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Preconception substance use and risk of unintended pregnancy

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Preconception substance use and risk of unintended pregnancy

**Submitted to
The School of Public Health
West Virginia University**

**In partial fulfillment of the requirements for the degree of
Doctor of Philosophy in
Epidemiology**

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Abstract

Background: In the United States, unintended pregnancy is a serious public health issue due to its persistent high prevalence. In the series of three studies, our first two investigations examined the risk and potential determinants of unintended pregnancy among substance and polysubstance using women of childbearing age. In the third study, we conducted a systematic review (SR) with meta-analysis (MA) to assess the association of illicit and recreational drugs to the risk of unintended pregnancy.

Methods: We performed a secondary data analysis on a subset of Pregnancy Risk Assessment Monitoring System (PRAMS) 2016-17 phase 8 data (n=75,543). The outcome variable was pregnancy intention. The exposure variable was substance use, including alcohol, cannabis, nicotine/tobacco, illicit/recreational drugs, and special medications, including prescription opioids, over-the-counter pain relief, and antidepressants. In the second study, the exposure variable was the use of alcohol in concert with other substances. We also evaluated the relation of specific sociodemographic and economic variables to the risk of unintended pregnancy. Data were analyzed using complex survey analysis. For the SR with MA, predetermined criteria were used to ascertain study eligibility. To identify eligible original studies for the full review, we screened abstracts from six electronic databases (PubMed (MEDLINE), Scopus, CINAHL, PsychINFO, and Web of Science) and citation indices from retrieved articles and recent reviews. The inverse variance method was used to calculate the pooled effect size.

Results: Overall, 41% of pregnancies were unintended. Approximately 57% of participants reported alcohol consumption, 17% reported smoking, and 10% cannabis use prior to conception. *Study 1:* Likelihood of unintended pregnancy was significantly associated with substance use, including cigarettes (Adjusted Odds Ratio (AOR):1.5, 95% CI: 1.4-1.6); use of other nicotine/tobacco products (AOR:1.4, 95% CI: 1.3-1.5); cannabis (AOR: 1.9, 95% CI: 1.5-2.3); illicit/recreational drugs (AOR:1.7, 95% CI: 1.2-2.4), prescription opioids (AOR:1.4, 95% CI: 1.02-1.9), and prescription antidepressants (AOR 1.8, 95% CI: 1.1-3.0). Among substance users, factors significantly associated with unintended pregnancy included maternal age <17, living in urban areas, lower educational attainment, annual income <FPL, not being married, and poor mental health. *Study 2:* The likelihood of unintended pregnancy was significantly elevated in those reporting co-use of alcohol with cigarette smoking (AOR: 1.5, 95%CI:1.4 – 1.6), cannabis (AOR: 2.0, 95%CI:1.6 – 2.4), tobacco/nicotine (AOR: 1.6, 95%CI:1.4 – 1.7), and illicit/recreational drugs (AOR: 1.8, 95%CI: 1.1 – 2.7). In addition, living in urban areas, income below the federal poverty level, and not being married were significant predictors of unintended pregnancy. *Study 3:* Our SR with MA included eight observational studies (N=38,520 women). Pooled findings indicated that illicit and recreational drugs use during the preconception period was significantly and positively associated with the likelihood of unintended pregnancy (pooled odds ratio (POR)=1.84, 95% CI: 1.4-2.4).

Conclusion: Findings of our two studies in a large representative sample of US women suggest that substance and polysubstance use during the preconception period significantly increases the likelihood of unintended pregnancy. Consistent with these results, the pooled findings of our SR with MA indicated a significant and positive association between the use of illicit and recreational drugs and the risk of unintended pregnancy. Collectively, these findings support a potential causal link between preconception substance use and subsequent risk of unintended pregnancy. These findings highlight the need for tailored screening, educational, and treatment programs and integrated family planning services to help reduce both substance use and unintended pregnancy among women of childbearing age.

Dedication

I dedicate my doctoral dissertation to my parents and my siblings. I cannot thank you enough for your love, support, and encouragement throughout my life.

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First, I would like to acknowledge and pay my warmest regards to my dissertation committee chair, Dr. Lesley Cottrell, whose invaluable expertise during this process and her insightful feedback pushed me to bring my work to a higher level. I would like to extend my sincere gratitude to all my committee members Dr. Kim Innes, Dr. Amna Umer, Dr. Toni Rudisill, and Dr. Wei Fang, for their indispensable guidance and support. I would like to thank the PRAMS working group for providing me with the data of my dissertation, the faculty and the staff of WVU School of Public Health, and Susan J. Arnold (WVU Health Sciences Library). A special thanks to Dr. Ubolrat Piamjariyakul for her support and guidance. My family and friends gave me love and support during this journey. Lastly, I wish to thank my brother Imran for being the biggest support during this phase of my life.

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Chapter 1

Introduction and Background

Unintended pregnancy

Unintended pregnancy remains a significant public health issue in the United States (US).¹ The persistent high prevalence of unintended pregnancies indicates unmet sexual and reproductive healthcare needs of women of reproductive age.² Experiencing unintended pregnancy is associated with poor health and lower psychological well-being of women and their families.³⁻⁴ About half of unintended pregnancies end in abortions, and nearly half are live births, with both outcomes having personal, social, and economic consequences.⁵ In 2010, the resulting national costs from unintended pregnancies leading to miscarriages, abortions, and births were approximately \$21 billion.⁶

An unintended pregnancy occurs when no children or no more children are desired, or it happens earlier than planned, i.e., unwanted or mistimed.⁷ While ambivalent pregnancies are defined as "unresolved or contradictory feelings about whether one wants to have a child at pregnancy recognition."⁸ Unintended pregnancies are associated with delayed and inadequate prenatal care, poor birth outcomes, including but not limited to premature birth, low birth weight (LBW), and poor child health and development.⁹ It is noted that unwanted pregnancies had higher odds of preterm delivery,¹⁰ while women who were ambivalent about their pregnancies had higher odds of having an LBW infant.¹¹ The evidence about mistimed pregnancies causing LBW is inconsistent.^{12,13} It is reported that women with unintended pregnancies are less likely to modify harmful behaviors, less vigilant in detecting maternal health problems and practicing healthy behaviors.¹⁴⁻¹⁵ Women with unintended pregnancies are more likely to experience household dysfunction, psychological and physical abuse.¹⁶ A systematic review and meta-

analysis on the association between unintended pregnancy and perinatal depression revealed a two-fold prevalence of perinatal depression with unintended pregnancy.¹⁷ Given the high prevalence of unintended pregnancies and their impact on maternal and child health, prevention efforts should be given a public health priority.

Risk factors of Unintended Pregnancy

Although all women of childbearing age (15-44) years are at risk of unintended pregnancy, sexually active, fertile, and women neither their partners using contraception and not trying to become pregnant are considered in this pool.⁴ Unintended pregnancy has been attributed to a range of demographic, social, economic, and behavioral risk factors. These factors include maternal age, race, levels of education, socioeconomic status, marital status, pregnancy history, mental health, maternal childhood experiences, physical or emotional abuse, and substance use.

Studies on maternal age show that teenage women are more likely to describe their pregnancy as unintended than older women.¹⁸ However, some studies have suggested that women aged thirty-five years or older are more likely to describe their pregnancies as unintended as they may already have the desired number of children.¹⁹ Usually, women at the beginning or end of their childbearing age are more likely to experience unintended pregnancy; however, a study shows that women from 18-24 years of age made the most significant proportion of unintended births, i.e., 81 per 1000 women.¹

Racial and ethnic minorities women are more likely to experience unintended pregnancies and births than White women. A study based on the National Survey of Family Growth exploring racial/ethnic differences in unintended pregnancies noted a higher prevalence of unintended pregnancy among Black (63%), followed by Hispanics (48%) compared to White

women (42%).²⁰ In another study, 16% of Black women of childbearing age compared with 9% of Asian, Hispanic, or White women were not using contraception.²¹

Women with less than or equal to high school education were at higher risk of unintended pregnancy than women with graduate education. Moreover, women with less than or equal to a high school diploma perceive that pregnancy may jeopardize their educational or career aspirations.²²

Low socioeconomic status is known as an independent risk factor for unintended pregnancy.²³ Women who are young, unmarried, and have low socioeconomic status have disproportionately higher levels of unintended childbearing.²⁴ This also raises the question of whether the mother's socioeconomic disadvantage or her pregnancy intention leads to poor health outcomes.

Literature shows that women who do not have a partner were three times more likely to describe their pregnancy as unintended than those with a partner or significant other.²⁵ Mothers with lower social support during pregnancy and conflict within their relationships are less likely to describe their pregnancy as intended.^{26,27} Physical and emotional abuse is also associated with unintended pregnancy. Abusive relationships and an environment of fear may limit women's fertility control, leading to unintended pregnancy.²⁸

Data on contraception shows inconsistent, incorrect, or no use of effective contraceptive methods are associated with a high prevalence of unintended pregnancy. It may happen due to the perceived low risk of pregnancy, lack of contraceptive knowledge, misperception of side effects, and barriers to using healthcare services.²⁹

The impact of mental health on reproductive health and pregnancy outcomes has been a seldom focus in the scientific literature. Although depression and anxiety are the most common

health problems linked with risky sexual behaviors, few studies have examined their relationship with pregnancy intention. A prospective cohort study with a representative sample reported that women with depression and stress symptoms had higher unintended pregnancy rates than women without these symptoms.³⁰ Another longitudinal cohort study found a significant association between adverse life experiences and the risk of unintended pregnancy among adolescents and young women.³¹ In literature, there is a range of factors linked to pregnancy intention. However, more research is needed to address this public health issue and the underlying disparities in unintended pregnancy rates.

Substance use among women of childbearing age

Substance use among women of childbearing age is associated with poor physical, mental, and social health outcomes.¹⁵ These substances include tobacco, alcohol, over-the-counter and prescription medicines, and illicit drugs.³² In a national survey (2012-13) administered among women ages 15-44, about 24.0% of women reported smoking, 55.4% alcohol consumption, 27% reported binge drinking, with 4.6% having at least one episode of binge drinking during the last one-month, and about 11.4% revealed the use of illicit drugs.³³ About one in six women between 15-44 years are prescribed opioid medication annually.³⁴

The preconception period or the time before pregnancy is crucial for subsequent maternal and child health.³⁵ Although most women tend to stop using the substance after pregnancy recognition, a large proportion of pregnancies are unintended. Pregnancy recognition takes 4-6 weeks after conception, resulting in exposures affecting fetal growth and development.³⁶ The adverse effects of substance use during pregnancy on fetal development are well-documented and widely comprehended. However, data is limited on the preconception substance use

affecting the newborn infant. A Canadian study on beliefs about the preconception period revealed that only 38% believed that alcohol consumption during the preconception period might affect fetal development.³⁷ Preconception substance use predicts continued or limited usage during the prenatal period and is linked with poor health outcomes.³⁸ For example, cigarette smoking during pregnancy has been associated with LBW, preterm and stillbirth, poor growth, and reduced cognitive development.¹⁴ Alcohol consumption during pregnancy can cause miscarriage, stillbirth, and Fetal Alcohol Spectrum Disorders (FASDs).³⁹ The use of cocaine, cannabis, and Marijuana is linked to preterm labor, small for gestational age (SGA), LBW, Neonatal Intensive Care Unit (NICU) admissions, poor cognition, and behavior.^{40,41,42,43,44} Similarly, the use of heroin and prescription pain medication before pregnancy is associated with stillbirth, premature birth, and Neonatal Abstinence Syndrome (NAS).⁴⁵

Women with substance use suffer poor sexual and reproductive health, inconsistent or ineffective contraception use, and a high prevalence of unintended pregnancies.²⁹ These women also face individual and systemic challenges while accessing treatment and family planning services including, medical and psychological comorbidities, history of neglect and abuse, the stigma of substance use, emotional and economic difficulties and, fear of losing child custody.⁴⁶ A recently published systematic review described women who use substances as a diverse population based on their sociodemographic, reproductive, and behavioral characteristics.⁴⁷ Providers must be aware of the unique needs of these women and the implications surrounding substance use.¹⁵ To provide treatment and family planning services, evidence-based, integrated, clinical, and behavioral interventions are needed.⁴⁸ A systematic review found theory-based interventions, on-site counseling, and the provision of effective contraception methods more effective than traditional educational materials.⁴⁹ These findings suggest the need for further

research to determine the characteristics and needs of these women; such information may help to provide a critical foundation for developing and implementing evidence-based interventions to prevent unintended pregnancies among substance-using women.

