dataset, such as Hospital Episodes Statistics (HES), Office for National Statistics (ONS) mortality register, community prescribing data, or the Avon Longitudinal Study of Parents and Children. All studies included data on female patients; three studies also reported preconception indicators for male patients.

Prevalence of preconception indicators

Articles reported findings on 30 preconception indicators across seven of the 12 domains identified in our scoping review.[9] Most studies included people of reproductive age irrespective of past/future

pregnancy (n=26), while other studies included women with a pregnancy or birth recorded during the study period (n=15) or women with a recorded pregnancy and their partners (n=1) (Supplementary Table 5).

To obtain population-level estimates of preconception indicators, prevalence data were extracted only if reported (or could be calculated) for the overall study population of females or males of reproductive age (i.e. not if reported only in sub-populations such as patients with a specific condition or characteristic) (Table 3). Data on overall prevalence were available for 21 of the 42 studies, with the other 21 studies reporting prevalence estimates only in sub-populations. Additional preconception indicators reported in sub-populations included housing, domestic abuse, routine GP check-up in the past year, paternal age, previous pregnancy loss, history of assisted reproduction, alcohol consumption, substance misuse, cervical screening, and cardiovascular disease (Supplementary Table 4).

The prevalence of preconception indicators reported across studies and primary care databases varied widely, possibly due to differences in preconception indicator definitions, year of data collection (Table 3), and study populations (Supplementary Table 5). The prevalence of preconception indicators defined in line with our scoping review (i.e. excluding individual methods of contraception, and prescribed folic acid supplements),[9] ranged from 0.01% for sickle cell disease to >20% for each of advanced maternal age, previous caesarean section (among those with a recorded pregnancy), overweight, obesity, smoking and diagnosis of depression and anxiety among female patients (irrespective of pregnancy). Only three studies reported preconception indicators for male patients, showing for example that the prevalence of depression among fathers (9.2%) was lower compared with mothers (22.2%),[17] and the proportion of patients prescribed valproate was comparable among female (0.31%) and male patients (0.37%) in 2004, but much lower among females (0.16%) than males (0.36%) in 2018.[18]

Associations of preconception indicators with maternal and offspring outcomes

Five studies reported associations of preconception indicators (contraception prescription [n=1], sexually transmitted disease [n=1] and polycystic ovary syndrome [PCOS] [n=3]) with pregnancy and birth outcomes (Table 4). Outcome data were obtained from primary care data and/or linked HES data. Where two studies reported on comparable indicators and outcomes, consistent findings were shown for associations of PCOS with preterm delivery (<37 weeks gestational age) (positive association), high birthweight (>4kg) (no association) and low birthweight (<2.5kg) (inconclusive findings).[19, 20]

Risk of bias and data quality

Risk of bias for findings on the prevalence of preconception indicators was generally low (n=18/21 studies), however, none of the studies received a minimal score (no bias) (Supplementary Table 2). Potential biases were introduced based on representativeness and sampling frame (e.g. excluding women with no pregnancy reported or no linked data available), and indicator definition and measurement (e.g. reporting individual methods of contraception rather than population prescribed contraception, or reliance on medication prescription rather than dispensing data). Moreover, details of non-response (e.g. impact of missing data) were not reported in approximately half the studies. Data quality for studies examining associations of preconception indicators with health outcomes was rated as good for four of the five studies (Supplementary Tables 3A-3B).

Discussion

Summary

This systematic review found that UK routine primary care data can provide valuable information on patients' medical, behavioural and social risk factors before (a potential) pregnancy. Based on 42 included studies among people of reproductive age or women with a pregnancy recorded during the study period, the prevalence of 30 preconception indicators was reported. Findings showed that >20% of female patients of reproductive age would benefit from support with smoking cessation, and management of weight, depression and anxiety. This would optimise their own health, and improve their chance of a successful pregnancy and healthy baby if that is something they want. Limited research has used primary care data to examine preconception indicators among male patients, or associations of preconception indicators with pregnancy outcomes and longer-term maternal and offspring health outcomes.

Strengths and limitations

This is the first systematic review to demonstrate how national routine primary care databases can be used to describe the population's preconception health, to inform clinical practice and future research directions. Comprehensive, prospectively registered review methods were used. Our search was limited to UK primary care data and findings may not be generalisable to other countries. Preconception indicators were selected based on our previous scoping review;[9] so potentially relevant indicators not included in this review or not reported in the included studies would have been missed. Moreover, some preconception indicators (such as dietary intake and physical activity) are not routinely recorded in general practice.

Comparison with existing literature

Findings from our review complement our previous preconception report card based on the MSDS,[10] showing that national routine health data are a valuable resource to describe and monitor women's preconception health. Half of the preconception indicators identified in this review were also reported in the MSDS, with comparable prevalence estimates for most indicators (e.g. teenage pregnancy, previous caesarean delivery, overweight, obesity), while other indicators may be underreported in primary care (e.g. over the counter folic acid supplementation) or in the MSDS (e.g. mental health conditions).[10] Published primary care data reported an additional 15 indicators not included in the MSDS (e.g. fertility problems, contraception, relevant medical conditions, teratogenic medication use). Linkage of these (and other) national routine health datasets would enhance the quality of preconception report cards and surveillance (Box 1). Based on linkage of primary care and HES datasets, findings from our review (n=2 studies[19, 20]) confirm the previously reported association of PCOS with increased risk of preterm delivery.[21]

Findings from our review are also in line with previous research reporting primary care data quality issues.[22-24] Studies included in our review documented substantial missing data (20-60%) for ethnicity and BMI category, likely varying across sub-populations. Coding quality is related to financial incentives such as the Quality and Outcomes Framework (QOF), which may improve accurate recording of selected indicators but also distort prevalence estimates over time.[22] The prevalence of some preconception indicators may be underestimated as not all conditions are solely diagnosed and coded in general practice (e.g. sexually transmitted disease),[25] or medications and supplements prescribed (e.g. contraception, folic acid supplements).[26] Another commonly reported limitation is the representation of selected general practices in research databases,[22, 23] often limited to practices that use one of four main software platforms to manage electronic patient records (EPRs) and further determined by voluntary 'opt ins'.[22, 23] As a result, primary care databases may

underrepresent specific regions and bias national prevalence estimates of preconception indicators and associations with health outcomes.

