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Maternal Demographic Patterns in Medication use During Pregnancy: A Nationwide Register Study

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ABSTRACT

In recent years, medication use during pregnancy has increased, yet its association with maternal characteristics remains unclear. To address this gap, we aimed to investigate how maternal age, pre-gestational body mass index (BMI), smoking, parity, ethnic origin and employment status relate to medication use during pregnancy. We conducted a nationwide Danish registry study, including 698 447 clinically recognised pregnancies with a gestational age of at least 10 weeks, spanning from 2008 to 2018. Medication use was estimated based on prescription redemptions during pregnancy and stratified by the demographic factors of interest. Overall, 60.3% of pregnant women redeemed at least one prescription, while 28.9% redeemed multiple medications. Notably, higher usage was observed among women aged 35 or older, those with a BMI of 30 kg/m^2 or more, smokers, multipara, Black women, and early retirees. Medication combination patterns differed with the demographic subgroups. These findings highlight notable differences in medication use among demographic groups during pregnancy, underscoring the need for tailored healthcare strategies during pregnancy.

1 | Background

The global use of medications during pregnancy is increasing [1–6], with prevalence rates reaching 93% in France, 85% in Germany and 64% in the United States [7–9]. However, these estimates vary due to differences in data quality and data inclusion, such as prescription, over-the-counter, and hospital medications and supplements. Consequently, use of multiple medications (≥2 medications) prevalence during pregnancy ranges from 4.9 to 62.4% [10]. The safety and potential side effects of use of multiple medications in pregnancy, especially if used concurrently, remain largely undetermined due to the inherent complexity of drug interactions and physiological changes during pregnancy [11]. Factors such as drug–drug interactions, drug–disease interactions, and variations in maternal, placental and foetal physiology and genetics can influence the pharmacokinetics, pharmacodynamics, and risk of adverse effects of medications used in pregnancy [12–16]. Medication use during pregnancy is highest in the first trimester, coinciding with the period of highest risk of serious foetal impact due to organogenesis [1, 6]. Furthermore, observational studies linking medication use and health outcomes are often biased by indication, where the condition leading to the prescription rather than the medication itself may be responsible for the

Summary

In a large Danish study of nearly 700 000 pregnancies from 2008 to 2018, we explored how often pregnant women used medications during pregnancy and how this varied with factors like maternal age, BMI, smoking, number of previous births, ethnicity and employment status. Over 60% filled at least one prescription, and almost 30% used multiple medications. Older women, those with obesity, smokers, Black women and early retirees were more likely to use medications, and in different combinations. These findings show that medication use during pregnancy varies among different groups.

observed association. Use of multiple medications during pregnancy frequently results from pre-existing or emerging multimorbidity [5, 17], further complicating safety studies due to strong confounding by indications. Accordingly, counselling pregnant women on multiple medications during is challenging and rests on scarce evidence. Few studies have investigated the associations between use of multiple medications and maternal demographic characteristics. This knowledge gap hampers the identification of vulnerable subgroups of pregnant women and the opportunity to provide individualised advice on medication. By understanding how different subgroups of pregnant women use medications and the unique challenges they face, healthcare providers may offer more tailored, patient-centric medication guidance. This study aimed to describe the use of one or multiple prescription medications during pregnancy in relation to maternal age, pre-gestational BMI, smoking, parity, ethnic origin, and employment status.

2 | Materials and Methods

2.1 | Cohort Selection

The study was conducted in accordance with the Basic & Clinical Pharmacology & Toxicology policy for experimental and clinical studies [18]. The Danish national cohort used in this study has previously been presented in detail [1]. Briefly, we identified all clinically recognised pregnancies with gestational age (GA) above or equal to 10 weeks in the Danish National Patient Registry (based on diagnosis codes) and the Danish Medical Birth Register (all registered records) between 2008 and 2018 (Figure 1), see previous study for more details [1]. The final study cohort included 698 447 pregnancies. GA was estimated based on ultrasound measurements in early pregnancy or, if missing, last day of last menstrual period. All pregnancies had complete information on date for end of pregnancy and GA.

2.2 | Maternal Characteristics

We retrieved data from various national Danish registers during the pregnancy period, including prescription redemptions from Danish National Health Service Prescription Database [19], employment status from Employment Classification Module [20], maternal age at conception from Danish Civil Registration System [21], and pre-gestational BMI, smoking status, parity, and ethnic origin from Danish Foetal Medicine Database [22]. Information on pre-gestational BMI and parity was included from the Danish Foetal Medicine Database only if not available from the Danish Medical Birth Registry. Employment status was grouped according to Statistics Denmark's categories: "In education", "Early retiree", "Self-employed or working spouse", "Transfer payment", "Unemployed", "Wage earner", "Wager earner—management level" [23]. These classifications reflect the Danish welfare system, which provide universal, state-guaranteed financial aid. "Early retiree" refers to women retired early due to chronic health-related problems, while "transfer payment" denotes those receiving state financial support due to temporary inability to work caused by health- or social-related problems. "Unemployed" women are those not currently employed and not classified under the other employment categories. Ethnic origin, documented in the Danish Foetal Medicine Database, is assessed during the first trimester scan by the sonographer in collaborations with the pregnant women, following subgrouping approach by the Foetal Medicine Foundation (see subgrouping specifications in Table 2) [24–26].

2.3 | Observed Medication Redeemed

Use of one or multiple prescription medications during pregnancy was reported for two time periods; the first trimester and the complete pregnancy. The first trimester was defined as from 4 weeks before the conception date to 69 days after (until GA 11 + 6) or to abortion (if the pregnancy ended before GA 11 + 6), while the complete pregnancy period was defined as from 4 weeks before the conception date to the end of pregnancy (birth or abortion). The conception date was calculated by identifying the date for the end of the pregnancy in the register, subtracting the GA in days and adding 14 days. From the Danish National Health Services Prescription Database, we collected information on redemption date and the Anatomical Therapeutics Chemical (ATC) classification code for each redeemed prescription [27]. As we were interested only in the number of redeemed unique medication types during pregnancy (and not the total number of redeemed prescriptions), we removed duplicates of the exact same ATC code at the fifth level within the period of interest. Use of multiple medications was defined as at least two redeemed unique medication types within the time period of interest.

2.4 | Statistical Analysis

The prevalence of one or multiple medications during the entire pregnancy period and the first trimester was reported overall and stratified by maternal age (<25 years, 25–29 years, 30–34 years, ≥ 35 years), pre-gestational BMI (<18.5 kg/m^2, 18.5 to <25 kg/m^2, 25 to <30 kg/m^2, ≥30 kg/m^2), smoking status (no smoking, former smoker, smoking during pregnancy), parity (nulliparity, multiparity), ethnic origin (Black, East Asian, Other, South Asian, White) and employment status (in education, early retiree, self-employed or working spouse, receiving transfer payments, unemployed, wage earner, wage earner at management level) [23–26]. Prevalence stratified by employment status was reported crude and age-adjusted, with the reference population being the entire study cohort. In a sub analysis, prevalence was