Polysubstance Use

Consuming more than one substance over a period of time is termed polysubstance use. Polysubstance use can refer to substances used either simultaneously or within the same period.⁵⁰ It includes co-use of alcohol, nicotine, cannabis, medical and non-medical prescription medications, cocaine, heroin, and hallucinogens.⁵¹ In a CDC report, about 40% of pregnant women who drank alcohol during pregnancy reported co-using other substances, including tobacco, cannabis, cocaine, and heroin.⁵²

Although polysubstance use is not a new practice, it is becoming a serious concern due to high rates of non-medical use of opioids along with other substances.⁵³ In addition, the policy changes surrounding efforts to legalize marijuana are also leading to the increasing use of marijuana concurrently with other substances.⁵⁴ Although polysubstance use is common, it remains underreported due to the associated stigma and legal implications.⁵⁵ Polysubstance use among women of childbearing age raises concerns among public health circles due to its increasing prevalence and adverse pregnancy and birth outcomes.⁵³ To address this public health issue, there is a need to understand polysubstance patterns and the sociodemographic factors predicting poor reproductive health.

Summary

The US has the highest rates of unintended pregnancy among the developed nations. These rates are particularly elevated among U.S. women aged 18-24 years, women with low education attainment, low-income, unmarried, and minority women.⁵⁶ More research is needed to determine the factors underlying disparities in the unintended pregnancy rates.

Previous studies suggest that women who use substances, including tobacco, alcohol, illicit drugs, and opioids, are at higher risk for unintended pregnancies.⁵⁷⁻⁵⁸ However, investigations regarding the association of substance use to unintended pregnancy have to date been limited to small-scale and hospital-based studies.⁵⁹⁻⁶⁰ Moreover, to our knowledge, no studies have yet been conducted in a nationally representative sample to estimate the prevalence and risk of unintended pregnancy and its subtypes among women with different types of substance use. To help address this gap, the first aim was to determine the prevalence of unintended pregnancy in a representative sample of women who use substances and to assess the associations of sociodemographic factors to unintended pregnancy risk in this population.

Additionally, polysubstance use is another emerging public health challenge with detrimental effects on maternal and child health. There is a need to identify the prevalence and patterns of polysubstance use among women of childbearing age to inform effective policies and practices. For this purpose, our second aim was to investigate the prevalence of polysubstance use and the risk associated with unintended pregnancy.

Illicit and recreational drugs are a serious public health problem with potentially adverse maternal and child health effects.⁶¹ According to national statistics, about 19.5 million (15.4%) of US women above 18 years used illicit and recreational substances.⁶² Although many studies investigated the risk of unintended pregnancy among women using illicit and recreational

drugs,^{63,64,65} these studies vary widely in study population characteristics, study design, and the determinants assessed. However, to our knowledge, systematic reviews regarding the potential association of preconception use of illicit and recreational drugs to risk for unintended pregnancy in women of child-bearing age are lacking. The authors are unaware of any systematic review (SR) or meta-analysis (MA) that estimated the risk of unintended pregnancy with illicit and recreational drug use among women of childbearing age. Understanding the link between these factors is particularly important in light of the high prevalence of substance use and unintended pregnancy among women of childbearing age. For this purpose, our third study aimed to conduct a systematic review with meta-analysis to establish evidence essential for policy and practice efforts to improve maternal and child health.

The *long-term goal* of this project was to examine the association of unintended pregnancy with substance use among women of childbearing age. The overall *objective* of this project was to determine the associations of unintended pregnancy to preconception substance use and sociodemographic factors in women of childbearing age. The *central hypothesis* was that substance use is an independent risk factor of unintended pregnancies. Precisely, this dissertation project is planned to investigate the following specific aims.

Specific aims

Specific Aim 1: Examine the association between preconception substance use (alcohol, smoking, illicit drugs) and unintended pregnancy among women of childbearing age in the US. If an association exists, compare substance use between subtypes of unintended pregnancies: 1) mistimed; 2) unwanted and ambivalent.

Aim 1b: Assess the association between sociodemographic factors and unintended pregnancies among women who use substances.

Specific Aim 2a: Examine the association between polysubstance use and unintended pregnancy among women of childbearing age. If a significant association is identified, compare polysubstance use between sub-types of unintended pregnancies: 1) mistimed, 2) unwanted and 3) ambivalent.

Aim 2b: Assess the association between sociodemographic factors and unintended pregnancies among women with polysubstance use.

Specific Aim 3: To conduct a systematic review with meta-analysis to assess the relation of illicit and recreational drugs use and the likelihood of unintended pregnancy among women of childbearing age.

The three specific aims correspond to chapters two, three, and four, respectively. Chapter five comprises the overall discussion, including the summary of key findings, strengths, limitations, potential public health implications, and suggestions and recommendations for future research. Unintended pregnancy is associated with poor maternal and child health and substantial economic, healthcare, and individual costs. Thus, determining the risk of unintended pregnancy among substance-using women of childbearing age and its correlates will aid public health, policy, and practice efforts to plan and implement informed preventive measures.

Chapter 2

Preconception Substance Use and Risk of Unintended Pregnancy

Abstract

Objective: This study examined the association between preconception substance use and unintended pregnancy in a large, nationally representative sample of women.

Methods: In this cross-sectional study, we used data from the Pregnancy Risk Assessment Monitoring System (PRAMS), comprising 74,543 women who had birth during 2016-17. Logistic regression was used to assess the independent association of unintended pregnancy overall and by subtypes to preconception substance use (smoking and other nicotine/tobacco use, alcohol consumption, and use of cannabis, illicit/recreational drugs) and specific medication, including prescription opioids, antidepressants and over the counter pain relief. Four highly prevalent substance use groups were identified for aim 1(b), including alcohol, tobacco/nicotine, opioids, and illicit/recreational drugs. Stratified descriptive analyses were performed to compare the sociodemographic indicators among each group. After controlling for potential confounders, individual models were created for each sociodemographic determinant for each substance-using group. Logistic regression was used to yield odds ratios with 95%CI and p-value.

Results: Overall, 41% of pregnancies were unintended. Nearly 57% of participants reported alcohol consumption during the preconception period, with 32% indicating binge drinking, 17% reported preconception smoking, and 10% cannabis use. Unintended pregnancy was significantly associated with substance use, including smoking (AOR:1.5, 95% CI: 1.4-1.6); as well as the use of other nicotine/tobacco (AOR:1.4, 95% CI: 1.3-1.5); cannabis (AOR: 1.9, 95% CI: 1.5-2.3); illicit/recreational drugs (AOR:1.7, 95% CI: 1.2-2.4), prescription opioids (AOR:1.4, 95% CI: 1.02-1.9), and prescription antidepressants (AOR 1.8, 95% CI: 1.1-3.0). The likelihood of unintended pregnancy was significantly elevated with heavy smoking, heavy alcohol consumption, and binge drinking. Analyses by unintended pregnancy subtype yielded similar results. The sociodemographic determinants of unintended pregnancy among all substance-using groups including maternal age <17, living in urban areas, not having a graduate degree, annual income <FPL, not being married, and having depression or anxiety increased the likelihood of unintended pregnancy, with a varying magnitude of risk. The risk of unintended pregnancy with race and ethnicity also varied among substance-using groups.

Conclusions: Preconception substance use was significantly and positively associated with unintended pregnancy. Among all substance-using groups, maternal age <17, living in urban areas, not having a graduate degree, annual income <FPL, not being married, and having depression or anxiety increased the risk of unintended pregnancy. This study's findings underscore the importance of recognizing and addressing preconception substance use among women of childbearing age. Evidence-based interventions are needed addressing substance use behavior and effective contraceptive use to prevent unintended pregnancy and related harmful effects on maternal and child health.

Introduction

Unintended pregnancy increases the risk of adverse outcomes for both maternal and child. Women with unintended pregnancies are at risk of receiving inadequate prenatal care, postpartum depression, experiencing depression and anxiety later in their lives, and being less likely to breastfeed.⁶⁶⁻⁶⁷ Unintended pregnancy may lead to preterm birth, LBW, and child maltreatment.⁶⁸⁻⁶⁹ In the US, about half of the pregnancies are unintended and compared to the general population, the rates are even higher among women who use substances.⁷⁰ A study conducted among opioid-using women revealed that 9 out of 10 pregnancies were unintended.⁷¹ Although the adverse effects of substance use on women's overall health are published in the literature, little attention has been given to pregnancy intention.¹⁵ Together, it suggests unmet reproductive health needs and poor sexual health among substance-using women.

There is a range of sociodemographic, economic, and behavioral risk factors identified for unintended pregnancy. According to the literature, these factors include lower SES, maternal age, i.e., adolescence and the end of childbearing age when no more children are desired, lacking social support, inconsistent or no contraception.^{1,56} These risk factors tend to be stable across cultures worldwide. However, a paucity of studies focused on the risk factors of unintended pregnancy among women who use substances. These women suffer poor sexual and reproductive health and face challenges while accessing family planning services.⁴⁶ To address the incidence of high-risk pregnancies, there is a need to identify the indicators among this high-risk group and develop and implement interventions to provide counseling and effective contraception. To fill this gap in the literature, this study aimed to; *specific aim 1*: examine the association of preconception substance use (alcohol, smoking, illicit drugs) and unintended pregnancy among women of childbearing age in the US. If an association exists, compare substance use between

subtypes of unintended pregnancies: 1) mistimed; 2) unwanted and ambivalent. And *aim 1b*: assess the association between sociodemographic factors and unintended pregnancies among women who use substances.

For this purpose, large national representative data from PRAMS was used. The current study's findings may underscore the importance of recognizing and addressing preconception substance use and developing policy and practice measures to reduce unintended pregnancy and related dire consequences among women of childbearing age.

Materials and Methods

Data Source

We used data from the Pregnancy Risk Assessment Monitoring System (PRAMS) in the current study. Secondary analysis on a cross-sectional subset of the PRAMS 2016-17 (phase 8) data was performed. PRAMS is a national, state-specific, population-based surveillance system that collects maternal and neonatal health indicators' data covering 83% of the US births.⁷² Originating in 1987 and designed to monitor maternal and child health indicators, selected maternal behaviors during preconception, pregnancy, and postpartum periods. PRAMS collects data from 39 states and New York City. These states include Alaska, Alabama, Arkansas, Colorado, Connecticut, Delaware, Georgia, Hawaii, Iowa, Illinois, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Missouri, Montana, Nebraska, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Oklahoma, Pennsylvania, Puerto Rico, Rhode Island, South Dakota, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, Wyoming. The current minimum response rate threshold for participating states is 55%.⁷²

PRAMS Questionnaire

Phase 8 is the most recent PRAMS questionnaire and consists of core questions used by all states and standard questions as optional selections by the states.

PRAMS data collection

Each state participating in PRAMS draws a stratified systematic sample of 100- 250 women who recently gave birth. Mailed questionnaires or surveys on the phone are used for data collection. PRAMS data are weighted for sample design, nonresponse, and non-coverage. The annual sample consists of 1000-3400 women per state. Survey responses have been linked to birth certificate data and demographic and medical information from the state's vital record system. Stratified samples drawn from all births make the data representative of women of childbearing age in each state. PRAMS survey design and methods are explained elsewhere.⁷² The CDC institutional review board approves the current study. The Institutional review board of West Virginia University exempted the study from IRB approval (protocol number 1908660609).

Measures:

Women who gave live birth in the United States during 2016-17 were included in the study. Demographic and background characteristics were generated from the birth certificate (e.g., age, education, race/ethnicity, marital status) and income, insurance, prenatal care, substance use, abuse, and childhood adversity from the PRAMS questionnaire.

Pregnancy Intention

The outcome variable pregnancy intention was assessed by responding to the following question" Thinking back to just before you got pregnant with your new baby, how did you feel

about getting pregnant? The responses "I wanted to be pregnant then" or "I wanted to be pregnant sooner" were classified as intended pregnancies. The answer "I wanted to be pregnant later" was classified as mistimed, "I did not want to be pregnant then or at any time in the future" was classified as unwanted. The response "I was not sure what I wanted" was categorized as ambivalent. For binary analysis, mistimed, ambivalent, and unwanted were grouped as unintended pregnancies based on literature.⁷³

Substance Use

Smoking was assessed by the yes/no question about smoking three months before pregnancy; women who answered yes were considered smokers. The smoking intensity (no smoking, moderate and heavy smoking) was built on the number of cigarettes/ days. Based on the literature, less than ten cigarettes/day was considered moderate smoking, and ten and more were regarded as heavy smoking⁷⁴.

For **alcohol consumption**, those responding yes to drinking three months before pregnancy were categorized as alcohol consumers. The number of alcoholic drinks /week was used to define moderate (up to 7drinks/week) and heavy drinking (8-14 drinks/week) according to dietary guidelines for Americans.⁷⁵ Binge drinking was defined as having four or more drinks in 2 hours span at least once during three months before pregnancy⁷⁶.