Implications for research and clinical practice

Our findings demonstrate that many preconception indicators are routinely recorded in EPRs, allowing primary healthcare professionals to search for risk factors and provide individualised preconception care. A digital risk screening template has been developed in the Ardens Clinical Decision Support System based on the NICE Clinical Knowledge Summary,[6] to support primary healthcare professionals to improve their preconception care practice, screening, coding and recording of indicators. Further work is required to co-develop practical guidance and resources to support integration of preconception care into every day clinical practice (Box 1).

Our findings identify the need to use standardised definitions when reporting preconception indicators (Box 1). Due to heterogeneity in definitions, the prevalence of preconception indicators across UK nations, and changes over time, could not be directly compared across studies. However, Lee and colleagues applied standardised definitions to CRPD (UK) and SAIL data (Wales), showing comparable prevalence estimates for some indicators (e.g. obesity, depression), but higher (e.g. smoking, underweight, anxiety, asthma) or lower (e.g. advanced maternal age) prevalence for other indicators, when comparing pregnant women in Wales with those in the UK overall .[27] Moreover, standardised reporting within the same database showed, for example, increases over time in the prevalence of type 2 diabetes (1995-2017),[29] alongside decreases in poor diabetes control (2004-2017).[29, 30]

Lastly, the limited reporting of male preconception indicators, and associations of preconception health with pregnancy, maternal and offspring health outcomes, calls for further research. Many of the preconception indicators reported for female patients are also relevant to male patients (e.g. smoking, obesity), with increasing evidence suggesting better paternal preconception health is associated with reduced risks of infertility and adverse pregnancy and offspring health and developmental outcomes.[31-33] To enable further research, improvements are needed in the way that families (i.e. biological parents and their children) can be identified and data linked.[17, 34] Primary care data also provide a unique opportunity to examine trajectories of preconception health during reproductive years irrespective of pregnancy, and to quantify the extent to which these reduce adverse pregnancy and offspring health outcomes. Future research would be enhanced by linkage of primary care and other routine health datasets beyond the identified existing linkages (e.g. MSDS and Community Services Data Set) to determine the short- and longer-term benefits of preconception care (Box 1).

Conclusion

Routinely collected primary care data in the UK provide a valuable resource for research and surveillance, and can guide to provision of preconception care. Improvements in coding and reporting, and linkage of general practice systems and other national routine health datasets, would inform evidence-based provision of preconception care in primary care.

Acknowledgements

Funding: DS is supported by the National Institute for Health and Care Research (NIHR) through an NIHR Advanced Fellowship (NIHR302955) and the NIHR Southampton Biomedical Research Centre (NIHR203319). MM is supported by the UK Medical Research Council (MR/W01498X/1). KMG is supported by the UK Medical Research Council (MC_UU_12011/4), the NIHR (NIHR Senior Investigator (NF-SI-0515-10042) and NIHR Southampton Biomedical Research Centre (NIHR203319)) and Alzheimer's Research UK (ARUK-PG2022A-008). For the purpose of Open Access, the author has applied a Creative Commons Attribution (CC BY) licence to any Author Accepted Manuscript version arising from this submission.

Competing interests: KMG has received reimbursement for speaking at conferences sponsored by companies selling nutritional products, and is part of an academic consortium that has received research funding from Abbott Nutrition, Nestec, BenevolentAI Bio Ltd. and Danone, outside the submitted work. No competing interests declared for other authors.