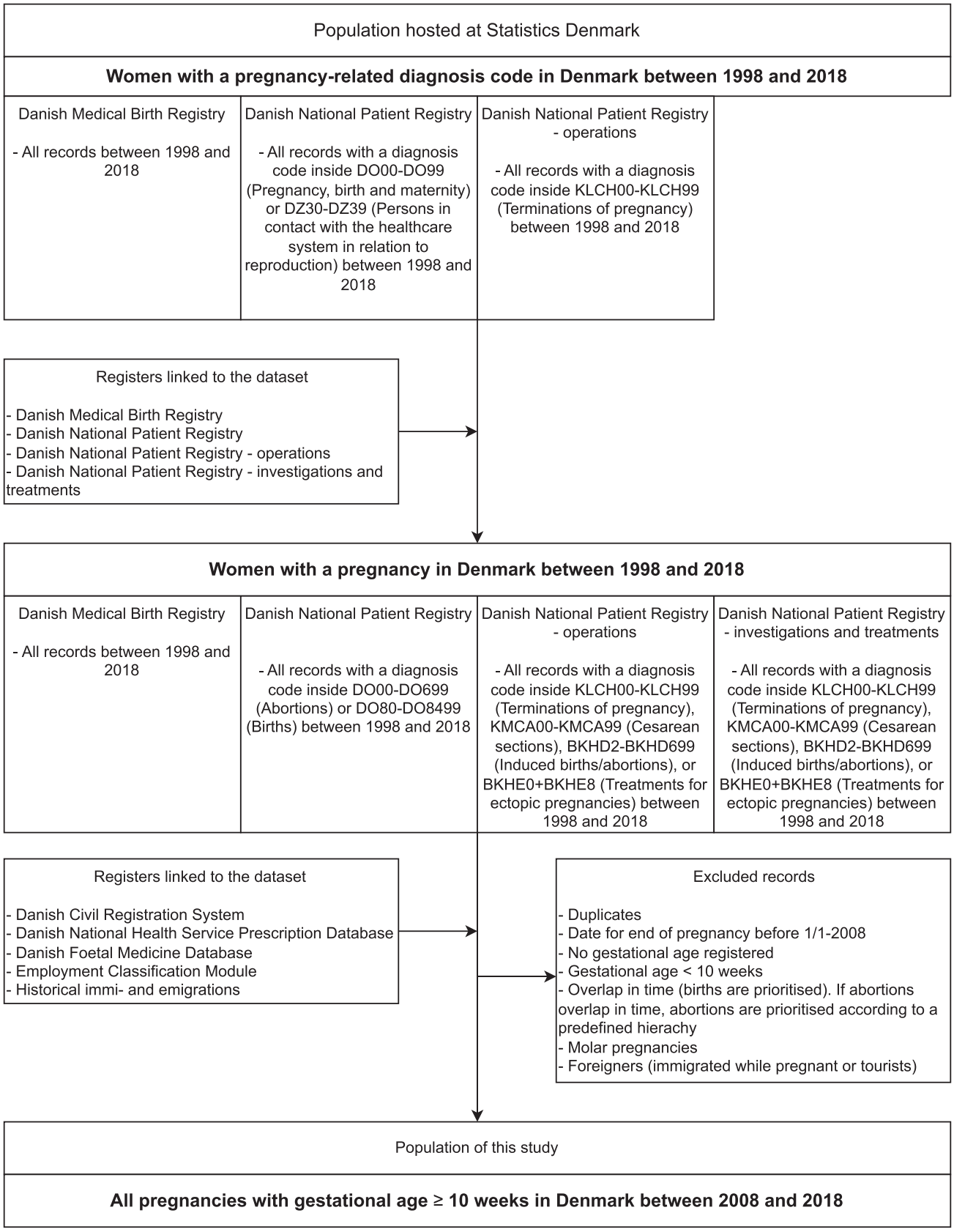

FIGURE 1 | Flowchart of merge of registers and identification of included pregnancies.

further stratified by employment status and then by ethnic origin and smoking status. The 10 most prevalent ATC codes for the entire pregnancy period were reported at the first level of the ATC code. The prevalence of pairwise medication combinations at the fist ATC level, stratified by employment status, was shown as bar plots in polar coordinates (polar plot). The 10 most

prevalent combinations at the second ATC level, stratified by employment status, were presented as a bar plot. Data management, analyses and graphs/visualisations were conducted and presented in R Studio version 2022.12.0 (RStudio Team, Boston, USA) with R version 4.2.1 at Statistics Denmark.

2.5 | Ethics

The study was approved by the Danish Data Protection Agency (Aarhus University journal number 2016-051-000001, serial number 2227, 2 March 2021). Scientific ethics committee permission is not required for register-based studies in Denmark.

3 | Results

The cohort comprised 698 447 pregnancies with a GA of 10 weeks or more, resulting in either abortions (GA < 22 weeks) or births (GA ≥ 22 weeks) between 2008 and 2018. Most of the pregnancies led to births (91.4%), and among these, most were singleton pregnancies (98.0%) (Table 1). Table 2 shows the characteristics of the study population. The majority of the pregnant women in the dataset were non-smokers (89.1%) between 25 and 34 years of age (65.9%), had a healthy pre-gestational BMI in the 18.5 to <25 kg/m^2 range (61.2%), and were White (93.4%). The largest employment status group was wage earners (49.2%), while only 0.8% were early retirees. Slightly more than half of all pregnancies were carried by multiparous women (53.5%) (Table 2).

TABLE 1 | Pregnancy characteristics.

Characteristics, $N = 698\,447$	*n* (%)
Type of pregnancy	
Abortions (GA < 22 weeks)	59 917 (8.6%)
Births (GA ≥ 22 weeks)	638 530 (91.4%)
Number of foetuses	
Multiple pregnancy	12 594 (2.0%)
Singleton pregnancy	625 936 (98.0%)
Missing	*59 917*
Gestational age at end of pregnancy	
Early abortion (GA < 12 weeks)	39 112 (5.6%)
Late abortion (GA ≥ 12 weeks to GA < 22 weeks)	20 805 (3.0%)
Extremely preterm births (GA ≥ 22 weeks to GA < 28 weeks)	2756 (0.4%)
Very preterm births (GA ≥ 28 weeks to GA < 32 weeks)	4042 (0.6%)
Moderate to late preterm births (GA ≥ 32 weeks to GA < 37 weeks)	30 980 (4.4%)
Term births (GA ≥ 37 weeks to GA < 42 weeks)	579 846 (83.0%)
Postterm births (GA ≥ 42 weeks)	20 906 (3.0%)

TABLE 2 | Maternal characteristics.

Characteristics, $N = 698\,447$	*n* (%)
Maternal age	
< 25 years	111 434 (16.0%)
25–29 years	232 917 (33.3%)
30–34 years	227 918 (32.6%)
≥ 35 years	126 133 (18.1%)
Missing	*45*
Pre-gestational BMI	
<18.5 kg/m^2 (underweight)	28 010 (4.4%)
18.5 to <25 kg/m^2 (normal weight)	391 809 (61.2%)
25 to <30 kg/m^2 (overweight)	137 184 (21.4%)
≥ 30 kg/m^2 (obese)	83 246 (13.0%)
Missing	*58 198*
Smoking status during pregnancy	
No	514 307 (89.1%)
Former smoker	9487 (1.6%)
Yes	53 724 (9.3%)
Missing	*120 929*
Parity	
Nullipara	298 194 (46.5%)
Multipara	343 595 (53.5%)
Missing	*56 658*
Ethnic origin[a]	
Black	7009 (1.2%)
East Asian	13 391 (2.4%)
Other	10 172 (1.8%)
South Asian	7260 (1.3%)
White	531 181 (93.4%)
Missing	*129 434*
Employment status	
Early retiree	5247 (0.8%)
In education	48 983 (7.0%)
Receiving transfer payment	156 831 (22.5%)
Self-employed or working spouse	13 795 (2.0%)
Unemployed	6.254 (0.9%)
Wage earner	343 087 (49.2%)
Wage earner—management level	123 188 (17.7%)
Missing	*1062*

[a]Black origin refers to African, Caribbean and Afro-American. East Asian origin refers to Chinese, Korean and Japanese. South Asian origin refers to Indian, Pakistani and Bangladeshi. White origin refers to European, Middle East, North African and South American. Other origin refers to both mixed racial origin and racial origin not fitting into the other categories.