The **illicit drug/recreational drugs** variable was created by combining the yes/no questions about the use of the following drugs during the month before pregnancy:

1. Adderall, ritalin, or another stimulant
2. Methadone, naloxone, subutex, or suboxone
3. Heroin (smack, junk, black tar, chiva)
4. Amphetamines (uppers, speed, crystal meth, crank, ice, agua)

5. Cocaine (crack, rick, coke, blow, snow, nieve)
6. Tranquilizers (downers, ludes) hallucinogens (LSD/acid, PCP/angel dust, ecstasy, molly, mushrooms, bath salts)
7. Sniffing gasoline, glue, aerosol spray cans, or paint to get high (huffing).

Cannabis use was assessed by asking respondents for their use of Marijuana one and three months before pregnancy.

The variable **nicotine and other tobacco forms** was created by combining the yes/no variables about hookah, electronic cigarettes, cigars, cigarillos, flavored cigars, nicotine, betel nut or betel quid, and chewing tobacco, snuff, snus, and dip. These variables were combined due to fewer respondents (ranging from 0.7%-6.6%) in each variable.

Among specific medications, **prescription antidepressants** were defined as the use of prescribed antidepressant and anti-anxiety medication before pregnancy. **Prescription opioids** were defined as the use of prescription pain relievers such as hydrocodone (Vicodin), oxycodone (Percocet), or codeine before pregnancy. **OTC pain relief** was assessed using over-the-counter pain relievers such as aspirin, Tylenol, Advil, or Aleve three months before pregnancy.

Covariates

The covariates include rural/urban status, maternal age, race, ethnicity, level of education, marital status, poverty, insurance status, parity, adequacy of prenatal care, maternal childhood experiences, experiencing physical/emotional abuse, and depression and anxiety were measured as below.

1. **Rural/urban status** was assigned using National Center of Health Statistics (NCHS) codes.

2. **Maternal age** at conception was categorized as ≤ 17 , 18-24, 25-34, and 35+ years.
3. **Race** The Respondents' Race categories include Asian, White, Black, and others. For aim b, we combined race and ethnicity into a single variable with categories including Asian, non-Hispanic White, Hispanic White, Black, and others.
4. **Maternal education** was categorized using maternal years of education as less than high school (less than 12), high school (12 years), Some college (13-15 years), and graduate (≥ 16).
5. **The poverty status** was based on the income-to-needs ratio derived from family income (median of the income categories) variables and family size (number of dependents plus self). The poverty threshold adjusted for a family was divided by annual household income size using the Census Bureau's guidelines to determine the poverty threshold adjusted for family size (2016-17, respectively).⁷⁷ The variable income-to-need ratio was then dichotomized below the federal poverty level and at or above the federal poverty level. (<1 below FPL, 1 and above/at and above FPL).⁷⁸
6. **Parity** was defined using the categorical question about previous live births.
7. **Adequacy of Prenatal Care (PNC)** was assessed using the Kessner Index.⁷⁹ It is a composite index defined by a fixed combination of values based on the time of entry into prenatal care, number of prenatal visits, and the gestational age at the time of birth. Kessner scale consists of three categories, i.e., adequate PNC, intermediate PNC, and inadequate PNC.⁸⁰ In PRAMS data, unknown PNC was used for incomplete information.

8. **Health insurance:** Pre-pregnancy insurance status was categorized as no insurance, Medicaid, and others, including insurance paid by work, military, Tricare, someone else, or other private insurance sources.
9. **Marital status** was dichotomized as married and others, including unmarried or living with a partner or parents.
10. **Childhood adversity** was based on seven questions about maternal childhood experiences. Total ACE scores were calculated and classified as 0, 1-3, and ≥ 4 .⁸¹
11. The **abuse** status was assessed by the pre-pregnancy physical/emotional abuse as yes/no in the PRAMS questionnaire.
12. **Depression and anxiety** were assessed by the questions about pre-pregnancy health conditions having depression and anxiety. Depression and anxiety were combined into a single variable called depression/anxiety.
13. **Mental Distress:** was assessed by the question about feeling depressed or sad during the preconception period.

Statistical Analysis

All statistical analyses were conducted in SPSS (IBM SPSS Statistics for Windows, Version 26.0)⁸² using complex survey procedures advised by the Center for Disease Control and Prevention (CDC).

Specific aim 1(a)

For descriptive analysis, frequencies and weighted percentages with 95% CI were computed using weights assigned to each observation in the PRAMS dataset. Bivariate analysis was performed using chi-square statistics for pregnancy intention by substance use and sociodemographic factors. The binomial logistic regression procedure was used to compute the

odds of unintended pregnancy for each type of substance use after adjusting for all sociodemographic factors. For subtypes of unintended pregnancy, i.e., mistimed, unwanted, and ambivalent multinomial logistic regression procedure was used for each type of substance use after adjusting sociodemographic factors. Crude and adjusted odds ratios with 95%CI and p-value were calculated.

Results 1(a)

Sample Characteristics. Of the 74,543 women who participated in PRAMS 2016-17, the majority were White (69.6%), non-Hispanic (80.3%), and living in urban areas (78.3%). Table 1 provides information about the sample characteristics. The mean age was 23.48±5.8 (range 12-46) years. More than half (58.9%) of women were between 25-35 years of age. A large proportion (62.1%) were married. About 12.9% did not complete their high school degree, and 36.2% had obtained a graduate degree. Nearly 14% did not have health insurance, and 27.7% reported living below the federal poverty level. Almost a half (46%) reported physical or emotional abuse, while 6.6% of women reported having experienced four or more adverse childhood experiences. One in six women (17.3%) reported having depression or anxiety.

Pregnancy Characteristics of Sample. More than 40% of pregnancies were reported as unintended; of those reports, 19.5% were mistimed, 6.2% were unwanted, and 15.3% were described as ambivalent. Preconception contraception use was reported by 41% of women. About two-thirds (68.5%) of the sample had adequate prenatal care, 19.1% mentioned having intermediate PNC, 5.8% did not have adequate PNC, while for 6.6%, the information on the adequacy was not available.

Substance Use. OTC pain relief was found to be most commonly used (70%), followed by alcohol (56.6%). One-third (31.8%) of women reported binge drinking. Seventeen percent

documented smoking, while 10.6% reported nicotine/tobacco use other than smoking. Cannabis use was described by 10%, followed by prescription antidepressants (7.1%), prescription opioids (5.2%), and illicit/recreational drugs (4.2%).

Maternal Substance Use and Unintended Pregnancy. Table 2(a) shows the association of preconception substance use behavior and pregnancy intention (unintended vs. intended). Crude and adjusted ORs indicated increased odds of unintended pregnancy with all types of substance use. Unintended pregnancy was significantly and positively associated with smoking (AOR: 1.5, 95% CI: 1.4-1.6), with risk estimates highest in those reporting heavy smoking (AOR: 1.9, 95%CI: 1.5-2.3). The dichotomous measure of preconception alcohol consumption demonstrated no risk of unintended pregnancy (AOR: 1.05, 95%CI: 1.0-1.1). However, those documenting heavy drinking were almost twice as likely to report unintended pregnancy (AOR: 1.9, CI: 1.5-2.2) compared to no drinking. Binge drinking was also found to be significantly associated with unintended pregnancy (AOR:1.2, 95%CI:1.04-1.4). Similarly, the likelihood of unintended pregnancy was elevated considerably in participants reporting the use of nicotine/tobacco (AOR: 1.4, 95% CI: 1.3-1.5), cannabis (AOR: 1.9, 95% CI: 1.5-2.3), illicit/recreational drugs (AOR: 1.7, 95% CI: 1.2-2.4).

Also, the use of specific medications was significantly associated with increased odds of unintended pregnancy, including prescription opioids (AOR:1.4, 95% CI: 1.02-1.9), and antidepressants (AOR:1.8, 95% CI: 1.1-3.0).

Maternal Substance Use and Unintended Pregnancy Subtypes. Table 3(a) presents the distribution of intended and three subtypes of unintended pregnancy, i.e., ambivalent, mistimed, and unwanted pregnancy with substance use. The prevalence of all three subtypes was higher with substances including smoking, heavy and binge drinking, nicotine/tobacco, cannabis, illicit

drugs, and prescription opioids. However, the number of unwanted pregnancies was reduced to half among participants who documented using prescription antidepressants compared to those who did not (6.3% to 3.5%). The highest unwanted pregnancy rates were observed with prescription opioids (12.8%) and illicit/recreational drugs (12.7%). The rates of mistimed were higher with cannabis use (28.6%).

Tables 4(a) illustrate substance use associations with unintended pregnancy subtypes. Preconception smoking and use of nicotine/tobacco, cannabis, illicit drugs, and prescription opioids significantly increased the likelihood of ambivalent, mistimed, or unwanted pregnancies. AORs for unintended pregnancy subtypes ranged from 1.1 to 2.3, with estimates appearing highest overall for unwanted pregnancy.

The association between ambivalent (AOR: 1.0, 95%CI: 0.9-1.1) and unwanted pregnancy (AOR: 0.9, 95%CI: 0.8-1.0) with dichotomous alcohol use and unwanted pregnancy with prescription antidepressants was not statistically significant (AOR: 0.7, 95%CI: 0.2-1.9).

Statistical analysis (1b)

Four substance-using groups were identified, including alcohol, tobacco/nicotine (including smoking cigarettes and tobacco and nicotine products), prescription opioids, and illicit and recreational drugs. Stratified descriptive analysis was performed for the above four substances to describe and compare their characteristics, yielding frequencies, and weighted percentages. The classification of the outcome variable and other covariates is explained in the methods section. The bivariate analysis was performed using Chi-square statistics for each substance use group by pregnancy intention. Variables not significantly associated (p -value < .05) with pregnancy intention were excluded from the multivariable analysis. For each substance

use group, separate models were created for each sociodemographic indicator after adjusting for potential confounders. Crude and adjusted odds ratios with 95% CI and p-value were calculated.

Results (1b)

Population characteristics. Table 1(b) presents the sample characteristics of the women that gave live births during 2016-17 and participated in the PRAMS, stratified by the substance use categories. The total sample consisted of 74,543 women. Among those, 39,831(56.6%) reported alcohol consumption, 17,535 (22.1%) mentioned tobacco and nicotine products, prescription opioid use was revealed by 848(5.2%), and illicit and recreational drugs by 1889(10.8%) of the participants. Among all women and four substance-using groups, more than two-thirds of the women ($\approx 78\%$) resided in urban areas; a majority were non-Hispanic Whites and were between 25-35 years of age. Among alcohol-using women, a larger fraction (45.6%) had a graduate degree than the other three groups, where more immense proportions had high school or less than high school. Regarding the socio-economic status, among alcohol using women (19.6%), tobacco/nicotine (41.6%), prescription opioids (46.4%), and illicit/recreational drugs (53.3%) of women documented their annual income below the FPL. Among all women (62.1%) and alcohol users (65.6%), about two-thirds of the participants reported their marital status as married, while among illicit/recreational drug users, only one-third (31.4%) were married. Almost a double number of women among illicit/recreational drugs (37.5%) and prescription opioids (38.5%) users have depression or anxiety compared to all women (17.3%). Overall, about a half of the women ($\approx 46\%$) reported having physical or emotional abuse before pregnancy, a much high prevalence was noted among opioid users (68.8%), followed by illicit/recreational drugs users (58.2%).

Pregnancy characteristics of the sample. Among all women and alcohol users, about (40%) of the pregnancies were unintended, while in prescription opioid users (55.8%), tobacco/nicotine (56.9%), and the highest prevalence was noted among illicit/recreational drug users (65.1%). Three out of four illicit/recreational drugs users (74.2%), two-thirds of the tobacco/nicotine (63.3%) users revealed not using any contraception. The adequacy of prenatal care assessed by the Kessner Index indicated that a more significant fraction of alcohol users had adequate PNC (73.5%) compared to tobacco/nicotine users (64.5%) and opioids users (63.3%). In comparison, only a half (55.7%) of illicit/recreational drug-using women had adequate PNC. (Table 1b).

Socio-demographic indicators of unintended pregnancy among substance-using women

Alcohol consumption. Among women who reported alcohol consumption, living in urban areas (AOR: 1.2, 95%CI: 1.1-1.3), Black race (AOR: 2.1, 95%CI:1.7-2.6), annual income less than FPL (AOR:2.2, 95%CI: 1.9-2.4), not being married (AOR: 3.2, 95%CI: 2.9 – 3.5), having depression or anxiety (AOR:1.3, 95%CI:1.2-1.4) were statistically significant predictors of unintended pregnancy. Maternal age groups less than 35 years of age were also found to have a higher risk, with the highest magnitude observed among those ≤ 17 (AOR: 7.0, 95%CI: 1.9-25.3), and 18-24 years (AOR:2.1, 95%CI: 1.8-2.3) of age. After adjusting with potential confounders, physical or emotional abuse did not significantly relate to unintended pregnancy (AOR: 0.96, 95%CI: 0.9-1.04). (Table 2b).