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Figures

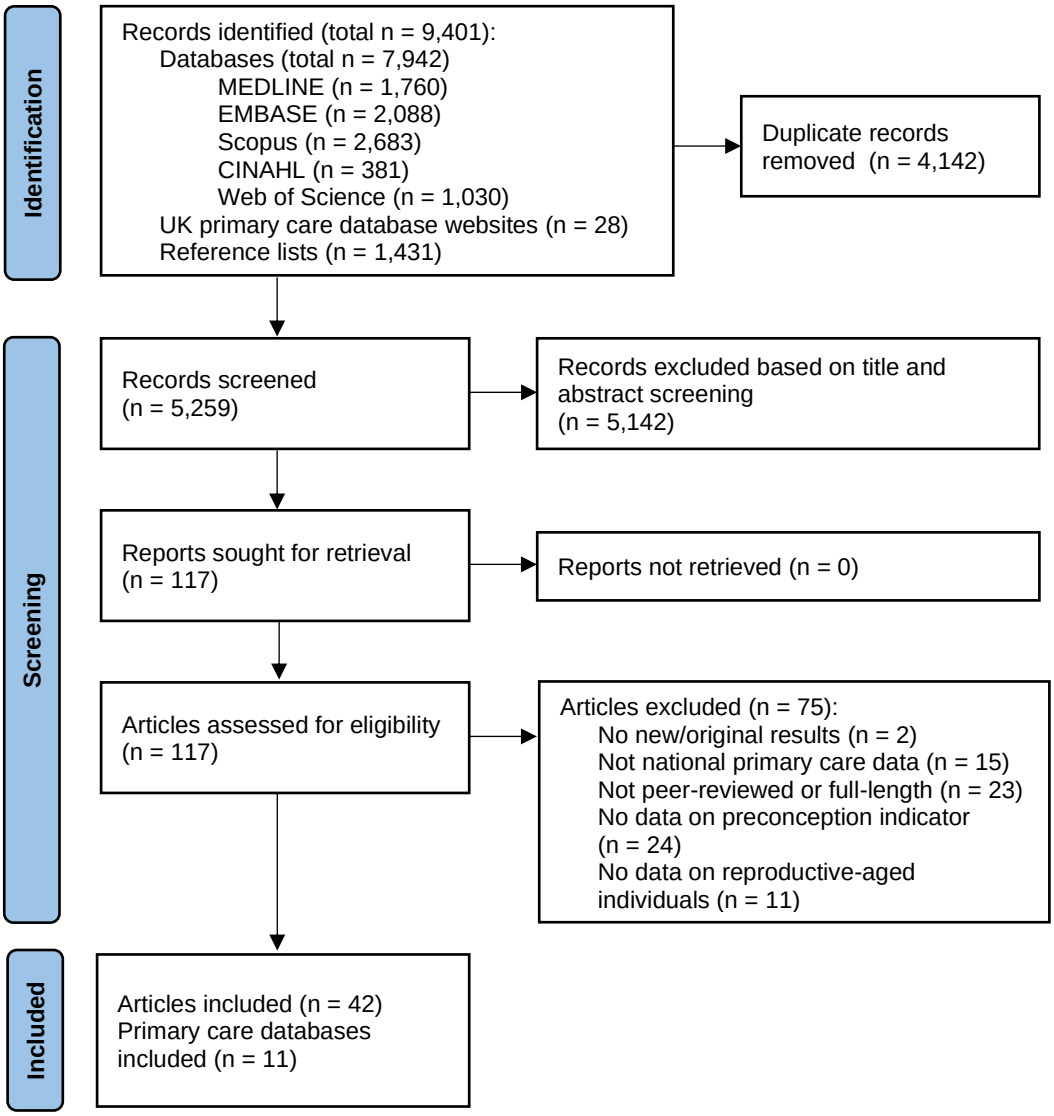

Figure 1. PRISMA flow diagram for the identification and selection of studies included in the review.

- Routine use of a standardised digital risk screening template (i.e. existing template in Ardens Clinical Decision Support System) to support implementation of the NICE Clinical Knowledge Summary on preconception advice and management.[6]
- Development of coding practice standards with appropriate incentives to improve data quality.
- Standardisation of reporting of preconception indicators and pregnancy and offspring health outcomes, for example through the development of core outcome sets.
- Improvements in the coding and identification of family and household members to enable linkage of data from biological parents and their children.
- Nationwide linkage of general practice systems, and linkage of primary care datasets with other routine health datasets (such as Hospital Episode Statistics, Maternity Services Data Set and Community Services Data Set).

Box 1. Recommendations to improve the use of UK routine primary care data for clinical practice, research and surveillance of preconception health and care.

Tables

Table 1. PICOS statement

Population	Individuals of reproductive age who may or may not be(come) pregnant/conceive a pregnancy (any gender, aged 15-49 years).
Intervention/ exposure	Preconception indicators as identified in Schoenaker et al.[9] Preconception indicators are defined as medical, behavioural and social risk factors or exposures as well as wider determinants of health that may impact potential future pregnancies among all individuals of reproductive age. Studies do not have to identify relevant factors or exposures as 'preconception indicators'.
Comparator/ control	Not applicable.
Outcome	Maternal health outcomes: any outcome that may occur during pregnancy (e.g. gestational diabetes), delivery (e.g. caesarean section), postpartum (e.g. mortality), or beyond (no age limit) (e.g. type 2 diabetes). Offspring health and developmental outcomes (including social/educational outcomes): any outcome that may occur during pregnancy (e.g. stillbirth), delivery (e.g. preterm birth), infancy (e.g. neonatal intensive care unit admission), or beyond (no age limit) (e.g. learning difficulty).
Study design	Observational studies (including cohort, cross-sectional and case-control studies).

Table 2. Characteristics of included studies reporting on the prevalence of preconception indicators in the overall population of people of reproductive age

First author, year (reference)	Dataset	Country	Study design	Data collection period	Total or maximum sample size	Population characteristics: sex, age	Preconception indicators reported	Maternal and offspring outcomes reported
Clinical Practice Research Datalink (CPRD)								
Lee, 2022 ([27])	CPRD GOLD	UK	Cross-sectional study	2018	37,641	Female, 15-49 years	Maternal age, ethnicity, deprivation, weight, smoking, depression, anxiety, severe mental health condition, asthma, PCOS, infertility, thyroid disease, eating disorder, endometriosis, hypertension, thromboembolism, sickle-cell disease, epilepsy, diabetes	None
Hope, 2022 ([35])	CPRD GOLD	UK	Cohort study	1990-2017	2,680,149	Female, 14-45 years	Ethnicity, mental health condition	None
Subramanian, 2022 ([19])	CPRD GOLD linked with HES	England	Cohort and case-control study	1997-2020	299,866	Female, 15-49 years	Ethnicity, PCOS	Preterm delivery, mode of delivery, high or low birthweight, stillbirth, small and large for gestational age
Syed, 2022 ([36])	CPRD GOLD linked with HES and Office for National Statistics (ONS) mortality register	England	Cohort study	2004- 2018	211,393	Female, 16-55 years	Deprivation, ethnicity, maternal age	None
den Heijer, 2019 ([25])	CPRD GOLD linked with IMD	England	Cohort	2000-2013	857,324	Female, 12-25 years	Smoking, deprivation, folic acid supplementation, sexually transmitted disease, PCOS, endometriosis, thyroid disease	Ectopic pregnancy
General Practice Research Database (GPRD)								

First author, year (reference)	Dataset	Country	Study design	Data collection period	Total or maximum sample size	Population characteristics: sex, age	Preconception indicators reported	Maternal and offspring outcomes reported
Briggs, 2013 ([37])	N/A	UK	Repeated cross-sectional study	2004-2010	1,103,669	Female, 15-49 years	Contraception	None
Rowlands, 2000 ([38])	N/A	UK	Cohort study	1994-1997	95,007	Female, 14-29 years	Contraception	None
The Health Improvement Network (THIN)								
Smith, 2020 ([39])	N/A	UK	Cohort study	2006-2016	241,662	Female, 15-49 years	Maternal age, deprivation, previous caesarean delivery, smoking	None
Cea Soriano, 2018 ([40])	N/A	UK	Cohort study and case-control study	1995-2012	251,581	Female, 15-45 years	Diabetes mellitus	None
Coton, 2016 ([30])	N/A	UK	Cohort study	1995-2012	301,794	Female, 16 and over	Diabetes mellitus	None
Ban, 2015 (2) ([41])	N/A	UK	Cohort study	1990-2010	2,141,503	Female, 15-44 years	Inflammatory bowel disease	None
Cea Soriano, 2014 ([28])	N/A	UK	Cohort study	2004-2010	N/R	Female, 18-44 years	Contraception	None
Cea Soriano, 2013 ([42])	N/A	UK	Cohort study	2008	574,185	Female, 12-49 years	Contraception	None
Dhalwani, 2013 ([43])	N/A	UK	Cohort study	1990-2010	1,776,746	Female, 15-49 years	Fertility problems	None
Ban, 2012 ([44])	N/A	UK	Cohort study	1994-2009	116,457	Female, 15-45 years	Depression, anxiety, serious mental illness, deprivation	None
Dave, 2010 ([17])	Use of family identification number to link mothers, fathers and children living in the same household	UK	Cohort study	1993-2007	86,957	Female and male, 15-≥35 years	Depression	None
Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) network								