3.1 | Use of One or Multiple Medications During Pregnancy

In our cohort, 60.3% of all pregnancies were exposed to at least one prescription medication (Table 3), with 36.6% redeeming a prescription in their first trimester. Use of multiple medications, defined as redemption of at least two prescriptions during pregnancy, was observed in 28.9% of pregnancies. The prevalence of medication use was above the overall prevalence among women aged ≥ 35 years (65.1%), those with a pre-gestational BMI ≥30 kg/m^2 (68.6%) (eTable 1), and among smokers (66.0%), multipara (62.4%), Black women (64.5%) (eTable 2), and women in early health-related retirement (78.8%) (Table 3). These groups also had an above overall prevalence of first trimester medication use and use of multiple medications during pregnancy and in their first trimester (except according to parity where nullipara had comparable use of multiple medications in the first trimester relative to multipara (30.0% for nullipara versus 29.5% for multipara)). Variations in medication use between employment status groups did not change when adjusted for maternal age (Table 3).

Medication use during pregnancy varied with maternal age, being most prevalent among women above 35 years (65.1%) and under 25 years (59.2%), and while women aged 25–29 years had the lowest prevalence at 58.1%. Medication use varied also by pre-gestational BMI, with higher BMI levels showing higher proportions of use (eTable 1). The prevalence of medication use was 66.0% among smokers, 63.6% among former smokers, and 60.9% among never-smokers. Early retirees had an absolute >15% higher overall medication use and an absolute >22% higher use of multiple medications compared to women receiving transfer payments, who had the second-highest prevalence (Table 3). Variations in medication use during pregnancy were observed across employment status, including within subgroups stratified by ethnic origin and smoking status (eTable 3).

3.2 | Variations in Medication Use Among Subgroups

Anti-infective medications for systemic use (ATC code J), including antibiotics for systemic use (ATC code J01), were the most prevalent prescription medications during pregnancy (28.4%) (eTable 4). This pattern remained evident when stratifying by maternal age, pre-gestational BMI, smoking status, parity, ethnic origin, and employment status. In general, we observed a similar pattern of medication type redemptions among all subgroups according to maternal age, pre-gestational BMI, smoking status and parity, albeit subgroup prevalences differed. However, when stratified by ethnic origin, we found that among Black women medications addressing conditions within the alimentary tract and metabolism (ATC code A) constituted a higher proportion of the prescriptions redeemed in pregnancy (18.2%) (Figure 2A). The most prevalent A-group ATC code medication among Black women was medications for acid-related disorders (ATC code A02) (9.0%) and medications for functional gastrointestinal disorders (ATC code A03) (6.1%) (eTable 4). Noticeably, when stratified by employment status, pregnant women in early health-related retirement had an overall higher prevalence of all medications; especially nervous system medications (ATC code N) were highly prevalent in this group (36.5%) (Figure 2B). Analgesics (ATC code N02) (15.2%) and psychoanaleptics (ATC code N06) (17.3%) were the most redeemed prescriptions among N-group ATC code medications. This group of pregnant women also frequently used medications for conditions within the alimentary tract and metabolism group (ATC code A) (21.7%) (Figure 2A), where the most frequently used medication type was medications for acid-related disorders (ATC code A02) (11.3%) (eTable 4).

3.3 | Combinations of Medication Types

The most prevalent combination of medication used in the first trimester was anti-infectives (ATC code J) and medication used to treat conditions in the genito-urinary system, including sex hormones (ATC code G) (Figure 3A). When we examined use of medication in the first trimester based on the second level of the ATC codes, the most prevalent combination was an antibiotic for systemic use (ATC code J01) combined with a sex hormone or genital system modulator (ATC code G03) (Figure 4A).

A distinct pattern emerged when stratifying by employment status (Figure 3). Pregnant women in early retirement exhibited a notably higher prevalence of medication combinations containing nervous system medications (ATC code N) during their first trimester. Conversely, the other employment status groups used combinations at a much lower prevalence where combinations predominantly contained anti-infectives (ATC code J) and medications for the genito-urinary system and sex hormones (ATC code G), except for pregnant women receiving transfer payments (Figure 3D). At the second level of the ATC codes, early retired pregnant women commonly used combinations of antibiotics (ATC code J01) and psychoanaleptics (ATC code N06) (Figure 4). Within the top 10 most prevalent combinations at this level, we also saw combination with psycholeptics (ATC code N05), analgesics (ATC code N02) and antiepileptics (ATC code N03) (Figure 4B).

Overall, pregnant women who were in education, receiving transfer payments, or unemployed exhibited similar patterns, with combinations predominantly containing anti-infectives (ATC code J). Conversely, wage earners, management-level wage earners, and self-employed women or working spouses more frequently used combinations containing medications for the genito-urinary system and sex hormones (ATC code G) (Figure 3). At the second level of the ATC codes, self-employed women or working spouses and management-level wage earners in particular used combinations containing sex hormones or modulators of the genital system (ATC code G03) (Figure 4E,H).

4 | Discussion

4.1 | Principal Findings

We found that redemption of one or multiple medications during pregnancy was more prevalent among women above the age of 35 years, women with obesity, smokers, Black women and, especially, among women in early retirement. Differences in medication combination patterns were particularly notable among pregnant women in early retirement, reflecting variations in maternal demographics and potential underlying health conditions.

TABLE 3 | Prevalence of redemption of one or multiple medications during pregnancy stratified by employment status.

Characteristics	At least 1 redeemed medication during pregnancy		At least 1 redeemed medication during first trimester		Use of multiple medications during pregnancy[a]		Use of multiple medications during first trimester[a]	
	Crude prevalence, *n* (%)	Age-adjusted prevalence, %	Crude prevalence, *n* (%)	Age-adjusted prevalence, *n*	Crude prevalence, *n* (%)	Age-adjusted prevalence, *n*	Crude prevalence, *n* (%)	Age-adjusted prevalence, *n*
Overall								
N = 698 447	421 268 (60.3%)		255 535 (36.6%)		201 832 (28.9%)		104 154 (14.9%)	
Employment status								
Early retiree, *N* = 5247	4136 (78.8%)	77.8%	3250 (61.9%)	60.1%	2841 (54.1%)	51.8%	2023 (38.6%)	36.0%
In education, *N* = 48 983	27 710 (56.6%)	58.2%	16 949 (34.6%)	35.8%	12 006 (24.5%)	27.0%	6020 (12.3%)	14.0%
Receiving transfer payments, *N* = 156 831	99 413 (63.4%)	63.9%	61 691 (39.3%)	40.2%	50 043 (31.9%)	32.8%	25 483 (16.2%)	17.2%
Self-employed or working spouse, *N* = 13 795	7948 (57.6%)	56.6%	4781 (34.7%)	33.0%	3736 (27.1%)	25.7%	1977 (14.3%)	13.1%
Unemployed, *N* = 6254	3677 (58.8%)	59.0%	2348 (37.5%)	37.8%	1645 (26.3%)	26.5%	911 (14.6%)	14.7%
Wage earner, *N* = 343 087	206 600 (60.2%)	60.1%	124 089 (36.2%)	36.1%	97 936 (28.5%)	28.4%	50 221 (14.6%)	14.5%
Wage earner—management level, *N* = 123 188	71 613 (58.1%)	56.6%	42 353 (34.4%)	32.8%	33 540 (27.2%)	25.4%	17 486 (14.2%)	12.6%
Missing	*171*		*74*		*85*		*33*	

[a]Two or more redeemed prescriptions.