Tobacco/nicotine use. Table 3b indicates the association of maternal characteristics with unintended pregnancy among women using tobacco or nicotine. Elevated risks for unintended pregnancy were noted with urban living (AOR:1.2, 95%CI:1.02-1.3), Black race (AOR: 1.5, 95%CI: 1.02-2.1), annual income below FPL (AOR:1.9, 95%CI:1.7-2.1), not married (AOR: 2.4, 95%CI: 2.1- 2.7), and having depression or anxiety (AOR:1.1, 95%CI: 1.01-1.3). Maternal age

≤ 17 (AOR:5.2, 95%CI: 2.1-12.6), 18-24 years (AOR: 1.8, 95%CI: 1.5-2.2), and 25-35 years (AOR: 1.2, 95%CI: 1.01-1.4) showed increased risk. Maternal education level <HS (AOR: 1.7, 95%CI: 1.4-2.1), HS only (AOR:2.1, 95%CI:1.7-2.5), and some college (AOR:2.0, 95%CI:1.7-2.3) indicated a higher likelihood of unintended pregnancy than women having a graduate degree among women using tobacco/nicotine.

Prescription opioid use. A substantially high risk of unintended pregnancy with opioid use was noted among women living in urban areas (AOR:3.5, 95%CI: 1.8-6.8) than other substance users. Contrary to other groups, Hispanic White (AOR: 2.8, 95%CI:1.01-7.7) and other races (AOR:4.0, 95%CI:1.9-8.5) had increased odds of unintended pregnancy. No significant association was observed with the maternal age groups 18-24 years (AOR: 1.2, 95%CI:0.4-3.5), 25-35 years (AOR: 0.74, 95%CI: 0.3-1.6), and educational attainment <HS (AOR:1.2, 95%CI:0.3-4.2), HS only (AOR:1.7, 95%CI:0.6-4.7), and some college (AOR: 2.0, 95%CI: 0.8-5.2). Having income <FPL (AOR: 3.0, 95%CI:1.6-5.7), marital status other than married (AOR: 1.8, 95%CI: 1.01-3.4), and having depression and anxiety (AOR: 2.0, 95%CI: 1.05-3.9) depicted increased risk for unintended pregnancy with preconception opioid use. (Table 4b).

Illicit and recreational drug use. Table 5b presents the results of the multivariable analysis conducted to determine the indicators of unintended pregnancy among women using illicit and recreational drugs during the preconception period. A higher likelihood of unintended pregnancy was noted among those residing in urban areas (AOR: 2.7, 95%CI:1.7-4.1), others racial group (AOR: 3.3, 95%CI:1.9-5.8), women aged ≤ 17 (AOR: 11.3, 95%CI: 1.7-76.2), have some college education (AOR: 2.3, 95%CI: 1.2-4.4), had annual income <FPL (AOR:2.2, 95%CI: 1.4-3.4), and had marital status other than married (AOR: 2.4, 95%CI: 1.4-3.9).

Discussion

Findings (Aim 1a)

Our results of the population-based, representative sample of women of childbearing age substantiated that preconception substance use is associated with unintended pregnancy. The three sub-types of unintended pregnancy were also associated with substance use. To the authors' knowledge, it is the study first examining the distribution of unintended pregnancy and its subtypes and the relation of preconception substance use to these outcomes in a large national sample of women.

Many of the associations found in the current study are previously reported in the literature, such as smoking, illicit drugs, tobacco, and cannabis.⁸³⁻⁸⁴⁻⁸⁵ The likelihood of unintended pregnancy was significantly elevated with heavy smoking, high alcohol consumption, and binge drinking, similar to what is reported in the literature.⁷³ Analyses by unintended pregnancy subtype yielded similar results overall, and the magnitude of the associations varied modestly. However, overall highest risk estimates were observed for unwanted pregnancies.

Lower contraceptives could explain high rates of unintended pregnancy since six in ten women in the current sample revealed no contraceptive use. It may happen due to perceived low risk of pregnancy, lack of understanding of the risk of substance-exposed pregnancy, and barriers to using healthcare services.⁸⁶ Women with substance use suffer from poor sexual and reproductive health. They encounter individual and systemic challenges, including medical and psychological comorbidities, neglect and abuse, mistrust of healthcare services, guilt, denial, and embarrassment regarding substance use, fear of losing child custody, and poor access to family planning services.⁸⁷ These high-risk situations indicate the significance of recognizing and

reducing substance use among women of childbearing age and facilitating effective contraceptive use among women tending to avoid pregnancy.

About half (46%) of the women reported physical or emotional abuse in the current study. An abusive relationship and environment of fear may limit women's control of their fertility, leading to unintended pregnancy.²⁸ The physical and mental health consequences of abuse are known. Having an abusive relationship or a traumatic past is also associated with higher odds of substance use.⁸⁸ Thus screening and identifying women with a history of physical and emotional abuse is crucial for implementing best practices known to improve survivor's outcomes.⁸⁹

Findings (Aim 1b)

Our findings from a large representative sample of the US women of childbearing age revealed that around a half of the women were consuming alcohol, 1 in five were using tobacco or nicotine products, about 5% were using prescription opioids, and 1 in ten were using illicit or recreational drugs during the preconception period. The results of the multivariable analysis indicated a higher risk of unintended pregnancy among substance-using women who were living in urban areas, were ≤ 17 of age, did not have a graduate education, had an annual income less than FPL, were not married, and had depression or anxiety during the preconception period. The magnitude of risk varied among racial and ethnic groups. The likelihood of unintended pregnancy was significantly higher among Black women using alcohol, tobacco/nicotine, opioid using non-Hispanic Whites, and illicit/recreational drugs using women from other races. To the authors' knowledge, this is the first study investigating the sociodemographic indicators of unintended pregnancy among various substance-using groups in a representative sample of US women.

The prevalence of alcohol, tobacco/nicotine products, and illicit/recreational drugs noted in the current sample are similar to what is reported in another national sample of US women.³³ However, a slightly higher prevalence of non-medical opioid use was reported by the NSDUH sample of women of childbearing age.⁵³

Among all substance-using groups, illicit and recreational drug users noted a considerably high prevalence of unintended pregnancy. In literature, other population-based studies have also reported similar findings.⁹⁰ This suggests that illicit and recreational drugs are an essential risk factor for poor reproductive and sexual health among women of childbearing age and requires a comprehensive approach to address the issue.

One of the strongest predictors of unintended pregnancy among all substance-using groups was urban living. Urban living women using prescription opioids were three times more at risk of unintended pregnancy than women in rural areas. In contrast, a twofold risk was observed among illicit and recreational drug users. This aligns with a study's findings conducted in New York City, where illegal use of drugs was significantly associated with unintended pregnancy.⁹¹ Although rural populations had a higher proportion of adolescent pregnancies.⁹² The higher prevalence of substance use among urban populations may lead to poor reproductive health, leading to unintended pregnancies among urban women.⁹³⁻⁹⁴

Poor socioeconomic status is a well-known risk factor for poor sexual and reproductive health, leading to unintended pregnancy.²³ In the present study, we also found that having an annual income less than FPL was a strong predictor of unintended pregnancy among all substance users, specifically among prescription opioid users, who were three times more likely to report unintended pregnancies. These findings are consistent with the existing literature showing that less annual income than FPL was independently associated with pregnancy

intention.⁹⁵ It is also reported that women below FPL were five times more likely to experience an unintended pregnancy.¹ A study conducted among urban poor women revealed that the majority of women did not have access to effective contraception and family planning services.⁹¹

In our findings risk of unintended pregnancy tend to decrease with maternal age. Among all substance users, age < 17 was a significant predictor of unintended pregnancy compared to the women aged 35 years and above. These findings are consistent with the existing literature.⁹⁶ The proportion of unintended pregnancy tends to decrease with age, and the adolescents aged 15-19 had the highest rates of unintended pregnancy than any other age group.⁹⁷ Furthermore, educational attainment less than graduate-level was also found to increase unintended pregnancy among all substance-using women. Another study aimed to determine the risk factors of unintended pregnancy among substance-using women reported similar findings.¹⁶

Another significant factor associated with an unintended pregnancy is marital status. The current study's findings revealed 2-3 folds increased risk of unintended pregnancy among women whose marital status was others. Unintended pregnancy was found to be highly correlated with marital status, where unmarried women were five times more likely to experience them.⁹⁸ A national study found a higher rate of unintended births among cohabiting women (141 per 1,000) than married women (33 per 1,000).¹ Having depression or anxiety during the preconception period also emerged as a determinant of unintended pregnancy among women using substances. Past studies have shown that women with poor mental health were more likely to use substances and experience poor sexual and reproductive health.⁹⁹⁻¹⁰⁰

Women from racial and ethnic minorities are at increased risk of experiencing an unintended pregnancy.¹⁰¹ Our study found an increased risk among Black women using alcohol and tobacco/nicotine, opioids using non-Hispanic Whites, and illicit/recreational drugs using

women from other races. Various social and economic factors contribute to health disparities. A study based on National Survey of Family Growth data reported age, relationship status, annual income, education, and insurance contributing factors to the higher likelihood of unintended pregnancy.²⁰

The women using substances before or during pregnancy are also likely to have inadequate PNC.¹⁰² In current findings, substance-using women reported inadequate PNC; specifically, about a half of women using illicit and recreational drugs had inadequate PNC. The women who do not have adequate PNC are at higher risk of preterm birth, low birth weight, and other adverse outcomes.¹⁰³

Public health implications

Given the high prevalence of substance use and the risk of unintended pregnancy among women of childbearing age, it is essential to identify and educate them for healthy decision-making. Brief culturally sensitive interventions are recommended in primary care, obstetrics and gynecologic, and family planning services.¹⁰⁴ The findings of our study also provide a deeper insight into the factors contributing to the poor reproductive health among all and specific women with substance use. It is essential to identify the women at higher risk and ensure that younger women, minorities, and women with poor socioeconomic status have information and access to reproductive and family planning services.¹⁰⁵ The current study's findings also have serious implications for providing adequate PNC among substance-using women, specifically women using illicit substances, for improving birth outcomes.¹⁰⁶ Providers must be aware of the women's unique needs and implications surrounding substance use.³⁸ To identify the women at

risk, educate them and provide treatment and family planning services, there is a need for evidence-based, integrated, clinical, and behavioral interventions.⁸⁸

Strengths and Limitations

The current study utilized data from a large, population-based, representative sample of women with detailed information on a wide range of potential confounders, pregnancy intention, sub-types, and the range of substances used. The study used a granular approach and provided insight into a range of social demographic, and economic risk factors of unintended pregnancy among various substance-using women.

Despite the strengths, the study has a few limitations that should be considered while interpreting the study's findings. First, the analysis is limited to women giving live births, leading to underreporting adverse outcomes (miscarriage or stillbirth) associated with unintended pregnancy and substance use. Additionally, nearly half of unwanted pregnancies end up in abortion.¹ Relation between abortion and prior substance use is also documented in the literature; our study did not have this information. Secondly, due to retrospective measurement, recall bias may influence pregnancy intention. However, studies on the reliability of pregnancy intendedness conducted a detailed analysis of the National Longitudinal Study of Youth¹⁰⁷, National Longitudinal Study of Adolescents Health¹⁰⁸, and National Survey of Family Growth.¹⁰⁹ They found aggregate levels estimated relatively stable across repeated measurements with small inconsistent reports in both directions. Third, PRAMS questionnaires are self-reported and may be subjected to under-reporting of behaviors perceived to be unhealthy. Substance use is prone to underreporting owing to social desirability bias and the

stigma of illicit drug use. However, women may be more willing to disclose their behaviors on a confidential survey as PRAMS data than other sources.¹¹⁰

Conclusion

Substance use is known to have detrimental effects on maternal and child health. After accounting for several maternal characteristics, the findings from this large population-based sample of US women indicated that substance use was significantly and positively associated with unintended pregnancy. This study also determined the indicators of unintended pregnancy among different substance users. We found strong evidence that maternal age <17, living in urban areas, not having a graduate degree, annual income <FPL, and not being married increased all substance users' risk of unintended pregnancy. Having depression and anxiety before pregnancy was associated with unintended pregnancy among alcohol, nicotine and tobacco, and prescription opioid users. This study's findings underscore the importance of recognizing and addressing preconception substance use among women of childbearing age, counseling, and provision of effective contraception methods to reduce unintended pregnancy and associated adverse effects on maternal and child health.