First author, year (reference)	Dataset	Country	Study design	Data collection period	Total or maximum sample size	Population characteristics: sex, age	Preconception indicators reported	Maternal and offspring outcomes reported
Gaudio, 2022 ([18])	N/A	England	Repeated cross-sectional study	2004-2018	729,662	Female and male, 12-46 years	Valproate prescription	None
Gaudio, 2021 ([29])	N/A	England	Repeated cross-sectional study	2004-2017	465,898	Female, 16-45 years	Diabetes mellitus	None
Enhanced Prescribing Database (EPD)								
Given, 2020 ([45])	EPD linked with GP Patient Registrations Index	Northern Ireland	Cohort study	2010-2016	560,074	Female, 12-49 years	Contraception	None
Wemakor, 2014 ([46])	EPD linked with the 2010 Northern Ireland Multiple Deprivation Measure (NIMDM)	Northern Ireland	Cross-sectional study	2009	268,917	Female, 15-45 years	Deprivation, anti-depressant use	None
Other datasets								
Lee, 2022 ([27])	Secure Anonymised Information Linkage (SAIL) Databank	Wales	Cross-sectional study	2018	27,782	Female, 15-49 years	Maternal age, ethnicity, deprivation, weight, smoking, mental health problem, severe mental health condition, asthma, PCOS, infertility, thyroid disease, eating disorder, endometriosis, hypertension, thromboembolism, sickle-cell disease, epilepsy, diabetes	None
Pasvol, 2022 ([47])	IQVIA Medical Research Data (IMRD) database	UK	Repeated cross-sectional study	2000-2018	2,705,638	Female, 15-49 years	Contraception	None

ALSPAC, Avon Longitudinal Study of Parents and Children; CPRD, Clinical Practice Research Datalink; EPD, Enhanced Prescribing Database; HES, Hospital Episodes Statistics; IMD, index of multiple deprivation; PCOS, polycystic ovary syndrome; SD, standard deviation.

Table 3. Prevalence of (and trends in) preconception indicators reported for people of reproductive age in UK routine primary care data

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
Domain: Wider determinants of health					
Indicator: Deprivation					
Ban, 2012 ([44])	1994-2009	THIN	Percentage of women [with a pregnancy during the study period] living in the most socio-economically deprived area (based on Townsend Index of Deprivation quintiles)	116,457	14.2
den Heijer, 2019 ([25])	2000-2013	CPRD	Percentage of women living in the most socio-economically deprived area (based on IMD quintiles)	857,324	13.6
Syed, 2022 ([36])	2004-2018	CPRD	Percentage of women [with a live birth recorded during the study period] living in the most socio-economically deprived area (based on IMD quintiles)	211,393	18.5
Smith, 2020 ([39])	2006-2016	THIN	Percentage of women [who gave birth to a single live infant during the study period] living in the most socio-economically deprived area (based on Townsend Index of Deprivation quintiles)	277,114	16.0
Wemakor, 2014 ([46])	2009	EPD	Percentage of women living in the most socio-economically deprived area (based on NIMDM quintiles)	264,798	22.6
Lee, 2022 ([27])	2018	CPRD (England)	Percentage of women [with a conception date during the study period] living in the most socio-economically deprived area (based on IMD quintiles)	9,800	19.5
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] living in the most socio-economically deprived area (based on IMD quintiles)	24,538	15.6
Indicator: Ethnicity					
Hope, 2022 ([35])	1990-2017	CPRD	Percentage of women [with a pregnancy during the study period] from an ethnic minority background	2,680,149	15.1
Coton, 2016 ([30])	1995-2012	THIN	Percentage of women [with a pregnancy during the study period] from an ethnic minority background	301,794	14.9
Subramanian, 2022 ([19])	1997-2020	CPRD	Percentage of women [with a record of delivery during the study period] from an ethnic minority background	299,866	20.0
Syed, 2022 ([36])	2004-2018	CPRD	Percentage of women [with a live birth recorded during the study period] from an ethnic minority background	211,393	13.7
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] from an ethnic minority background	37,641	12.8
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] from an ethnic minority background	27,782	15.1

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
Domain: Reproductive health and family planning					
Indicator: Teenage pregnancy					
Syed, 2022 ([36])	2004-2018	CPRD	Percentage of women [with a live birth recorded during the study period] aged ≤19 at time of childbirth	211,393	3.3
Smith, 2020 ([39])	2006-2016	THIN	Percentage of women [who gave birth to a single live infant during the study period] aged 15-19 at time of most recent pregnancy	309,573	3.1
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] aged 15-19 at time of index pregnancy	37,641	6.7
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] aged 15-19 at time of index pregnancy	27,782	5.5
Indicator: Advanced maternal age					
Syed, 2022 ([36])	2004-2018	CPRD	Percentage of women [with a live birth recorded during the study period] aged ≥40 at time of childbirth	211,393	27.0
Smith, 2020 ([39])	2006-2016	THIN	Percentage of women [who gave birth to a single live infant during the study period] aged 35-49 at time of most recent pregnancy	309,573	26.1
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] aged 35-49 at time of most recent pregnancy	37,641	20.1
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] aged 35-49 at time of most recent pregnancy	27,782	15.1
Indicator: Previous caesarean delivery					
Smith, 2020 ([39])	2006-2016	THIN	Percentage of women [who gave birth to a single live infant during the study period] with a previous caesarean delivery (based on most recent pregnancy)	98,932	23.7
Indicator: Fertility problems					
Dhalwani, 2013 ([43])	1990-2010	THIN	Percentage of women with a history of fertility problems (at least one record for a fertility problem based on Read codes)	1,776,746	3.3
Lee, 2022 ([27])	2018	CRPD	Percentage of women [with a conception date during the study period] with a history of fertility problems (based on Read codes for (possible) female infertility)	37,641	3.81 (3.62-4.01)
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with a history of fertility problems (based on Read codes for (possible) female infertility)	27,782	1.18
Indicator: Contraception					
Rowlands, 2000 ([38])	1994-1997	GPRD	Percentage of women who use contraception (assessed based on prescription codes for all regular methods, excluding emergency contraception)	95,007	70.1