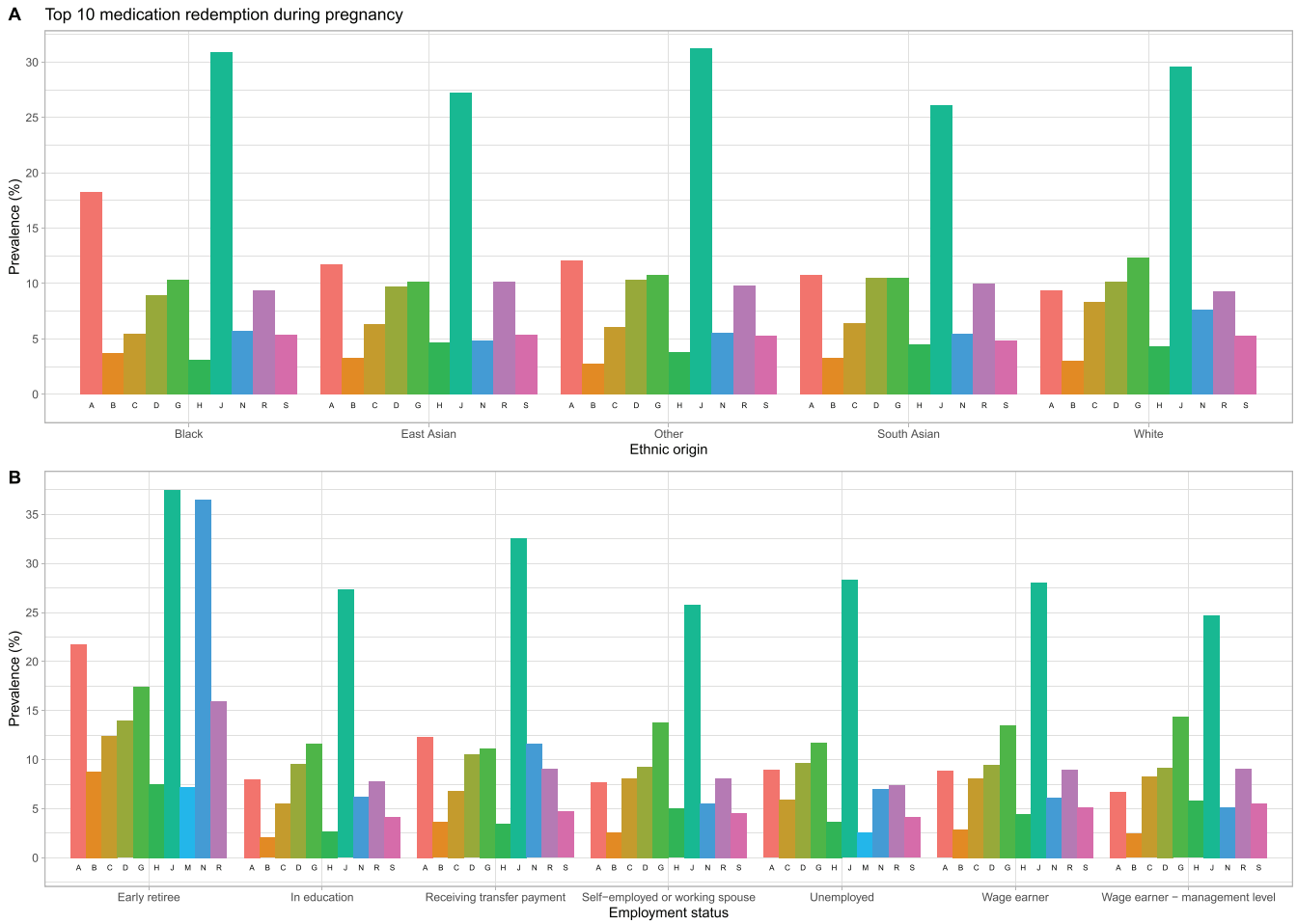

FIGURE 2 | Top 10 most prevalent medication types (first level of the ATC code) during pregnancy in Denmark, 2008–2018, stratified by ethnic origin (A) and employment status (B). A, alimentary tract and metabolism; B, blood and blood forming organs; C, cardiovascular system; D, dermatologicals; G, genito-urinary system and sex hormones; H, systemic hormonal preparations, excluding sex hormones and insulins; J, anti-infective for systemic use; M, musculo-skeletal system; N, nervous system; R, respiratory system; S, sensory organs.

4.2 | Interpretation

Our findings align with previous studies linking maternal demographics to medication use [2, 3, 5, 17, 28–35]. The high prevalence of medication use among the youngest and oldest pregnant women likely reflects the combination of health needs, awareness of risks, and socioeconomic factors.

We found that higher frequency of medication use was observed in women with a higher BMI (eTable 1), consistent with prior research [2, 5, 28, 31]. Women with higher BMI often present with comorbidities such as diabetes or hypertension, necessitating medication during pregnancy [36]. For instance, women with obesity are more likely to require antihypertensive or antidiabetic medications, contributing to a higher use of multiple medications. This reflects the significant burden of multimorbidity in this group, which often extends into pregnancy.

Smokers and former smokers demonstrated elevated medication use, consistent with their increased prevalence of chronic conditions and health complications [2, 28, 30, 31, 37, 38]. Notably, former smokers—those who quit before pregnancy—also exhibited higher medication use compared to never-smokers, indicating that pre-pregnancy smoking status may have long-term health implications affecting medication needs during pregnancy [5, 33].

Contradictory findings exist for parity, with both nulliparity and multiparity linked to higher medication use during pregnancy [31, 37, 39]. Use of multiple medications is reported as more common among multipara [5]. In our study, medication redemption was 1.5% higher in multipara than nullipara, possibly reflecting age differences between groups.

Black women exhibited unique medication patterns, with higher use of alimentary tract and metabolic medications (ATC code A) (Figure 2A), differing from both women of White origin and other ethnic minority groups. While all non-White groups in this study are considered minorities in the Danish context, the medication patterns of women of East Asian, South Asian, and other origin were similar to those of White origin. A distinct pattern of medication use among ethnic minorities has been reported in other studies [3, 5, 29, 40]. Potential factors include disparities in healthcare access, symptom recognition, underlying genetic predispositions, or socioeconomic challenges. The small sample size and descriptive nature of this study limit definitive conclusions, but these findings highlight the need for further