Chapter 3

Polysubstance Use and Risk of Unintended Pregnancy

Abstract

Background: Polysubstance use among women of childbearing age poses serious risks to maternal and child health. However, information regarding the relation between polysubstance use and unintended pregnancy in this population is limited. To address this gap, we investigated the prevalence and patterns of polysubstance use in a population-based sample of reproductive-aged US women, assessed the association of specific polysubstance use patterns to the risk of unintended pregnancy, and examined the relation of sociodemographic factors to unintended pregnancy in women co-using alcohol and other substances.

Methods: In this cross-sectional study, we used data from the Pregnancy Risk Assessment Monitoring System (PRAMS) representing 39 states and New York City. The sample comprised 74,543 women giving live births and participating in PRAMS 2016-17. Stratified descriptive analyses were used to compare women's characteristics with polysubstance use. Binary and multinomial logistic regression analyses were used to estimate the risk of unintended pregnancy, its subtypes (unwanted, mistimed, and ambivalent), and sociodemographic correlates of unintended pregnancy in participants reporting alcohol use (n=39,831). All multivariable analyses were adjusted for demographics, rurality, and other potential confounders.

Results: Prevalence of polysubstance use was high in the current sample. Among alcohol users (21.5%) were also smoking cigarettes, and (13%) were using cannabis. Similarly, among cigarette smokers, about two-thirds (70%) were also consuming alcohol, 50% were heavy, or binge drinkers and one-fourth (25%) were using cannabis. Larger fractions of women reporting heavy drinking and heavy smoking reported co-using other substances. Relative to the alcohol use, only the likelihood of unintended pregnancy was significantly elevated in women co-using alcohol with heavy smoking (AOR: 1.5, 95%CI:1.4 – 1.6), cannabis (AOR: 2.0, 95%CI:1.6 – 2.4), tobacco/nicotine (AOR: 1.6, 95%CI:1.4 – 1.7), and illicit/recreational drugs (AOR: 1.8, 95%CI: 1.1 – 2.7). Odds of unintended pregnancy were particularly high among heavy or binge drinkers who smoked cigarettes (AOR: 1.9, 95%CI: 1.5 – 2.4), used cannabis (AOR: 2.1, 95%CI: 1.4 – 3.1), or consumed other tobacco/nicotine products (AOR: 2.3, 95%CI: 1.7 – 3.1). Analysis by unintended pregnancy subtype yielded similar findings overall, with unwanted pregnancy showing the strongest association ranging from an AOR = 1.8 (95%CI: 1.5 - 2.1) with smoking and alcohol to an AOR = 4.7 (95%CI: 2.7 – 8.2) with co-using alcohol with illicit drugs. Living in urban areas and income below FPL were significant predictors of unintended pregnancy among all groups of polysubstance use.

Conclusion: In this large sample of reproductive-aged US women, polysubstance use during the preconception period was positively and significantly associated with increased odds of unintended pregnancy. Urban residence, low education, poverty, and having depressive symptoms prior to conception were significant correlates of unintended pregnancy among women co-using substances. The findings of this study may aid in identifying women at risk of poor reproductive health when developing tailored and culturally sensitive screening and treatment interventions to improve maternal and child health outcomes.

Introduction

Polysubstance use is defined as using more than one substance used simultaneously or within a period.¹¹¹ It refers to the co-use of substances, including but not limited to heavy or binge drinking of alcohol, nicotine, cannabis, medical and non-medical use of prescription medications, stimulants (cocaine), opioids (heroin), and hallucinogens.¹¹²

Despite the high prevalence of substance use among women of childbearing age,¹¹³ limited literature is published on polysubstance use. A study that used pooled data (2005-2014) from National Survey on Drug Use and Health (NSDUH) on reproductive-aged women in the United States (US) found polysubstance use common among respondents.¹¹⁴ They found that about 50% of women who used prescription opioids for non-medical reasons were binge drinking.¹¹³ Another NSDUH study using 2015-18 data to investigate alcohol use and co-use of other substances among women of childbearing age found that 38.2% of pregnant respondents who indicated consuming alcohol also reported using one or more additional substances.¹¹² These substances included tobacco (28.1%), marijuana (20.6%), opioids, and other substances. The women who continued use during pregnancy also reported substance use in the preconception period.¹¹² Another study documented co-using opioids with smoking cigarettes during pregnancy.¹¹⁵ The findings from eight US states' data noted that about two-thirds of women using cannabis before and during pregnancy also smoked cigarettes.¹¹⁶ Substance use is also associated with increased odds of unprotected sex, prior abortion, sexually transmitted infections (STI) symptoms,¹¹⁶ and a higher risk of developing comorbid health and psychiatric conditions.¹¹⁷ A recent study based on PRAMS data from 6 US states reported the prevalence of preconception marijuana of 8%. Among these users, 55% also smoked tobacco, and 77.4% consumed alcohol.¹¹⁸ Only a few studies have documented polysubstance use among women of

childbearing age, and lesser is known about their reproductive health. A higher prevalence of polysubstance use was observed among non-Hispanic Whites and women with low educational attainment.¹¹⁴ The paucity of studies on polysubstance use among women points to the gap in the literature.

Treatment and prevention strategies for polysubstance use are limited compared to single substance use.¹¹⁹ In addition, women with polysubstance use suffer poor reproductive and sexual health¹¹⁴ and are likely at increased risk for unintended pregnancy.¹²⁰ The prevalence, patterns, and sociodemographic correlates of polysubstance use among women merit additional investigation. This information could help identify at-risk women and guide the prevention and treatment efforts to improve maternal and child health outcomes. To address this gap, the current cross-sectional study assessed the prevalence and patterns of polysubstance use, the likelihood of unintended pregnancy associated with polysubstance use, and the sociodemographic correlates of unintended pregnancy among women with polysubstance use in a national representative sample.

Specific aim 2

Specific Aim 2a: Examine the association of polysubstance use and unintended pregnancy among women of childbearing age. If analyses indicate a significant association, compare polysubstance use between sub-types of unintended pregnancies: 1) mistimed, 2) unwanted and 3) ambivalent.

Aim 2b: Assess the association between sociodemographic correlates and unintended pregnancies among women with polysubstance use.

Materials and Methods

Data and measures

The current study is based on a cross-sectional, secondary data analysis of a subset of the PRAMS Phase 8 data. For a complete description, refer to Chapter 2.

Outcome Variables:

Pregnancy Intention. The outcome variable pregnancy intention was assessed by response to the following question, "Thinking back to just before you got pregnant, how did you feel about getting pregnant? The responses, "I wanted to be pregnant then" or "I wanted to be pregnant sooner," were classified as intended pregnancies. The response "I wanted to be pregnant later" was regarded as mistimed, and "I did not want to be pregnant then or in the future" was classified as unwanted. The response, "I was not sure," was categorized as ambivalent. Mistimed, ambivalent, and unwanted were grouped as unintended pregnancies for binary analysis.¹²¹

Exposure variables: Substance use included the following substances.

Alcohol consumption: For alcohol consumption, those who responded yes to drinking were categorized as drinkers. The number of alcoholic drinks /weeks was used to define moderate (up to 7 drinks/week) and heavy drinking (8-14 drinks/week).¹²² Binge drinking was described as having four or more drinks in 2 hours, at least once during the preconception period.¹²³

Cigarette smoking: Preconception smoking was assessed by a yes/no question about smoking three months before pregnancy. Smoking levels were built on the number of cigarettes/ days, <10 cigarettes/day were considered moderate smoking, and ≥ 10 were regarded as heavy smoking.^{124,125}

Cannabis: Cannabis use was assessed by one- and three-month usage before pregnancy.

Opioids (Prescription) were defined as hydrocodone (Vicodin), oxycodone (Percocet), or codeine.

Illicit/recreational drugs: The variable illicit/recreational drugs was created by combining the yes/no questions about the following drugs: 1- adderall, 2-methadone, 3-heroin, 4-amphetamines, 5- cocaine, 6- tranquilizers, and 8- sniffing gasoline, glue, aerosol spray cans, or huffing

Nicotine/Tobacco products other than smoking: Due to the small number of respondents (ranging from 0.7%-6.6%), new variable nicotine/tobacco forms were created by combining the use of hookah, electronic cigarettes, cigars, cigarillos, flavored cigars, nicotine, betel nut or betel quid, and chewing tobacco, snuff, snus, and dip.

Polysubstance was defined as using two or more of the above substances by the participants.

Covariates: The covariates included maternal age, race/ethnicity, education, rurality, income to needs ratio, and having mental distress. Rural/urban status was assigned using National Center of Health Statistics (NCHS) codes. Maternal age at conception was categorized as ≤ 17 , 18-24, 25-34, and 35+ years. The race was classified as Asian, White, Black, and others. Education was based on years of education as less than high school (< 12 years), high school (12 years), some college (13-15 years), and graduate (≥ 16). The income-to-needs ratio was derived from family income (median of the income categories) and family size (number of dependents plus self) variables. The poverty threshold adjusted for a family was divided by annual household income size using the Census Bureau's guidelines to determine the poverty threshold adjusted for family size (2016-17, respectively).¹²⁶ The variable was dichotomized as < 1 below the federal poverty level (FPL) and ≥ 1 as at/above FPL.¹²⁷ The question about feeling sad or depressed before the current pregnancy defined mental distress.

Due to the smaller number of participants in a few polysubstance using groups, age, education, and race/ethnicity were recategorized for the sociodemographic indicators. Participants were categorized as ≤ 19 , 20-34, and 35+ years of age. Maternal education was classified as \leq high school, some college, and graduate. Due to a few respondents in the Asian category of race and ethnicity, this group was merged with the ‘other’ race category. The race/ethnicity categories included Non-Hispanic White, Hispanic White, Black, and Others. A detailed description of the above variables is mentioned in chapter 2.

Statistical Analysis

All statistical analysis was conducted in SPSS version 26 (IBM corp. Armonk NY) using complex survey procedures advised by the Center for Disease Control and Prevention (CDC).¹²⁸ For the descriptive analyses, frequencies and weighted percentages with 95% confidence interval (CI) were computed using weights assigned to each observation in the PRAMS dataset.

Specific aim 2(a)

Bivariate analysis was performed using chi-square statistics to identify the polysubstance use patterns. Binary and multinomial logistic regression were used to assess the independent association of unintended pregnancy overall and by subtype (unwanted, mistimed, and ambivalent) to polysubstance use (smoking, alcohol consumption, and use of marijuana, illicit/recreational drugs, and prescription opioids). Multivariable analyses were adjusted for demographics, rurality, and other potential confounders.

Specific aim 2(b)

Descriptive analyses were performed to study and compare the sociodemographic characteristics of women co-using alcohol with other substances, yielding frequencies and weighted percentages. We identified three highly prevalent patterns of substance use involving

alcohol, including use of alcohol only, alcohol use in concert with cigarette smoking, use of alcohol with cannabis, and use of alcohol in addition to illicit/recreational drugs. To assess the relation of sociodemographic characters to unintended pregnancy among these groups of substance users, we created individual models for each sociodemographic variable. These factors include maternal age, race/ethnicity, level of education, annual income, marital status, and rurality.

Results

Sample characteristics

Of the 74,543 women of childbearing age who participated in the PRAMS 2016-17 survey, 39831 (56.6%) consumed alcohol, with one-third (33%) being involved in binge or heavy drinking. The prevalence of cigarette smoking was 17.4%, and nearly one in four (27%) smokers reported heavy smoking during the preconception period. Table 1 shows participants' sociodemographic characteristics stratified by smoking and alcohol use. The majority of the women were located in urban areas (~ 80%), were non-Hispanic White, and were 25-35 years of age. Overall, 62.1% of the women were married, and among the smokers (36.4%) and heavy smokers (33%), one-third were married. Overall, 72.3% of women reported their income to need ratio at/above FPL, and the prevalence was higher for those who consumed alcohol (80.4%) than smoking cigarettes (55%). Also, a smaller proportion of smokers (12.8%) and heavy smokers (6.5%) had a graduate degree compared to women who drank alcohol (45.6%). Among all respondents, the prevalence of depressive symptoms (63.4%) and physical or emotional abuse (57%) were highest among heavy smokers. The inadequacy of prenatal care was noted among substance-using women; a higher proportion of women smoking cigarettes (8.2%) and heavy

smokers (8.5%) reported inadequate prenatal care compared to all women (5.8%). The rate of unintended pregnancies was 41% in the overall population and highest in the heavy smokers (62.5%), followed by smokers (58%), heavy/ binge drinkers (45%), and alcohol consumers (39%). Similarly, contraception use was lower in women smoking cigarettes (30%) than alcohol-consuming (41.3%). The breakdown of unintended pregnancy among subtypes, i.e., mistimed, unwanted, and ambivalent, showed that mistimed pregnancies (23.9%) and unwanted pregnancies (10.1%) were highest among smokers. In comparison, ambivalent was highest among heavy smokers (27.9%) compared to all other groups.