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
den Heijer, 2019 ([25])	2000-2013	CPRD	Percentage of women who use contraception (oral contraception)	857,324	5.7
Pasvol, 2022 ([47])	2000	IMRD	Percentage of women who use contraception (COCP, POP and LARC)	2,705,638	32.9 (32.7-33.0)
	2018	IMRD	As above	2,705,638	29.2 (29.1-29.3)
Cea Soriano, 2014 ([28])	2004	THIN	Percentage of women who use contraception (progesterone-only implant assessed using Read and MULTILEX codes)	N/R	0.5
	2010	THIN	As above	N/R	3.4
	2004	THIN	Percentage of women who use contraception (levonorgestrel releasing-intrauterine system (LNG-IUS) assessed using Read and MULTILEX codes)	N/R	3.1
	2010	THIN	As above	N/R	5.2
	2004	THIN	Percentage of women who use contraception (copper intrauterine devices assessed using Read and MULTILEX codes)	N/R	5.4
	2010	THIN	As above	N/R	4.8
	2004	THIN	Percentage of women who use contraception (progestogen-only injections assessed using Read and MULTILEX codes)	N/R	3.6
	2010	THIN	As above	N/R	3.2
Briggs, 2013 ([37])	2004	GPRD	Percentage of women who use contraception (assessed based on combined hormonal contraception prescription data)	1,018,835	19.6
	2005	GPRD	As above	1,040,629	19.6
	2006	GPRD	As above	1,053,353	19.1
	2007	GPRD	As above	1,067,462	18.7
	2008	GPRD	As above	1,085,149	18.2
	2009	GPRD	As above	1,100,002	17.4
	2010	GPRD	As above	1,103,669	16.3
Cea Soriano, 2013 ([42])	2008	THIN	Percentage of women who use contraception (combined oral contraceptive assessed using Read and MULTILEX codes)	574,185	16.2 (16.1-16.3)
	2008	THIN	Percentage of women who use contraception (progesterone-only pill assessed using Read and MULTILEX codes)	574,185	5.6 (5.5-5.6)
	2008	THIN	Percentage of women who use contraception (copper intrauterine device assessed using Read and MULTILEX codes)	574,185	4.5 (4.4-4.5)
	2008	THIN	Percentage of women who use contraception (levonorgestrel-releasing intrauterine system assessed using Read and MULTILEX codes)	574,185	4.2 (4.1-4.2)

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
	2008	THIN	Percentage of women who use contraception (progesterone-only implant assessed using Read and MULTILEX codes)	574,185	1.5 (1.5-1.6)
	2008	THIN	Percentage of women who use contraception (progestogen-only injection assessed using Read and MULTILEX codes)	574,185	2.4 (2.3-2.4)
	2008	THIN	Percentage of women who use contraception (contraceptive patch assessed using Read and MULTILEX codes)	574,185	0.1 (0.1-0.2)
Given, 2020 ([45])	2010	EPD	Percentage of women who use contraception (based on dispensed prescriptions of COCP, POP, emergency contraceptive, injection, implant, intrauterine device, transdermal patch, vaginal ring and gel)	465,912	25.7
	2016	EPD	As above	479,908	26.1
Domain: Health behaviours and weight					
Indicator: Folic acid supplementation					
den Heijer, 2019 ([25])	2000-2013	CPRD	Percentage of women prescribed folic acid supplementation	857,324	0.3
Indicator: Underweight					
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] in the underweight BMI category (<18.5 kg/m^2)	30,910	3.9
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] in the underweight BMI category (<18.5 kg/m^2)	21,802	5.9
Indicator: Overweight					
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] in the overweight BMI category (25.0-29.9 kg/m^2)	30,910	26.1
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] in the overweight BMI category (25.0-29.9 kg/m^2)	21,802	26.0
Indicator: Obesity					
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] in the obesity BMI category (≥30.0 kg/m^2)	30,910	23.2
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] in the obesity BMI category (≥30.0 kg/m^2)	21,802	24.6
Indicator: Smoking					
den Heijer, 2019 ([25])	2000-2013	CPRD	Percentage of women who currently smoke	857,324	25.8

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
Smith, 2020 ([39])	2006-2016	THIN	Percentage of women [who gave birth to a single live infant during the study period] who currently smoke	263,575	13.1
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] who currently smoke	36,339	22.7
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] who currently smoke	24,785	26.7
Domain: Immunisation and infections					
Indicator: Sexually transmitted disease					
den Heijer, 2019 ([25])	2000-2013	CPRD	Percentage of women diagnosed with gonorrhoea	857,324	0.01
Domain: Mental health conditions					
Indicator: Mental health condition					
Hope, 2022 ([35])	1990-2017	CPRD	Percentage of women [with a pregnancy during the study period] with a mental illness (assessed based on prescription, diagnosis and symptom data for depression, anxiety, psychosis, substance or alcohol misuse disorder, eating or personality disorder)	2680149	19.8
Indicator: Depression					
Dave, 2010 ([17])	1993-2007	THIN	Percentage of mothers with depression (assessed based on Read codes for unipolar depression and/or a prescription for an antidepressant for treatment of depression)	86,957	22.2
Dave, 2010 ([17])	1993-2007	THIN	Percentage of fathers with depression (assessed based on Read codes for unipolar depression and/or a prescription for an antidepressant for treatment of depression)	86,957	9.2
Ban, 2012 ([44])	1994-2009	THIN	Percentage of women [with a pregnancy during the study period] with depression during 9 months before pregnancy (assessed based on record of depression diagnosis and/or antidepressant prescription)	116,457	9.3 (9.1-9.4)
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with depression (based on read codes for diagnosis of depression and history of depression)	37,641	23.43 (23.01-23.87)
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with depression (based on read codes for diagnosis of depression and history of depression)	27,782	24.07 (23.57-24.58)
Indicator: Anxiety					
Ban, 2012 ([44])	1994-2009	THIN	Percentage of women [with a pregnancy during the study period] with anxiety during 9 months before pregnancy (assessed based on record of anxiety diagnosis and/or anxiolytic prescription & record of anxiety diagnosis and antidepressant prescription but no depression diagnosis)	116,457	4.1 (4.0-4.3)
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with anxiety (based on read codes for diagnosis of anxiety disorders and history of anxiety disorders)	37,641	18.98 (18.58-19.38)