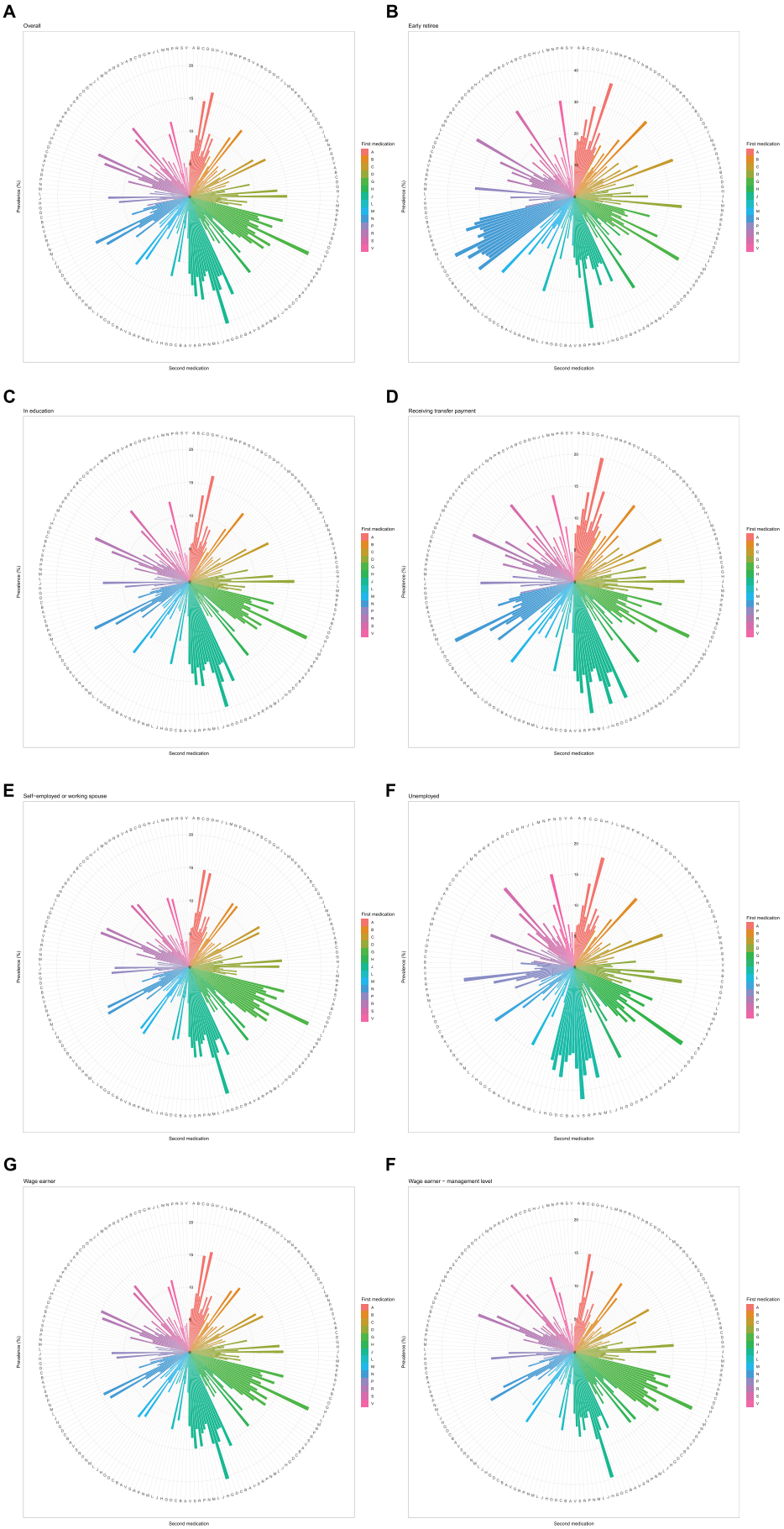

FIGURE 3 | Legend on next page.

FIGURE 3 | Combinations of prescription medications in the first trimester in Denmark, 2008–2018, overall and stratified by employment status. The polar plot illustrates the prevalence of two-drug combinations based on the first level of the ATC code. Different colours indicate the ATC code of the first medication in each combination, while each bar within the circular plot corresponds to the ATC code of the second medication. The radial distance from the centre reflects the prevalence of each combination. A, alimentary tract and metabolism; B, blood and blood forming organs; C, cardiovascular system; D, dermatologicals; G, genito-urinary system and sex hormones; H, systemic hormonal preparations, excluding sex hormones and insulins; J, anti-infective for systemic use; L, antineoplastic and immunomodulating agents; M, musculo-skeletal system; N, nervous system; P, antiparasitic products, insecticides and repellents; R, respiratory system; S, sensory organs; V, various.

research into medication use across different ethnic groups during pregnancy.

4.3 | Use of Multiple Medications in Pregnancy

Use of multiple medications, defined here as the redemption of two or more distinct medications during pregnancy, was more common among women with obesity, smokers, and those with more vulnerable employment status. While some use of multiple medications reflects appropriate management of chronic conditions [41], it raises concerns about potential drug interactions and risks to foetal development. The distinction between appropriate and inappropriate use of multiple medications is critical [41]. Appropriate use of multiple medications involves the rational management of comorbidities, whereas inappropriate use may result from fragmented care or insufficient consideration of potential risks. For example, the simultaneous use of medications with overlapping toxicities or limited benefit could pose additional risks to the mother and foetus. Future studies should investigate whether current prescribing practices adequately distinguish between these scenarios and ensure optimal care for pregnant women.

4.4 | Employment Status and Medication Use

Employment status disparities in medication use were evident in our study, with women on early health-related retirement or receiving transfer payments showing the highest rates of medication redemption. These women often used nervous system medications (ATC code N), which include analgesics and medications for mental health disorders. This pattern aligns with previous research [33, 35] suggesting that poor physical and mental health mediates the relationship between lower socioeconomic status and higher medication use [42, 43]. Additionally, the relationship between employment status and medication use appears to be complex and bidirectional. While more vulnerable employment status might contribute to higher medication use through poorer health, chronic health conditions requiring medication may also hinder educational attainment or stable employment, resulting in fewer resources and reinforcing socioeconomic disadvantages.

Vulnerable employment groups may face additional challenges, including limited health literacy, which can impair their ability to navigate complex healthcare systems and make informed decisions about medication use [44, 45]. This may lead to both higher overall medications use and a greater likelihood of inappropriate use. The more frequent use of nervous system medications (ATC code N) among early retirees reflects the intersection of health conditions and social factors. For instance, these patterns are consistent with findings that pregnant women with multimorbidity often use selective serotonin re-uptake inhibitors in the first trimester [5]. Addressing these disparities requires attention to health literacy and equitable access to preventive care and support, particularly for socioeconomically vulnerable populations.

These patterns may also be influenced by structural factors, such as a lack of awareness about available services or difficulties in utilising preventive care and support effectively. For example, early retirees in our study commonly used combinations of psychoanaleptics (ATC code N06) and antibacterials (ATC code J01) in the first trimester. The high prevalence of multiple medication combinations in this group may reflect a higher burden of multimorbidity, which could pose risks to maternal and foetal health, regardless of the specific combinations.

Despite Denmark's universal healthcare system, our findings show distinct and potentially suboptimal medication use patterns among groups with vulnerable employment status. Further research is needed to explore whether these groups experience higher medicalisation or face challenges in accessing and using health information and services effectively. These differences highlight the importance of considering medication patterns alongside demographic characteristics when addressing medication safety and health inequalities.

4.5 | Strength of the Study and Limitations of the Data

This study utilised a robust, nationwide cohort from Denmark with universal healthcare and complete follow-up for pregnancies. Data integration was facilitated by unique personal identifiers [46]. Pregnancies with a GA of 10 weeks or more were included to focus on those likely carried to term. Including all pregnancies would have required accounting for early medical abortions, but the decreasing abortion rate in Denmark reduces potential bias [47, 48]. GA was primarily determined by ultrasound (around 90% [49]), though some relied on less accurate last menstrual period estimates.

Maternal characteristics, such as age, BMI, and smoking status, were self-reported at the first trimester scan, introducing potential misclassification, especially due to social desirability. Ethnic origin was assessed collaboratively by sonographers and the pregnant women, raising risks of misclassification, particularly for non-White groups.