Polysubstance use

Alcohol was the most commonly used substance, with nearly half of the sample (56.6%) reported drinking and (33%) heavy or binge drinking. About 17% reported smoking, with 30% documenting heavy smoking. A higher prevalence of polysubstance use was noted in the current sample. Among women who mentioned heavy or binge drinking, one-third (31%) smoked cigarettes, 30% were co-using cannabis, 19.5% used tobacco/nicotine products other than smoking cigarettes, and 4.5% used illicit/recreational drugs. Polysubstance use was also common among cigarette-smoking women, two-thirds (70%) consumed alcohol, and a half (50%) were heavy or binge drinkers. Cannabis use (25.8%), illicit/recreational drugs (12.5%), other tobacco/nicotine products (33%), and opioids (10.4%) were also reported among smokers. The co-use of cannabis (31.8%), tobacco/nicotine products (37%), and opioids (13.6%) were highest among heavy smokers than all other groups (Table 1).

Association of unintended pregnancy with polysubstance use

Alcohol and heavy or binge drinking

Table 2 depicts the association of unintended pregnancy to co-using alcohol with other substances in a representative sample of US women. Statistically significant and positive association of unintended pregnancy was observed with heavy smoking (AOR: 1.5, 95%CI:1.4 – 1.6), cannabis (AOR: 2.0, 95%CI:1.6 – 2.4), tobacco/nicotine (AOR: 1.6, 95%CI:1.4 – 1.7), and illicit/recreational drugs (AOR: 1.8, 95%CI: 1.1 – 2.7). Higher odds of unintended pregnancy were noted among heavy or binge drinkers with smoking (AOR: 1.9, 95%CI: 1.5 – 2.4), cannabis use (AOR: 2.1, 95%CI: 1.4 – 3.1), tobacco/nicotine (AOR: 2.3, 95%CI: 1.7 – 3.1). The risk of unintended pregnancy was not statistically significant with co-use of opioids with alcohol (AOR: 1.3, 95%CI: 0.9 – 1.9) and heavy or binge drinking (AOR: 1.4: 95%CI: 0.6 – 3.6) after adjusting for potential confounders.

Association of mistimed, unwanted, and ambivalent pregnancies with polysubstance use

Table 3 shows the likelihood of unintended pregnancy sub-types, i.e., mistimed, unwanted, and ambivalent with preconception use of alcohol in concert with other substances. The risk estimates with polysubstance use among alcohol-consuming women varied between smoking (AOR: 1.3, 95%CI: 1.1 – 1.4) and illicit/recreational drugs (AOR: 2.7, 95%CI: 1.4 – 5.1). Among three sub-types, the magnitude of the association was higher for unwanted pregnancy with smoking (AOR: 1.8, 95%CI: 1.5 – 2.1), heavy smoking (AOR: 2.3, 95%CI: 1.4 – 3.9), cannabis (AOR: 2.8, 95%CI: 2.0 – 3.8), tobacco/nicotine use (AOR: 1.8: 95%CI: 1.5 – 2.3), illicit/recreational drugs (AOR: 2.7, 95%CI: 1.4 – 5.1) and opioids (AOR: 2.3, 95%CI: 1.3 – 4.0). The association of mistimed pregnancy with illicit/recreational drugs (AOR: 1.6, 95%CI: 1.0 – 2.6) and opioids (AOR: 1.2, 95%CI: 0.7 – 2.0) were not statistically significant (Table 4).

Socio-demographic indicators of unintended pregnancy among polysubstance users

In the current sample of US women who gave birth during 2016-17 and participated in PRAMS 2016-17, about a half (N=39,831) documented alcohol consumption in the preconception period. To identify and compare the sociodemographic characteristics of women who were co-using alcohol with other substances following groups were created; alcohol and smoking (N=9,145), alcohol and cannabis (N=1511), alcohol and illicit/recreational drugs (N=346), and smoking and cannabis (N=1091). Table 4 shows the maternal characteristics stratified by the polysubstance use patterns. A larger fraction of women co-using alcohol and illicit recreational drugs were located in urban areas (86.5%). The majority of women in all groups were 25-34 years of age, were non-Hispanic White, and had less than high school education. More women in the alcohol and cannabis group had graduate education (23.7%) than in other groups. More respondents in smoking and cannabis (55.4%) and alcohol and illicit/recreational drug (46.0%) users were below the FPL. Two-thirds (65.6%) of alcohol consumers reported their marital status as married, while a higher proportion of polysubstance users reported it as other. About half to two-thirds (69.3%) of the pregnancies were reported unintended in all polysubstance using groups. (Table 4).

Factors associated with unintended pregnancy among polysubstance users

After adjusting with other risk factors, living in urban areas, income below FPL, and marital status other than married were strong and significant predictors of unintended pregnancy among all polysubstance users. Women older than 35 years (AOR: 2.0, 95%CI: 1.3 – 3.0) and Black race (AOR: 1.4,95%CI: 1.1 – 1.7) increased the odds of unintended pregnancy among women co-using alcohol and smoking. (Table5). Having less than or equal to a high school

diploma was significantly associated with unintended pregnancy among alcohol and smoking (AOR: 2.8, 95%CI: 2.3 – 3.6) and alcohol and cannabis users (AOR: 2.6, 95%CI: 1.6 – 4.6). Women reporting marital status other than married had higher odds of unintended pregnancy among alcohol only (AOR: 3.2, 95%CI: 3.0 -3.5), alcohol and smoking (AOR: 2.4, 95%CI: 2.0 - 2.8), and alcohol and cannabis (AOR: 2.8, 95%CI: 1.8 – 4.4).

Discussion

Principal findings

Our findings from the current population-based representative sample of US women delivering live births during 2016-17 demonstrated a positive and statistically significant association between polysubstance use during the preconception period and the risk of unintended pregnancy. The prevalence of unintended pregnancy was 39% for alcohol consumers and the highest for heavy smokers (62.5%). However, when alcohol was used with smoking, illicit substances, or cannabis, the prevalence of unintended pregnancy in these sub-groups was nearly 60%. The analysis by the sub-types also yielded similar results, with higher odds observed for unwanted pregnancies. We observed a high prevalence of polysubstance use, and women drinking alcohol also smoked and co-used cannabis, illicit/recreational drugs, nicotine/tobacco, and opioids. Cannabis was the most commonly co-used substance both with smoking and alcohol. Compared to moderate drinking and smoking, women with heavy/binge drinking and heavy smoking had a high prevalence of polysubstance use.

The finding that co-using alcohol with other substances increased the odds of unintended pregnancy is previously reported. One study found alcohol use/abuse indicative of concurrent use of the illegal substance and risky sexual behavior, including not using contraception, among

adolescents and young women aged 18-29 years.¹²⁹ Another study noted a high prevalence of alcohol, tobacco, and cannabis among women of childbearing age, with the most frequent co-use pattern including alcohol, cannabis, and tobacco.¹³⁰ A similar polysubstance use pattern was observed in the present sample of women of childbearing age. In the current study, the association of co-using alcohol was not statistically significant with unintended pregnancy after adjusting for potential confounders, which contradicts the findings of Hail et al., where a high prevalence of unintended pregnancy was reported among opioid users. This shows the critical role of socioeconomic factors when examining this association in this study population.

In this study, the authors also performed a stratified analysis of demographic factors by most prevalent substance use pattern to compare the demographic indicators of unintended pregnancy. The results showed that most women reporting polysubstance use resided in urban areas, were 20-34 years of age, were non-Hispanic White, had education \leq high school, were not married, and their annual income was below the FPL. About two-thirds of the pregnancies among participants documenting polysubstance use were unintended. The multivariable analysis indicated that income less than FPL, living in urban areas, and not having a graduate degree were substantial and statistically significant predictors of unintended pregnancy. A study conducted in New York City that focused on the low-income urban population found an even higher prevalence (>80%) of unintended pregnancy in women who smoked, used drugs, and consumed alcohol compared to our study. They also found that alcohol consumption increased the odds of unintended pregnancies among low-income urban women.¹³¹

A precarious finding from our study was the reported depressive symptoms by a large proportion of the respondents. About 17% of women felt depressed in the preconception period, and among heavy alcohol users and smokers, the depression rate was more than 50%. This

alarming high prevalence of depression rate needs to be further examined since it is known to cause poor birth outcomes, including pre-term birth and LBW.¹³² In the current study, more women in the substance-using groups reported inadequacy of prenatal care. This is consistent with what is found in the literature, where women using substances are at an increased risk of inadequate prenatal care.¹³³⁻¹³⁴

The findings of our study suggest a potential sequel that starts with the initiation of substance use with the legal substances, particularly smoking and alcohol, and progressing towards heavy smoking/drinking and proceeding to co-using other substances. This pattern is in alignment with the gateway drug hypothesis. This hypothesis suggests the beginning of substance use with alcohol, tobacco, and cannabis that escalates to using more addictive substances, including illicit drugs.^{135,136}

The high prevalence of co-using cannabis with alcohol and smoking is notable concerning the policy changes and legalization efforts regarding cannabis use in a few states. A recently published study that used PRAMS 2016 data found higher use of cannabis among states that legalized its use. It occurs due to the general population's easy availability and acceptance of use among the general population.¹¹⁸

Public health implications

The preconception period is a critical time in women's life to promote healthy behavior that can significantly improve maternal and child health outcomes.¹³⁷ Implementing interventions to encourage healthy behaviors, including contraception use, screening women for substance use, and educating them on the harmful effects of substance use, can significantly improve maternal and child health outcomes.

Polysubstance use among women of childbearing age is common and leads to health risks for both maternal and child health. Our study's findings suggest the need for interventions addressing polysubstance use in women of childbearing age. The United States Preventive Services Task Force (USPSTF)¹³⁸, CDC¹³⁹, and American College of Obstetricians and Gynecologists (ACOG)¹⁴⁰ recommend universal screening of women of childbearing age and pregnant women. There is evidence suggesting the benefits of screening and concise interventions leading to a reduction in alcohol use, smoking, and illicit drug use^{141,142,143}.

In addition to the screening, counseling and treatment services should be offered or referred. Women with substance use who are not ready to quit or not planning to become pregnant should be given access to effective contraception methods. Addiction or substance use is a mental health issue and should be treated like other medical conditions. One of the barriers to accessing health care and family planning services is the social stigma of substance use.¹⁴⁴ Women with substance use experience social and structural stigma.¹⁴⁵ Education programs for the general population and healthcare providers to enhance non-stigmatizing behavior can help people cross these barriers.

The findings of this study also highlighted the increased odds of unintended pregnancy among urban and women below the FPL. This suggests implementing tailored interventions to address the needs of women at high risk for unintended pregnancy.

Overall, there is a need for appropriate educational, screening and treatment efforts to identify the women in need and provide treatment services integrated with family planning services.¹⁴⁶ When planning and implementing interventions, substance use prevention and treatment efforts should consider the critical determinants, including social, economic, environmental factors, social support, family structure, and cultural norms.¹⁴⁷ Screening and

assessment help provide information regarding these factors and information on mental health,¹⁴⁸ physical or emotional abuse,¹⁴⁹ childhood adversity¹⁵⁰ that are known determinants of substance use, and poor reproductive health among women. Screening and assessment from a perspective affirming the cultural values and beliefs facilitate the women's engagement in the screening leading to the treatment process.¹⁵¹ In addition to cultural differences, women from minorities, racial/ethnic groups, living in rural areas,¹⁵² and not speaking English experience unique challenges while pursuing substance use treatment.¹⁵³ A customized supportive therapy aimed to address the barriers identified in the screening and assessment process may help women contact and stay in the treatment services.¹⁵⁴

Women with substance use are at an increased risk of unintended pregnancy. An estimated nine out of ten opioid-using women¹⁵⁵ and eight out of ten pregnancies among illicit drug-using women¹³¹ were unintended. Inconsistent or a complete lack of effective contraception is one of the significant correlates of unintended pregnancy.¹⁵⁶ Women using substances report poor or no access to family planning services, even when they are in treatment services or after discharge.¹⁵⁷⁻¹⁵⁸ The most commonly reported barriers to family planning services include but are not limited to fear of criminalization, feeling of guilt and shame, lack of information, lack of insurance, difficulty getting appointments, and filling birth control prescriptions.¹⁵⁹ A systematic review on preventing unintended pregnancies among substance-using women found contraception counseling and provision more effective than traditional educational methods.¹⁶⁰ Another systematic review concluded that offering contraception services and substance use treatment could help reduce unintended pregnancy among these women.¹⁶¹ A qualitative study conducting in-depth interviews and focus groups with 115 women found that most women prefer family planning services conjugated with substance use

treatment.¹⁶² Thus, efficient screening followed by customized evidence-based interventions may help address substance-using women's reproductive needs.