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with anxiety (based on read codes for diagnosis of anxiety disorders and history of anxiety disorders)	27,782	23.05 (22.56-23.55)
Indicator: Serious mental illness					
Ban, 2012 ([44])	1994-2009	THIN	Percentage of women [with a pregnancy during the study period] with serious mental illness during 9 months before pregnancy (assessed based on record of bipolar disorder, schizophrenia or other psychotic disorders and/or prescription of lithium or mood stabilisers)	116,457	0.12 (0.11-0.14)
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with severe mental illness (based on read codes for diagnosis or history of bipolar disorder / affective psychosis and schizophrenia / non-affective psychosis)	37,641	2.42 (2.26-2.58)
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with severe mental illness (based on read codes for diagnosis or history of bipolar disorder / affective psychosis and schizophrenia / non-affective psychosis)	27,782	2.07 (1.91-2.24)
Domain: Physical health conditions					
Indicator: Epilepsy					
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with epilepsy (based on read codes for epilepsy diagnosis, treatment and advice)	37,641	1.44
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with epilepsy (based on read codes for epilepsy diagnosis, treatment and advice)	27,782	1.30
Indicator: Diabetes mellitus					
Cea Soriano, 2018 ([40])	1995-2012	THIN	Percentage of women [with a pregnancy during the study period] with type 1 diabetes	251,581	0.36
Cea Soriano, 2018 ([40])	1995-2012	THIN	Percentage of women [with a pregnancy during the study period] with type 2 diabetes	251,581	0.24
Coton, 2016 ([30])	1995	THIN	Percentage of women [who gave birth during the study period] with type 1 diabetes (based on diagnostic Read codes and prescriptions for antidiabetics from medical records)	N/R	0.16
Cea Soriano, 2018 ([40])	1995-2012	THIN	Percentage of women [with a pregnancy during the study period] with diabetes (any type) (based on Read codes suggestive of diabetes and for insulin prescriptions)	251,581	0.60
Coton, 2016 ([30])	1995	THIN	Percentage of women [who gave birth during the study period] with type 2 diabetes (based on diagnostic Read codes and prescriptions for antidiabetics from medical records)	N/R	0.23
Gaudio, 2021 ([29])	2004	RCGP RCS	Percentage of women with diabetes (any type)	316,461	1.0
Gaudio, 2021 ([29])	2004	RCGP RCS	Percentage of women with type 2 diabetes	316,461	0.6

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
Gaudio, 2021 ([29])	2004	RCGP RCS	Percentage of women with poor diabetes control (HbA1c ≥8.5%) (type 1 diabetes patients)	788	50.0
Gaudio, 2021 ([29])	2004	RCGP RCS	Percentage of women with poor diabetes control (HbA1c ≥8.5%) (type 2 diabetes patients)	1,098	33.1
Coton, 2016 ([30])	2008	THIN	Percentage of women [who gave birth during the study period] with type 2 diabetes (based on diagnostic Read codes and prescriptions for antidiabetics from medical records)	N/R	0.51
Coton, 2016 ([30])	2009	THIN	Percentage of women [who gave birth during the study period] with type 2 diabetes (based on diagnostic Read codes and prescriptions for antidiabetics from medical records)	N/R	0.67
Coton, 2016 ([30])	2012	THIN	Percentage of women [who gave birth during the study period] with type 2 diabetes (based on diagnostic Read codes and prescriptions for antidiabetics from medical records)	N/R	1.06
Coton, 2016 ([30])	2012	THIN	Percentage of women [who gave birth during the study period] with type 1 diabetes (based on diagnostic Read codes and prescriptions for antidiabetics from medical records)	N/R	0.41
Gaudio, 2021 ([29])	2017	RCGP RCS	Percentage of women with diabetes (any type)	465,898	1.4
Gaudio, 2021 ([29])	2017	RCGP RCS	Percentage of women with type 2 diabetes	465,898	0.9
Gaudio, 2021 ([29])	2017	RCGP RCS	Percentage of women with poor diabetes control (HbA1c ≥8.5%) (type 1 diabetes patients)	1,579	40.8
Gaudio, 2021 ([29])	2017	RCGP RCS	Percentage of women with poor diabetes control (HbA1c ≥8.5%) (type 2 diabetes patients)	3,041	24.7
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with type 1 diabetes	37,641	0.56
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with type 1 diabetes	27,782	0.49
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with type 2 diabetes	37,641	0.71
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with type 2 diabetes	27,782	0.68
Indicator: Polycystic ovary syndrome (PCOS)					
Subramanian, 2022 ([19])	1997-2020	CPRD	Percentage of women [with a record of delivery during the study period] with PCOS (based on Read codes for PCOS, polycystic ovaries or symptoms)	299,866	6.5
den Heijer, 2019 ([25])	2000-2013	CPRD	Percentage of women with PCOS	857,324	0.2
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with PCOS (based on read codes for PCOS, isosexual virilisation, polycystic ovaries, Stein - Leventhal syndrome, multicystic ovaries and endoscopic drilling of ovary)	37,641	4.66 (4.45-4.88)
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with PCOS (based on read codes for PCOS, isosexual virilisation, polycystic ovaries, Stein - Leventhal syndrome, multicystic ovaries and endoscopic drilling of ovary)	27,782	3.96 (3.73-4.20)
Indicator: Endometriosis					
den Heijer, 2019 ([25])	2000-2013	CPRD	Percentage of women with endometriosis	857,324	0.06