Medication data came from a registry of redeemed prescriptions, eliminating recall bias but not including hospital-prescribed,

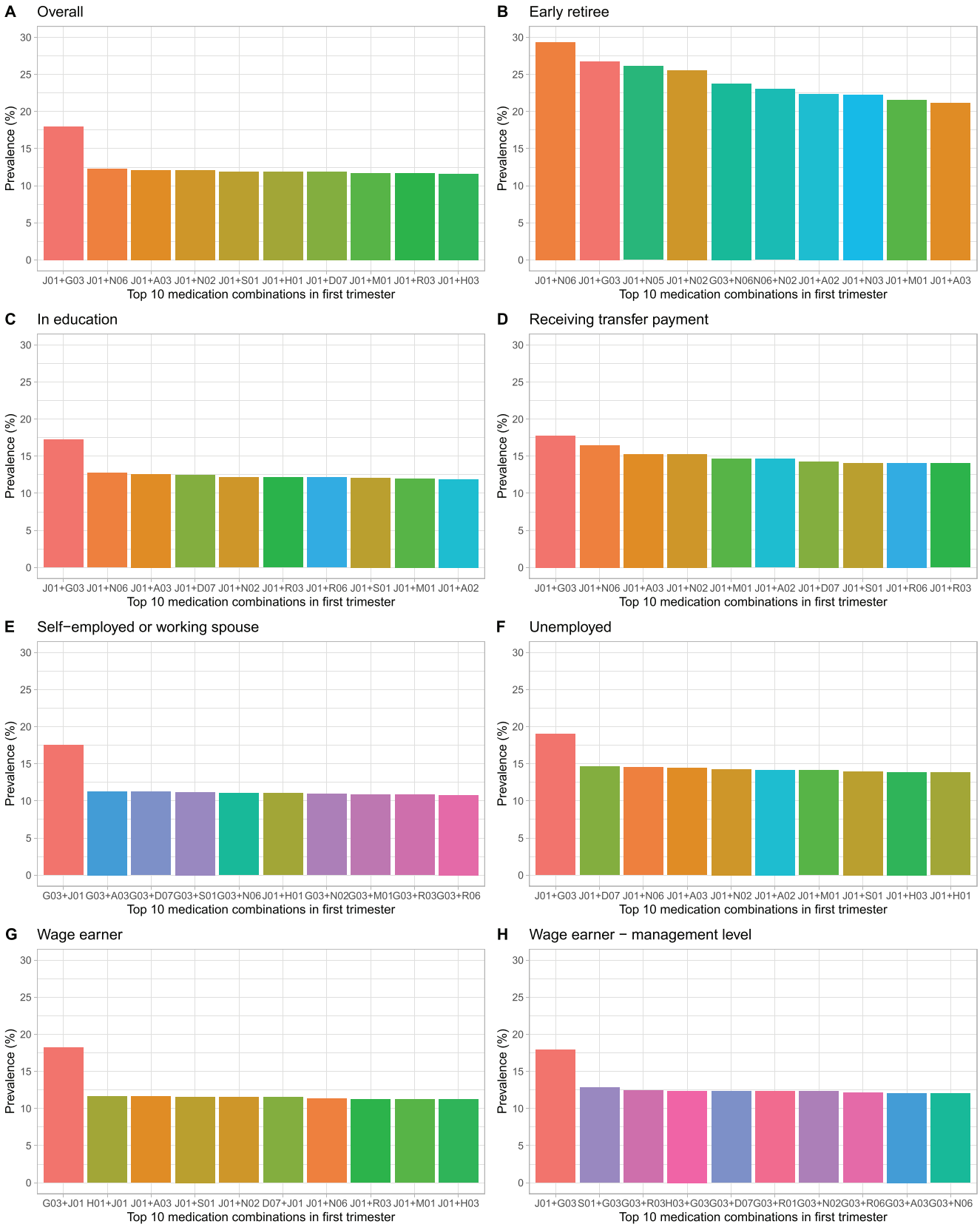

FIGURE 4 | Top 10 prevalent medication combinations at the second level of the ATC code among all pregnancies in first trimester, overall and stratified by employment status. A02, drugs for acid-related disorders; A03, drugs for functional gastrointestinal disorders; D07, corticosteroids, dermatological preparations; G03, sex hormones and modulators of the genital system; H01, pituitary and hypothalamic hormones and analogues; H03, thyroid therapy; J01: antibacterials for systemic use; M01, anti-inflammatory and antirheumatic products; N02, analgesics; N03, antiepileptics; N05, psycholeptics; N06, psychoanaleptics; R01, nasal preparations; R03, drugs for obstructive airway diseases; R06, antihistamines for systemic use; S01, ophthalmologicals.

over-the-counter, and self-medicated drugs. The analysis of multiple medication use focused on two distinct medications during defined periods, without accounting for dosage or treatment duration, limiting the ability to assess true concurrent use. While some prescriptions may reflect simultaneous medication use, others may represent sequential treatments for different conditions. Our broad definition of the first trimester, which included even contraceptives, might have overestimated the true use of medication during early pregnancy. However, this approach provides valuable insights into medication use patterns from conception onward, including transitions in treatment and potential cumulative exposures.

5 | Conclusions

Medication use during pregnancy was notably elevated among older women, those with a high BMI, smokers, Black women, and early retirees, with diverse combinations of medications observed across these maternal demographic subgroups. These variations highlight the potential for differences in medication safety, including teratogenic risk, driven by medication patterns rather than solely by inherent demographic characteristics. Future research on pregnancy medication safety should thoroughly consider these maternal demographic factors and medication patterns. This underscores the necessity for tailored interventions and healthcare strategies to optimise maternal and foetal health outcomes across diverse populations.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data cannot be placed in a public repository as the data are hosted by Statistics Denmark. Current register legislation and the data confidentiality principles of Statistic Denmark are therefore applicable.

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Appendix A

ETABLE 1 | Prevalence of redemption of one or multiple medications during pregnancy stratified by maternal BMI.

Characteristics	At least 1 redeemed medication in pregnancy, $N = 421\,268$ Crude prevalence, *n* (%)	At least 1 redeemed medication in first trimester $N = 255\,535$ Crude prevalence, *n* (%)	Use of multiple medications in pregnancy $N = 201\,832$ Crude prevalence, *n* (%)	Use of multiple medications in first trimester $N = 104\,154$ Crude prevalence, *n* (%)
$< 18.5\,kg/m^2$ (underweight)	16 532 (59.0%)	9519 (34.0%)	7444 (26.6%)	3520 (12.6%)
$18.5 - < 25\,kg/m^2$ (normal weight)	233 447 (59.6%)	134 057 (34.2%)	107 513 (27.4%)	52 172 (13.3%)
$25 - < 30\,kg/m^2$ (overweight)	87 960 (64.1%)	52 429 (38.2%)	44 289 (32.3%)	22 329 (16.3%)
$\geq 30\,kg/m^2$ (obese)	57 105 (68.6%)	35 213 (42.3%)	31 195 (37.5%)	15 930 (19.1%)
Missing	*26 224*	*24 317*	*11 391*	*10 203*

ETABLE 2 | Prevalence of redemption of one or multiple medications during pregnancy stratified by ethnic origin.