Strengths and limitations of the study

To the best of our knowledge, this is the first study examining the association between polysubstance use and unintended pregnancy among women of childbearing age in the US. This study used a large sample from population-based data of PRAMS. We also performed a stratified analysis to compare the characteristics of groups with highly prevalent patterns of co-using substances. The study also identified a range of predictors of unintended pregnancy women reporting polysubstance use.

The study also has a few limitations. First, this cross-sectional study cannot predict polysubstance use patterns over time. However, estimating preconception substance use might provide a temporal relationship to measure the risk associated with unintended pregnancy. Secondly, the analysis was limited to women with live births, potentially leading to underreporting adverse outcomes (miscarriage or stillbirth) related to unintended pregnancy and substance use. Additionally, nearly half of unwanted pregnancies end up in abortion.¹⁶³ Association between abortion and prior substance use has also been documented in the literature; our study did not have this information. Third, due to retrospective measurement, recall bias may influence pregnancy intention. However, detailed analyses regarding the reliability of self-reported pregnancy intendedness have been conducted using data from the National Longitudinal Study of Youth,¹⁶⁴ National Longitudinal Study of Adolescents Health,¹⁶⁵ and National Survey of Family Growth¹⁶⁶ indicate that, in aggregate, prevalence estimates remain relatively stable across repeated measurements with small inconsistent reports in both directions. Fourth, PRAMS questionnaires rely on self-report and may thus under-ascertain behaviors perceived as

unhealthy. Polysubstance use is prone to underreporting owing to social desirability bias and the widespread stigma of illicit drug use.¹⁶⁷ However, women may be more willing to disclose their behaviors on a confidential survey such as PRAMS than via other venues.¹⁶⁸ Fifth, Since PRAMS data only include women with a fixed address, this study did not include homeless or transient women.

Conclusion

In the current sample, the US women of childbearing age reporting polysubstance use during the preconception period were more likely to experience an unintended pregnancy. They were also likely to live in urban areas, not have a graduate-level education, not be married, and have less annual income than FPL. These factors should be considered in developing and implementing tailored screening and treatment interventions to prevent unintended pregnancy among women using substances to improve maternal and child health outcomes.

Chapter 4

Unintended Pregnancy Among Substance-Using Women: A Systematic Review with Meta-Analysis

Abstract

Background: Unintended pregnancy is an indicator of reproductive health and has severe consequences for women's and children's health and wellbeing. Although unintended pregnancy rates are higher among women who use illicit and recreational drugs, systematic reviews are lacking to estimate the pooled risk of unintended pregnancy in this population. In this study, we conducted a systematic review (SR) with meta-analysis (MA) to address this gap.

Methods: Predetermined criteria were used to determine study eligibility. To identify studies, we screened records from six electronic databases (PubMed (MEDLINE), Scopus, CINAHL, PsychINFO, and Web of Science) and reviewed citations from retrieved articles. Data from included studies were abstracted in a pretested codebook. Each study was assessed for risk of bias using the Newcastle-Ottawa Scale (NOS). The pooled effect size was calculated using the inverse variance method. Heterogeneity among studies was determined using I^2 statistics. A DOI plot with an *LFK* index was created to assess the risk of publication bias. In addition, we compared the prevalence of illicit and recreational drug use, unintended pregnancies, and its determinants across studies. Influence analysis was used to evaluate the robustness of pooled findings.

Results: Eight studies (1 case-control, 1 cohort, 6 cross-sectional) met criteria for inclusion in our review (N=38,520 women). Prevalence of reported illicit and recreational drug use ranged from 4.0-21.0%, and that of unintended pregnancy, from 5.3 - 82.0%. Pooled findings of our meta-analysis indicated that the use of illicit and recreational drugs during the preconception period was significantly and positively associated with the likelihood of unintended pregnancy (pooled odds ratio (POR)=1.84, 95% confidence interval 1.4-2.4). Influence analysis supported the robustness of these findings, with PORs ranging from 1.65 – 2.1, and all remaining significant. The DOI plot was asymmetrical, and the *LFK* index was 2.66 suggesting a potential small study effect. NOS scores indicated a moderate to low risk of bias across studies.

Conclusion: The findings of this SR with MA suggest that maternal preconceptual use of illicit and recreational drugs may substantially increase the risk for unintended pregnancy. Specific early interventions are needed to reduce substance use among women of childbearing age. If confirmed in additional large prospective studies, these findings may have important implications for public health and clinical education, practices, and policies designed to reduce the risk of unplanned pregnancy and improve reproductive health in this population.

Introduction

Unintended pregnancy is a significant global public health concern affecting the well-being of women and their families.¹⁶⁹ An unintended pregnancy can be mistimed or unwanted, indicating poor sexual health and unmet reproductive and family planning needs.¹⁷⁰ Unplanned pregnancy is a known risk factor for inadequate prenatal care, pregnancy complications, poor birth outcomes, including low birth weight and preterm birth, post-partum depression, and poor child health and development.¹⁷¹⁻¹⁷²⁻¹⁷³ Women experiencing unintended pregnancies report adverse effects on their physical¹⁷⁴ and mental health,¹⁷⁵⁻¹⁷⁶ as well as on social, economic, and cultural aspects of their lives.¹⁷⁷ Unplanned pregnancy has also been associated with adverse lifestyle behaviors during pregnancy, including inadequate vitamin intake, physical activity, weight gain, and the use of tobacco, alcohol, and other substances harmful to the developing fetus.¹⁷⁸⁻¹⁷⁹

In the United States, a significant proportion of women of childbearing age use substances.¹⁸⁰ The detrimental effects of substance use on women's health and pregnancy outcomes are well-known.¹⁸¹ Women using substances in the preconception period are more likely to continue use during pregnancy, increasing the risk for poor pregnancy and perinatal outcomes,¹⁸² including low birth weight (LBW), preterm birth, stillbirth, and Neonatal Abstinence Syndrome (NAS).^{183,184} Substance use during pregnancy is also linked to pregnancy intention in a few studies.^{185,186} Women with unintended pregnancies are more likely to continue substance use during pregnancy.¹⁸⁷ Higher rates of unintended pregnancy among substance-using women than non-substance users were also reported in another study.¹⁸⁸ A study among substance-using women revealed that 84% of pregnancies were unintended.¹⁸⁹ Although substance use during pregnancy and its impact on fetal health is well established in the

literature¹⁹⁰, less is known about illicit and recreational drugs during the preconception period and their relationship with pregnancy intention.

Moreover, there is conflicting evidence on recreational drug use's effects on fertility.¹⁹¹ Quitting substance use to increase fertility is also common among men and women.¹⁹² Chronic use of few drugs deteriorates sexual response among both males and females.¹⁹³ On the contrary, the use of illicit and recreational sexual aid is also reported.¹⁹⁴ In addition, it is also linked with risky sexual behaviors, including unprotected sex that elevates the risk of unintended pregnancies and sexually transmitted infections (STIs).¹⁹⁵ Another study reported intoxication during sexual activity and not using contraception as risk factors for unintended pregnancy.¹⁹⁶ In other studies, using illicit and recreational drugs during the preconception period increased the risk of unintended pregnancy.^{197,198,199} A recently published systematic review on preventing unintended pregnancies among women using psychoactive substances concluded that substance-using women vary widely in demographic, reproductive, and behavioral characteristics.²⁰⁰

Although several studies suggest that preconception use of illicit and recreational drugs may be associated with an increased likelihood of unintended pregnancy differences in study populations, sample sizes and study designs have limited conclusions regarding the significance and magnitude of these associations. A rigorous systematic review (SR) and meta-analysis (MA) of existing studies on this topic will help clarify the strength and magnitude of this relationship, aid in identifying limitations in the current literature on this topic and help inform future directions for research. However, to our knowledge, systematic reviews regarding the potential association of preconception use of illicit and recreational drugs to risk for unintended pregnancy in women of child-bearing age are lacking. To date, the author is not aware of any systematic review (SR) or meta-analysis (MA) that estimated the risk of unintended pregnancy with illicit

and recreational drug use among women of childbearing age. Understanding the link between these factors is particularly important in light of the high prevalence of substance use and unintended pregnancy among women of childbearing age. This study aimed to conduct a systematic review with meta-analysis to establish evidence essential for policy and practice efforts to improve maternal and child health. This chapter details specific aim 3 and statistical methods used to achieve this aim.

Specific Aim 3: To conduct a systematic review with meta-analysis to assess the relation of illicit and recreational drugs use and the likelihood of unintended pregnancy among women of childbearing age.

Research design and Methods

Purpose

The purpose of this study was to conduct a comprehensive SR with MA to examine the risk of unintended pregnancy among women using illicit and recreational drugs during the preconception period. The drugs include marijuana/cannabis, cocaine, ecstasy (3,4-methylenedioxymethamphetamine) or MDMA, hallucinogens, stimulants, and other street drugs. We conducted this SR with MA by following Cochrane Collaboration's recommendations and guidelines for conducting SR and MA for observational studies as well as the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement. This study was registered in PROSPERO, a prospective international registry for SRs (PROSPERO 2021; ID: CRD42021286231).

Study eligibility

A priori eligibility criteria were set for inclusion and exclusion of the studies. We utilized Population, Intervention, Comparison, Outcome (PICO) criteria, a Cochrane search, and an evaluation tool²⁰¹ to ensure all key study components were included in our study screening and assessment. Our review was limited to original studies published in English between January 2000 and June 2021 and conducted in Western developed countries (United States (US), Canada, Western European countries, Australia, New Zealand). Additional inclusion criteria were: 1) observational design (cross-sectional, case-control, or cohort); 2) study population/sample comprising women of childbearing age, including pregnant women and women who had a live birth; 3) explanatory variables included the use of any illicit and recreational drugs (e.g, marijuana/cannabis, cocaine, ecstasy (3,4-methylenedioxymethamphetamine or MDMA), hallucinogens, stimulants, and other street drugs) during the preconception period; 4) pregnancy intention assessed as either the primary outcome or a variable of interest, and 5) risk estimates presented (or calculable from available data) for the association of illicit and recreational drug use to unintended pregnancy.

We excluded from our SR the following: review articles, comments, and letters, studies where the outcome of unintended pregnancy was abortion, studies published in a non-English language, studies published only in abstract or dissertation form, unpublished studies, Studies conducted outside the general population including but not limited to sex workers, homeless women, incarcerated, or women in substance use treatments, and studies lacking quantitative outcome data.

The authors utilized several resources to identify the eligible studies. These methods include electronic databases and citation tracking from retrieved articles. Although we used numerous sources to identify the published literature, we did not include grey literature. It includes unpublished reports rejected or unsubmitted manuscripts.²⁰² Some researchers have shown concerns regarding the methodological quality of grey literature compared to the published studies due to the lack of peer reviews and formal quality control.^{203,204} Thus, the inclusion of grey literature may jeopardize the quality of MA, given that it depends on the quality of included studies in the analysis. However, there is limited evidence regarding the lower quality of grey literature than the published literature.²⁰⁵ It is also thought that excluding grey literature may overestimate the effect size (ES) since studies with non-significant findings are less likely to be published.²⁰⁶ In the current SR with MA, we excluded grey literature due to limited resources and difficulty accessing the unpublished literature.

Data sources

The literature search plan utilized numerous resources, including electronic searches in multiple databases, citation indices of pertinent review articles and papers identified as potentially eligible, and contact with experts in the field. To develop a specific search strategy for each database, an information retrieval specialist (Director Health Sciences Library, SA) guided the planning process to create correct search strings for each electronic database search. To begin the electronic databases search strings, MeSH (medical subject heading) and the Boolean operator were created. For the current study, we searched the following databases from October 18-26, 2021: (1) PubMed (MEDLINE), (2) Scopus, (3) CINAHL, (4) PsychINFO, and (5) Web of Science. All aspects of literature were documented, including data source, journal,

date, etc. We initiated the search by conducting a preliminary search in PubMed using MeSH terms. The Pubmed search strings, including MeSH term, were as follows:

("pregnancy, unplanned"[MeSH Terms] OR "pregnancy, unwanted"[MeSH Terms]) OR (unintended pregnancies OR unintended pregnancy) OR (unplanned pregnancies OR unplanned pregnancy) OR (unwanted pregnancies OR unwanted pregnancy) AND "drug abuse") OR "drug dependence") OR "drug addiction")) OR]) ("substance-related" AND "disorders") OR "substance-related disorders" OR ("drug" AND "habituation") OR "drug habituation").

Each search was conducted separately and was downloaded and saved as a separate file using Endnote(X9). The search on the electronic database was supplemented by a hand search for citation tracking from the reference list of the included articles and relevant review articles. The duplicates were removed both electronically and manually.