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with endometriosis (based on read codes for diagnosis of endometriosis and procedures of endometriosis)	37,641	1.68 (1.55-1.82)
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with endometriosis (based on read codes for diagnosis of endometriosis and procedures of endometriosis)	27,782	1.31 (1.18-1.45)
Indicator: Eating disorder					
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with an eating disorder (based on read codes for eating disorders, including anorexia, binge eating, bulimia, compulsive eating disorder, referral to eating disorder clinic)	37,641	1.88 (1.74-2.02)
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with an eating disorder (based on read codes for eating disorders, including anorexia, binge eating, bulimia, compulsive eating disorder, referral to eating disorder clinic)	27,782	1.80 (1.65-1.97)
Indicator: Thyroid disease					
den Heijer, 2019 ([25])	2000-2013	CPRD	Percentage of women with thyroid disease	857,324	0.07
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with thyroid disease (based on read codes for hyperthyroidism and hypothyroidism)	37,641	3.34 (3.16-3.52)
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with thyroid disease (based on read codes for hyperthyroidism and hypothyroidism)	27,782	2.45 (2.28-2.64)
Indicator: Hypertension					
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with hypertension (based on read codes related to hypertension)	37,641	0.87
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with hypertension (based on read codes related to hypertension)	27,782	0.67
Indicator: Thromboembolism					
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with thromboembolism (based on read codes for history, diagnosis or procedure for pulmonary embolism)	37,641	0.65
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with thromboembolism (based on read codes for history, diagnosis or procedure for pulmonary embolism)	27,782	0.60
Indicator: Asthma					

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with asthma (based on read codes on asthma, including diagnosis, treatment, education and review)	37,641	14.63 (14.27-14.99)
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with asthma (based on read codes on asthma, including diagnosis, treatment, education and review)	27,782	17.17 (16.73-17.62)
Indicator: Inflammatory bowel disease (IBD)					
Ban, 2015 (2) ([41])	1990-2010	THIN	Percentage of women [with a singleton live birth recorded during the study] with IBD (based on Read codes)	2,141,503	0.45
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with IBD (Crohn's disease, ulcerative colitis)	37,641	0.60
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with IBD (Crohn's disease, ulcerative colitis)	27,782	0.58
Indicator: Sickle cell disease					
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with sickle cell disease (based on read codes for diagnosis of sickle-cell anaemia or history of sickle-cell anaemia)	37,641	0.01
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with sickle cell disease (based on read codes for diagnosis of sickle-cell anaemia or history of sickle-cell anaemia)	27,782	<0.02
Indicator: Cancer					
Lee, 2022 ([27])	2018	CPRD	Percentage of women [with a conception date during the study period] with previous cancer diagnosis (breast, lung, bowel, cervical, ovarian, uterine, thyroid, skin, lymphoma, leukaemia, metastatic)	37,641	0.51
Lee, 2022 ([27])	2018	SAIL	Percentage of women [with a conception date during the study period] with previous cancer diagnosis (breast, lung, bowel, cervical, ovarian, uterine, thyroid, skin, lymphoma, leukaemia, metastatic)	27,782	0.60
Domain: Medication					
Indicator: Medication not recommended when planning pregnancy					
Gaudio, 2022 ([18])	2004	RCGP RCS	Percentage of women prescribed valproate	533,627	0.31 (0.18-0.44)
	2018	RCGP RCS	As above	729,662	0.16 (0.07-0.24)
	2004	RCGP RCS	Percentage of men prescribed valproate	N/R	0.37 (0.35-0.38)
	2018	RCGP RCS	As above	N/R	0.36 (0.34-0.37)

First author, year (reference)	Year for datapoint	Dataset	Preconception indicator measure	Sample size	Prevalence of preconception indicator (% with 95% CI)
Wemakor, 2014 ([46])	2014	EPD	Percentage of women prescribed anti-depressant medication	43,770	16.3 (16.1-16.4)

CI, confidence interval; COCP, combined oral contraceptive pill; CPRD, Clinical Practice Research Datalink; EPD, Enhanced Prescribing Database; IMD, index of multiple deprivation; LARC, long-acting reversible contraception; NIMDM, Northern Ireland Multiple Deprivation Measure; N/R, not reported; PCOS, polycystic ovary syndrome; POP, progestogen-only pill; SAIL, Secure Anonymised Information Linkage.

Table 4. Associations of preconception indicators with outcomes in women and offspring

First author, year (reference)	Reference and comparison group	Indicator data source	Maternal or offspring outcome	Outcome data source	Sample size	Statistical results definition	Result	Adjustment for confounders
Contraception								
Parker, 2016 ([48])	Intrauterine device (IUD) use prior to start of pregnancy vs. no IUD use prior to start of pregnancy (determined using procedure codes, drug codes and record review)	CPRD	Pre-eclampsia	CPRD	13,900	Adjusted OR (95% CI)	0.76 (0.58-0.98)	Age, general practice, year of delivery, BMI, smoking, parity, induced abortion, fertility problems, pre-existing diabetes
Sexually transmitted disease								
den Heijer, 2019 ([25])	Positive chlamydia test vs. negative chlamydia test	CPRD	Ectopic pregnancy	CPRD GOLD	2,484	Adjusted HR (95% CI)	1.87 (1.38-2.54)	Age, smoking status, history of gonorrhea
Polycystic ovary syndrome (PCOS)								
Subramanian, 2022 ([19])	PCOS vs. no PCOS (assessed based on Read codes for PCOS, polycystic ovaries or symptoms)	CRPD	Preterm delivery (< 37 weeks of gestational age at delivery)	HES	137,930	Adjusted OR (95% CI)	1.11 (1.06-1.17)	Age, ethnicity, deprivation, dysglycaemia, hypertension, thyroid disorders, numbers of babies born at the delivery, pre-gravid body mass index
Rees, 2016 ([20])	PCOS vs. no PCOS	CPRD	Preterm birth	HES and CRPD	19,502	Adjusted HR (95% CI)	1.24 (1.09-1.41)	Age, BMI, primary care practice, multiple gestation, number of previous births, smoking history