Characteristics	At least 1 redeemed medication in pregnancy, $N = 421\,268$ Crude prevalence, *n* (%)	At least 1 redeemed medication in first trimester $N = 255\,535$ Crude prevalence, *n* (%)	Use of multiple medications in pregnancy $N = 201\,832$ Crude prevalence, *n* (%)	Use of multiple medications in first trimester $N = 104\,154$ Crude prevalence, *n* (%)
Black	4519 (64.5%)	2635 (37.6%)	2109 (30.1%)	946 (13.5%)
East Asian	7886 (58.9%)	4613 (34.4%)	3650 (27.3%)	1716 (12.8%)
Other	6344 (62.4%)	3691 (36.3%)	2927 (28.8%)	1390 (13.7%)
South Asian	4220 (58.1%)	2432 (33.5%)	1934 (26.6%)	918 (12.6%)
White	327 911 (61.7%)	190 766 (35.9%)	156 735 (29.5%)	75 985 (14.3%)
Missing	*70 388*	*51 398*	*34 477*	*23 199*

ETABLE 3 | Prevalence of at least one prescription medication redemption during pregnancy, stratified by employment status and ethnic origin or smoking status.

		Ethnic origin					Smoking in pregnancy		
n/*N* (%)[a]		Black, 4519/7009 (64.5%)	East Asian, 7886/13391 (58.9%)	Other, 6344/10172 (62.4%)	South Asian, 4220/7260 (58.1%)	White, 27911/531181 (61.7%)	No, 314490/514307 (61.1%)	Former smoker, 6038/9487 (63.6%)	Yes, 35454/53724 (66.0%)
Employment status	Early retiree, 4136/5247 (78.8%)	52/64 (81.2%)	53/72 (73.6%)	55/72 (76.4%)	45/54 (83.3%)	2859/3531 (81.0%)	2245/2781 (80.7%)	55/67 (82.1%)	804/1006 (79.9%)
	In education, 27710/48983 (56.6%)	274/449 (61.0%)	447/796 (56.2%)	439/698 (62.9%)	225/407 (55.3%)	20392/35119 (58.1%)	20021/34730 (57.6%)	371/635 (58.4%)	1733/2753 (62.9%)
	Receiving transfer payments, 99413/156831 (63.4%)	2569/3934 (65.3%)	3322/5642 (58.9%)	2860/4525 (63.2%)	1726/2903 (59.5%)	71258/108353 (65.8%)	64501/100405 (64.2%)	1847/2762 (66.9%)	16530/24022 (68.8%)
	Self-employed or working spouse, 7948/13795 (57.6%)	43/71 (60.6%)	193/312 (61.9%)	106/175 (60.6%)	100/184 (54.3%)	6081/10266 (59.1%)	6162/10412 (59.2%)	86/154 (55.8%)	419/699 (59.9%)
	Unemployed, 3677/6254 (58.8%)	103/133 (77.4)	90/134 (67.2%)	98/157 (62.4%)	54/94 (57.4%)	2386/3815 (62.5%)	2186/3453 (63.3%)	78/113 (69.0%)	492/798 (61.7%)
	Wage earner, $N = 206600/343087$ (60.2%)	1367/2166 (63.1%)	3037/5127 (59.2%)	2375/3845 (61.8%)	1515/2603 (56.5%)	165659/269470 (61.5%)	158468/259065 (61.2%)	3182/5062 (62.9%)	14289/22474 (63.9%)
	Wage earner—management level, 71613/123188 (58.1%)	107/177 (60.5%)	735/1289 (57.0%)	404/678 (59.6%)	553/935 (59.1%)	59235/100517 (58.9%)	60837/103283 (58.9%)	419/693 (60.5%)	1183/1965 (60.2%)

[a]The numbers do not add up to the total population due to missing data in some variables.

ETABLE 4 | Top 10 most prevalent ATC codes at the first level and the most prevalent ATC code at the second level overall and stratified by employment status and ethnic origin.

		Employment status							Ethnic origin				
n/*N* (%)[a]	Overall, *N* = 698 447	In education, *N* = 48 983	Retiree, *N* = 5247	Self-employed or working spouse, *N* = 13 795	Transfer payment, *N* = 156 831	Unemployed, *N* = 6254	Wage earner, *N* = 343 087	Wage earner—management level, N 123 188	Afro-Caribbean, *N* = 7009	Asian, N = 13 391	Caucasian, *N* = 531 181	Oriental, *N* = 7260	Other, N = 10 172
A: Alimentary tract and metabolism	64 612 (9.3%)	3922 (8.0%)	1141 (21.7%)	1066 (7.7%)	19 364 (12.3%)	559 (8.9%)	30 277 (8.8%)	8249 (6.7%)	1277 (18.2%)	1572 (11.7%)	49 543 (9.3%)	780 (10.7%)	1225 (12.0%)
A02: Drugs for acid-related disorders	24 713 (3.5%)	1450 (3.0%)	595 (11.3%)	415 (3.0%)	8429 (5.4%)	244 (3.9%)	10 802 (3.1%)	2762 (2.2%)	632 (9.0%)	36 (4.7%)	18 864 (3.6%)	340 (4.7%)	588 (5.8%)
A03: Drugs for functional gastrointestinal disorders	19 146 (2.7%)	1246 (2.5%)	288 (5.5%)	313 (2.3%)	6353 (4.1%)	161 (2.6%)	8850 (2.6%)	1926 (1.6%)	429 (6.1%)	497 (3.7%)	14 376 (2.7%)	260 (3.6%)	447 (4.4%)
B: Blood and blood forming organs	20 504 (2.9%)	999 (2.0%)	461 (8.8%)	354 (2.6%)	5689 (3.6%)	148 (2.4%)	9850 (2.9%)	2988 (2.4%)	258 (3.7%)	442 (3.3%)	15 957 (3.0%)	236 (3.3%)	282 (2.8%)
B03 : Antianaemic preparations	12 241 (1.8%)	618 (1.3%)	293 (5.6%)	206 (1.5%)	3813 (2.4%)	86 (1.4%)	5772 (1.7%)	1443 (1.2%)	172 (2.5%)	338 (2.5%)	9509 (1.8%)	167 (2.3%)	202 (2.0%)
C: Cardiovascular system	53 448 (7.7%)	2715 (5.5%)	653 (12.4%)	1119 (8.1%)	10 710 (6.8%)	371 (5.9%)	27 737 (8.1%)	10 128 (8.2%)	380 (5.4%)	849 (6.3%)	43 997 (8.3%)	463 (6.4%)	618 (6.1%)
C05: Vasoprotectives	46 873 (6.7%)	2424 (4.9%)	430 (8.2%)	994 (7.2%)	9171 (5.8%)	321 (5.1%)	24 283 (7.1%)	9236 (7.5%)	323 (4.6%)	758 (5.7%)	39 072 (7.4%)	397 (5.5%)	547 (5.4%)
D: Dermatologicals	67 567 (9.7%)	4679 (9.6%)	731 (13.9%)	1282 (9.3%)	16 451 (10.5%)	605 (9.7%)	32 513 (9.5%)	11 280 (9,2%)	628 (9.0%)	1302 (9.7%)	53 847 (10.1%)	760 (10.5%)	1053 (10.4%)
D01: Antifungals	23 604 (3.4%)	1530 (3.1%)	305 (5.8%)	435 (3.2%)	6030 (3.8%)	216 (3.5%)	11 184 (3.3%)	3892 (3.2%)	239 (3.4%)	411 (3.1%)	19 020 (3.6%)	240 (3.3%)	417 (4.1%)
D07: Corticosteroids, dermatological preparations	30 341 (4.3%)	2048 (4.2%)	297 (5.7%)	577 (4.2%)	7420 (4.7%)	270 (4.3%)	14 904 (4.3%)	4812 (3.9%)	269 (3.8%)	708 (5.3%)	23 885 (4.5%)	419 (5.8%)	501 (4.9%)

(Continues)

ETABLE 4 | (Continued)