First author, year (reference)	Reference and comparison group	Indicator data source	Maternal or offspring outcome	Outcome data source	Sample size	Statistical results definition	Result	Adjustment for confounders
Subramanian, 2022 ([19])	PCOS vs. no PCOS (assessed based on Read codes for PCOS, polycystic ovaries or symptoms)	CPRD	High birthweight (>4kg) for at least one of the babies	HES	137,930	Adjusted OR (95% CI)	0.97 (0.92-1.01)	Age, ethnicity, deprivation, dysglycaemia, hypertension, thyroid disorders, numbers of babies born at the delivery, pre-gravid body mass index, gestational age
Rees, 2016 ([20])	PCOS vs. no PCOS	CPRD	High birth weight	HES	12,363	Adjusted OR (95% CI)	0.97 (0.67-1.41)	Age, BMI, primary care practice, multiple gestation, number of previous births, smoking history
Subramanian, 2022 ([19])	PCOS vs. no PCOS (assessed based on Read codes for PCOS, polycystic ovaries or symptoms)	CPRD	Low birthweight (<2.5 kg) for at least one of the babies	HES	137,930	Adjusted OR (95% CI)	1.03 (0.95-1.13)	Age, ethnicity, deprivation, dysglycaemia, hypertension, thyroid disorders, numbers of babies born at the delivery, pre-gravid body mass index, gestational age
Rees, 2016 ([20])	PCOS vs. no PCOS	CPRD	Low birth weight	HES	12,363	Adjusted OR (95% CI)	1.19 (1.00-1.42)	Age, BMI, primary care practice, multiple gestation, number of previous births, smoking history
Subramanian, 2022 ([19])	PCOS vs. no PCOS (assessed based on Read codes for PCOS, polycystic	CPRD	Emergency caesarean section	HES	137,930	Adjusted OR (95% CI)	1.10 (1.05-1.15)	Age, ethnicity, deprivation, dysglycaemia, hypertension, thyroid disorders, numbers of

First author, year (reference)	Reference and comparison group	Indicator data source	Maternal or offspring outcome	Outcome data source	Sample size	Statistical results definition	Result	Adjustment for confounders
	ovaries or symptoms)							babies born at the delivery, pre-gravid body mass index, gestational age
Subramanian, 2022 ([19])	As above	CPRD	Elective/ other/unspecified caesarean section delivery	As above	As above	Adjusted OR (95% CI)	1.07 (1.03-1.12)	As above
Subramanian, 2022 ([19])	As above	CPRD	Instrumental vaginal delivery	As above	As above	Adjusted OR (95% CI)	1.04 (1.00-1.09)	As above
Subramanian, 2022 ([19])	As above	CPRD	Stillbirth	As above	As above	Adjusted OR (95% CI)	0.99 (0.81-1.21)	Age, ethnicity, deprivation, dysglycaemia, hypertension, thyroid disorders, numbers of babies born at the delivery, pre-gravid body mass index
Subramanian, 2022 ([19])	As above	CPRD	Very preterm (<32 weeks of gestational age at delivery)	As above	As above	Adjusted OR (95% CI)	1.07 (0.97-1.18)	As above
Subramanian, 2022 ([19])	As above	CPRD	Extremely preterm (<28 weeks of gestational age at delivery)	As above	As above	Adjusted OR (95% CI)	1.13 (0.98-1.29)	As above
Subramanian, 2022 ([19])	As above	CPRD	Large for gestational age (>90th percentile) for at least one of the babies	As above	As above	Adjusted OR (95% CI)	1.00 (0.97-1.04)	As above
Subramanian, 2022 ([19])	As above	CPRD	Small for gestational age (<10th percentile) for at least one of the babies	As above	As above	Adjusted OR (95% CI)	1.03 (0.96-1.11)	As above

First author, year (reference)	Reference and comparison group	Indicator data source	Maternal or offspring outcome	Outcome data source	Sample size	Statistical results definition	Result	Adjustment for confounders
Berni, 2018 ([49])	PCOS vs. no PCOS (assessed based on Read codes C164.00, C164.12, C165.00)	CPRD	Offspring ADHD	HES	17,668	Adjusted OR (95% CI)	1.34 (0.96-1.89)	Age, body mass index category, primary care practice, history of prior mental health disorder
	As above	CPRD	Offspring autism spectrum disorder	As above	As above	Adjusted OR (95% CI)	1.75 (1.27-2.46)	As above
Rees, 2016 ([20])	PCOS vs. no PCOS	CPRD	Miscarriage resulting in hospital admission	HES	22075	Adjusted HR (95% CI)	1.70 (1.56-1.84)	Age, BMI, primary care practice, number of previous births, smoking history
Rees, 2016 ([20])	As above	CPRD	Pre-eclampsia	HES and CRPD	19,502	Adjusted HR (95% CI)	1.31 (1.16-1.49)	Age, BMI, primary care practice, multiple gestation, number of previous births, smoking history
Rees, 2016 ([20])	As above	CPRD	Gestational diabetes	HES and CRPD	19,502	Adjusted HR (95% CI)	1.42 (1.21-1.67)	As above
Rees, 2016 ([20])	As above	CPRD	Jaundice	HES	12,363	Adjusted OR (95% CI)	1.20 (1.03-1.39)	As above
Rees, 2016 ([20])	As above	CPRD	Respiratory complications (offspring)	HES	12,363	Adjusted OR (95% CI)	1.20 (1.06-1.37)	As above
Rees, 2016 ([20])	As above	CPRD	Hypoglycaemia (offspring)	HES	12,363	Adjusted OR (95% CI)	1.31 (0.99-1.74)	As above
Rees, 2016 ([20])	As above	CPRD	Feeding issues	HES	12,363	Adjusted OR (95% CI)	1.21 (0.96-1.52)	As above

CI, confidence intervals; CPRD, Clinical Practice Research Datalink; HES, hospital episodes statistics; HR, Hazard Ratio; OR, odds ratio; PCOS, polycystic ovary syndrome