		Employment status							Ethnic origin				
n/*N* (%)[a]	Overall, *N* = 698 447	In education, *N* = 48 983	Retiree, *N* = 5247	Self-employed or working spouse, *N* = 13 795	Transfer payment, *N* = 156 831	Unemployed, *N* = 6254	Wage earner, *N* = 343 087	Wage earner—management level, N 123 188	Afro-Caribbean, *N* = 7009	Asian, N = 13 391	Caucasian, *N* = 531 181	Oriental, *N* = 7260	Other, N = 10 172
G: Genito-urinary system and sex hormones	90 714 (13.0%)	5700 (11.6%)	914 (17.4%)	1907 (13.8%)	17 491 (11.2%)	733 (11.7%)	46 272 (13.5%)	17 672 (14.3%)	723 (10.3%)	1364 (10.2%)	65 275 (12.3%)	760 (10.5%)	1092 (10.7%)
G01: Gynaecological anti-infectives and antiseptics	27 302 (3.9%)	1593 (3.3%)	313 (6.0%)	535 (3.9%)	7374 (4.7%)	240 (3.8%)	13 322 (3.9%)	3915 (3.2%)	361 (5.2%)	453 (3.4%)	21 736 (4.1%)	275 (3.8%)	480 (4.7%)
G03: Sex hormones and modulators	63 528 (9.1%)	3866 (7.9%)	597 (11.4%)	1372 (9.9%)	10 044 (6.4%)	462 (7.4%)	33 183 (9.7%)	13 992 (11.4%)	368 (5.3%)	931 (7.0%)	44 671 (8.4%)	499 (6.9%)	638 (6.3%)
H: Systemic hormonal preparations, excluding sex hormones and insulins	30 374 (4.3%)	1304 (2.7%)	395 (7.5%)	688 (5.0%)	5400 (3.4%)	230 (3.7%)	15 247 (4.4%)	7100 (5.8%)	214 (3.1%)	624 (4.7%)	23 103 (4.3%)	327 (4.5%)	383 (3.8%)
H03: Thyroid therapy	14 109 (2.0%)	704 (1.4%)	181 (3.4%)	277 (2.0%)	2965 (1.9%)	127 (2.0%)	6703 (2.0%)	3144 (2.6%)	110 (1.6%)	382 (2.9%)	10 999 (2.1%)	163 (2.2%)	210 (2.1%)
J: Anti-infectives for systematic use	198 558 (28.4%)	13 376 (27.3%)	1966 (37.5%)	3558 (25.8%)	51 067 (32.6%)	1769 (28.3%)	96 267 (28.1%)	30 465 (24.7%)	2166 (30.9%)	3640 (27.2%)	157 167 (29.6%)	1892 (26.1%)	3176 (31.2%)
J01: Antibacterials for systemic use	185 086 (26.5%)	12 376 (25.3%)	1886 (35.9%)	3261 (23.6%)	48 482 (30.9%)	1665 (26.6%)	89 432 (26.1%)	27 895 (22.6%)	2062 (29.4%)	3492 (26.1%)	146 306 (27.5%)	1794 (24.7%)	3024 (29.7%)
M: Musculoskeletal system	16 584 (2.4%)	957 (2.0%)	377 (7.2%)	268 (1.9%)	5188 (3.3%)	158 (2.5%)	7611 (2.2%)	2019 (1.6%)	196 (2.8%)	253 (1.9%)	12 287 (2.3%)	148 (2.0%)	234 (2.3%)
M01: Anti-inflammatory and antirheumatic products	15 643 (2.2%)	907 (1.9%)	343 (6.5%)	251 (1.8%)	4846 (3.1%)	152 (2.4%)	7218 (2.1%)	1921 (1.6%)	174 (2.5%)	226 (1.7%)	11 609 (2.2%)	131 (1.8%)	215 (2.1%)

(Continues)

ETABLE 4 | (Continued)

		Employment status							Ethnic origin				
n/*N* (%)[a]	Overall, *N* = 698 447	In education, *N* = 48 983	Retiree, *N* = 5247	Self-employed or working spouse, *N* = 13 795	Transfer payment, *N* = 156 831	Unemployed, *N* = 6254	Wage earner, *N* = 343 087	Wage earner—management level, N 123 188	Afro-Caribbean, *N* = 7009	Asian, N = 13 391	Caucasian, *N* = 531 181	Oriental, *N* = 7260	Other, N = 10 172
N: Nervous system	51 701 (7.4%)	3060 (6.2%)	1914 (36.5%)	766 (5.6%)	18 175 (11.6%)	436 (7.0%)	20 968 (6.1%)	6366 (5.2%)	401 (5.7%)	642 (4.8%)	40 585 (7.6%)	396 (5.5%)	566 (5.6%)
N02: Analgesics	26 937 (3.9%)	1413 (2.9%)	795 (15.2%)	389 (2.8%)	8273 (5.3%)	217 (3.5%)	12 062 (3.5%)	3780 (3.1%)	292 (4.2%)	390 (2.9%)	21 712 (4.1%)	228 (3.1%)	327 (3.2%)
N06: Psychoanaleptics	20 846 (3.0%)	1384 (2.8%)	907 (17.3%)	294 (2.1%)	8833 (5.6%)	168 (2.7%)	7232 (2.1%)	2023 (1.6%)	69 (1.0%)	192 (1.4%)	16 125 (3.0%)	134 (1.8%)	189 (1.9%)
R: Respiratory system	62 476 (8.9%)	3812 (7.8%)	837 (16.0%)	1115 (8.1%)	14 141 (9.0%)	461 (7.4%)	30 888 (9.0%)	11 204 (9.1%)	655 (9.3%)	1361 (10.2%)	49 345 (9.3%)	726 (10.0%)	997 (9.8%)
R01: Nasal preparations	24 098 (3.5%)	1392 (2.8%)	234 (4.5%)	440 (3.2%)	4560 (2.9%)	150 (2.4%)	12 284 (3.6%)	5030 (4.1%)	257 (3.7%)	527 (3.9%)	19 403 (3.7%)	287 (4.0%)	381 (3.7%)
R03: Drugs for obstructive airways diseases	22 072 (3.2%)	1340 (4.2%)	398 (7.6%)	390 (2.8%)	5326 (3.4%)	161 (2.6%)	10 467 (3.1%)	3986 (3.2%)	167 (2.4%)	372 (2.8%)	17 407 (3.3%)	208 (2.9%)	334 (3.3%)
R06: Antihistamines for systemic use	21 025 (3.0%)	1446 (3.0%)	289 (5.5%)	351 (2.5%)	4954 (3.2%)	153 (2.4%)	10 336 (3.0%)	3490 (2.8%)	271 (3.9%)	579 (4.3%)	16 424 (3.1%)	286 (3.9%)	375 (3.7%)
S: Sensory organs	5030 (5.0%)	2037 (4.2%)	330 (6.3%)	625 (4.5%)	7398 (4.7%)	257 (4.1%)	17 541 (5.1%)	6835 (5.5%)	376 (5.4%)	713 (5.3%)	27 963 (5.3%)	354 (4.9%)	533 (5.2%)
S01: Ophthalmologicals	29 711 (4.3%)	1655 (3.4%)	268 (5.1%)	535 (3.9%)	5789 (3.7%)	208 (3.3%)	15 136 (4.4%)	6116 (5.0%)	317 (4.5%)	610 (4.6%)	23 709 (4.5%)	315 (4.3%)	429 (4.2%)

[a]Numbers do not add up due to missingness and potential classification differences. Note that multiple distinct ATC codes at the second level may correspond to a single ATC code at the first level, as duplicates have been removed.