Study Selection

Two researchers (SS and RM) independently screened studies based on pre-defined eligibility criteria for inclusion. We reviewed the titles and abstracts of individual studies. Full-text articles were retrieved and reviewed if they appeared to meet the inclusion criteria. After completing the individual study selection, the two reviewers screened every selection for agreement. A third reviewer (AU) resolved the matter in cases of disagreement. Using Cohen's kappa statistics,²⁰⁷ the overall agreement rate between the two researchers before correcting discrepancies was 0.86.

Data Abstraction

A detailed codebook was created in Microsoft Excel (version 2112). This codebook included studies' characteristics, i.e., authors' name, year of publication, region of study, data source, study design, sample size, outcome and exposure variables, population characteristics,

and statistical findings required to calculate the effect size. The codebook was pilot-tested and revised. The two authors (SS and RM) coded and extracted the information from each study independently to avoid any abstraction bias. The two researchers then compared the data for accuracy and consistency to reach 100% agreement. A third reviewer (AU) resolved the matter in case of disagreement.

Risk of Bias Assessment

After the full-text review of the studies included in the SR and MA, the risk of bias assessment was performed to capture and analyze variation among the studies. The risk of bias describes "a systematic error or deviation from the truth, in the results or inferences." The biases reported in observational studies include (1) selection bias (sampling frame, recruitment, retention, nonresponse, loss to follow-up), (2) social desirability bias, (3) recall bias, (4) confounding and residual confounding bias, (5) measurement bias, and (6) interviewer bias. Several tools have been used to evaluate the risk of bias and quality of studies with no gold standard established.²⁰⁸ However, one tool, the Newcastle-Ottawa scale (NOS), is commonly used.²⁰⁹

The NOS results from an ongoing collaborative effort between the Universities of Newcastle, Australia, and Ottawa, Canada. Separate scales are available for cohort, cross-sectional and case-control studies. Each scale consists of eight items, with three dimensions including selection, comparability, and outcome or exposure. A star system is used ranging from 0-9; the higher number of stars depicts the higher quality of studies. The content validity of the NOS is based on a critical review of the items by several experts who evaluated its clarity and completeness to assess the quality of studies included in SR and MA.²¹⁰

Statistical Analysis

After data cleaning in Microsoft Excel (version 2112), qualitative and descriptive analyses with frequencies and percentages were generated.

Qualitative Analysis

A detailed description of the included studies was created for quality analysis, including studies and populations characteristics.

Calculations for Effect Size

The effect size depicts the strength and the direction of association between two variables. In the current study, we used the OR with 95%CI as our effect size measure to estimate the risk of unintended pregnancy among women using drugs.

Pooling of Effect Size's

The inverse variance (IVhet) model analyzed and summarized the results using MetaXL (version 5.3).²¹¹ The IVhet model provides a quasi-likelihood-based expansion of the CI around the inverse variance weighted pooled estimate when studies exhibit heterogeneity (without inappropriate changes to individual study weights, as observed in the random-effects model), keeping the mean squared error (MSE) lower than with the random effects estimator.²¹² This method is regarded as the measure of precision and is inversely related to the size of confidence intervals (CIs). The study with more precision, i.e., smaller CIs, will contribute more to the overall ES than those with wider CIs. The IVhet method also takes sample size and within-sample heterogeneity into account. Larger sample sizes and those with less heterogeneity produce more precise estimates.²¹² Heterogeneity of the effect estimates of different studies was assessed using two statistics, Cochran's Q test statistic and its corresponding p-value, and I^2

statistics. The major purpose of conducting an MA is to investigate the potential sources of heterogeneity of results in the included studies.²¹³ I^2 statistics narrate the variations across the studies due to heterogeneity rather than chance.²¹³ It also summarizes the input and extent of heterogeneity to determine the robustness of overall conclusions.²¹⁴ I^2 is an intuitive expression of the inconsistency of studies results and is calculated as $100\% \times (Q - df)/Q$, where Q is Cochran's heterogeneity statistics, and df is the degree of freedom. For current study, I^2 was classified (0% - 25%) as trivial, (25.1% - 50%) as low, (50.1% - 75%) as moderate, and (75.1% - 100%) as high. The findings were interpreted regarding the magnitude and direction across studies, evidence for heterogeneity, and the clinical implications of the degree of inconsistency.²¹⁵

We created Forest plots to exhibit the distribution of effect estimates across studies. Publication bias, i.e., the tendency of authors to submit and journals to publish the articles with statistically significant findings. A DOI plot with an LFK index was used in the current study to assess any small study effect and publication bias. An asymmetrical DOI plot and *LFK* index value outside the +1 and -1 is considered a publication bias.²¹⁶ We also performed influence analysis to assure the robustness of the overall findings.²¹⁷ An influence analysis is meant to determine each study's influence on overall results and determine if the study with a larger influence can distort the overall ES.²¹⁸ A cumulative analysis was performed to detect the temporal trends in effect size.²¹⁹

Results

Search results

The flow chart diagram showing the comprehensive search for studies is presented in Figure 1. Of the 4920 records identified from five electronic databases, 152 were selected based

on title screening. After abstract screening and removing duplicates both electronically and manually, 22 potentially eligible articles were identified for detailed review. Of these, 14 were excluded. The excluded articles with reasons are listed in a supplemental file (Supplemental File 1). Eight studies meeting inclusion were included in the current SR with MA.

^{220,221,222,223,224,225,226,227}

Description of included studies

The included studies were published between 2004 and 2020, while the data collection period ranged from 1997 to 2016. Five studies were conducted in the US,^{220-223,226} two studies in the United Kingdom (England, Scotland, and Wales),^{225,227} and one study in Canada²²⁴. The studies included six cross-sectional investigations,^{220,223,227} one case-control study,²²¹ and one prospective cohort study.²²² (Table2) The study populations ranged from pregnant women,^{220,222,223} women delivering a live birth,^{221,226} to women of childbearing age.^{224,225,227} Only two studies utilized hospital data.^{222,223} The remainder were based on large nationally representative data sources, including the National Births Defects Prevention Study,²²¹ Pregnancy Risk Assessment Monitoring System (PRAMS),²²⁶ Office of Family Health, New York City Department of Health and Mental Hygiene,²²⁰ Maternity Experience Survey,²²⁴ and National Survey of Sexual Attitudes and Lifestyles (Natsal-3).^{225,227}

Table 3 provides a detailed description of the exposure and outcome variables. In addition to illicit and recreational drugs, smoking and alcohol consumption were also reported in seven of the eight studies.^{220-221,224-225} Substance use was assessed by employing self-reported questionnaires in all studies. The prevalence of illicit and recreational drugs varied from 4%-21%.^{220,223} A detailed description of population characteristics, including age, race and ethnicity,

marital/relationship status, education, insurance, rurality, and parity, is available in the additional file. (Supplemental file 3)

Prevalence and correlates of unintended pregnancy

Pregnancy intention was measured by validated tools, including London Measure of Unplanned Pregnancy (LMUP)^{223,225,227} PRAMS^{226,226}, or questions explicitly investigating the intention to become pregnant about their recent pregnancy.^{220,221,222} The prevalence of unintended pregnancies varied from 5.3%²²⁵ to 82%.^{220,220} (Table 3). The average crude prevalence in the seven studies using nationally representative samples was 44%. The most commonly reported determinants of unintended pregnancy included age <20 years,^{220-221,224,227} non-Hispanic White²²⁰ and Black race,²²¹ not married or not having a partner,^{220,224} having one or more previous pregnancies,²²⁴ previous adverse pregnancy outcomes,²²¹ lower educational attainment,^{224,227} and abusive relationship.²²⁴ Use of substances in addition to illicit and recreational drugs included smoking^{221-224,227} and alcohol consumption.^{220,223,225-227}

Risk of Bias Assessment

Risk of bias assessment was performed using NOS scales for cross-sectional, cohort, and case-control studies. Overall study level risks of bias are shown in Table 1, and results for each item from individual studies are shown in the additional file (Additional file 2). The studies ranged from 5- 8 out of 9 stars on the NOS scale, indicating a low to moderate risk of bias. Most study populations were representative of the target population, with large sample sizes (n's=2654²²³ to 8886²²⁰) in all but one study²²³. For substance use, self-reported data were used, prone to recall and other information bias. Similarly, studies used a retrospective self-reported validated questionnaire for outcome assessment, increasing the risk of recall bias.

Primary Outcome

The results of all studies, including crude and adjusted ORs and information on factors adjusted for, are detailed in Table 4. Overall, there was a statistically significant and positive association between preconception illicit or recreational drugs use and unintended pregnancy (Pooled OR=1.84, 95%CI=1.4 – 2.4). The inverse variance model MA results for the association between illicit and recreational drugs and unintended pregnancy are presented below. The forest plot exhibiting the effect estimates with 95%CI is shown in Figure 2. The Oulman et al., 2015 study had the smallest CIs and accounted for 28.5% of the overall estimates in the current MA.²²⁴ In contrast, the small cohort study by Lundsberg et al., 2020 accounts for only 0.7% of the overall estimates and reported (0.27 – 7.41) the widest confidence intervals (Figure 2. Forest plot).²²³ The overall pooled OR showed that the women using illicit and recreational drugs during the preconception period have a statistically significant increased likelihood of unintended pregnancy compared to women who did not use drugs (POR=1.84, 95%CI=1.4 – 2.4). A moderate heterogeneity ($I^2=66\%$) across studies, with significant Cochrane Q statistics ($Q=20.41$, $p\text{-value}=0.00$) was also noted. However, after deleting each study, the influence analysis results yielded pooled ORs ranging from 1.65 – 2.1 (Table 6). All ORs remained significant; the very modest variation in ES across studies suggests a lack of outliers or highly influential studies among the investigations included in the MA. The cumulative analysis comparing ORs by year of publication did not show significant changes in the magnitude of risk over the two decades. (2000-2020, Table 7). DOI plot (Figure 3. DOI plot) was asymmetrical, and the *LFK* index was 2.66 indicating a positive asymmetry. As illicit and recreational drug use is often considered a risk factor for unintended pregnancy, and studies yielding non-significant findings may be less likely to be published, investigations confirming an association are more

likely to be published. However, the interpretation regarding a bias requires caution due to the small number of studies (n=8), which increases the likelihood of an asymmetry.

Discussion

Principal finding

This comprehensive SR with MA assessed the relationship between illicit and recreational drugs during the preconception period and the likelihood of unintended pregnancy among women of childbearing age. Pooled findings of the eight eligible studies indicated a significant, 1.84-fold increased risk of unintended pregnancy in women reporting preconception use of illicit and recreational drugs, suggesting that these substances may increase the risk of unplanned pregnancy in women of childbearing age. The results of influence analysis support the robustness of these findings. However, moderate heterogeneity was noted across studies, likely reflecting differences in study population characteristics, measures of drug use, factors adjusted for, and other methodological components, potentially limiting definitive conclusions. The cumulative analysis indicated a consistent magnitude of risk over the two decades, adding to the robustness of the current findings.

The pooled findings of this SR also indicate a high prevalence of both illicit and recreational drug use and unintended pregnancy among women of reproductive age. Broadly consistent with our results, prior studies have suggested about half of the pregnancies in the US²²⁸ and one-third of those in the UK and other European countries are unintended.²²⁷ Unintended pregnancy is considered a global standard or benchmark of reproductive health and has severe consequences for women's and children's health and wellbeing.²²⁹⁻²³⁰ High prevalence

of unintended pregnancy indicates unmet reproductive and family planning needs among women of childbearing age.

Substance use poses serious health risks to women of childbearing age. As noted above, the reported prevalence of illicit and recreational drug use during the preconception period was high, varying from 4%²²⁰ – 21%²²³ in the studies included in this SR. Other studies investigating the prevalence of illicit drug use among women of childbearing age also reported similar findings.^{231,232} Preconception substance has been shown to increase the risk for substance use during pregnancy.¹⁸² These exposures have severe effects on fetal growth, development, and birth outcomes.²³³ Moreover, although most women stop using illicit and other substances upon pregnancy recognition, fetal exposure to these potential teratogens can still occur during the initial 4 – 6 weeks or later if the determination of pregnancy is delayed,²³⁴ specifically among women using substances in the preconception period.

Moreover, prior studies have suggested that women with unintended or unwanted pregnancies are more likely to continue substance use during pregnancy than are those with planned pregnancies.²³⁵ To address these outcomes, the advocates for women and child health suggest implementing programs to improve preconception health for all women of childbearing age.²³⁶ Researchers at the Center for Disease Control and Prevention (CDC) have identified several evidence-based interventions promoting preconception care and pregnancy-related outcomes, including risk screening and health promotion.²³⁷ An essential aspect of preconception care is pregnancy planning. Data from a telephonic survey conducted in Minnesota and Washington revealed that pregnancy planning was associated with health behaviors that influence birth outcomes, including vitamin intake and substance use.²³⁸ This emphasizes focusing the screening and education efforts to address substance use among women of

childbearing age, promoting public awareness of the effects of substance-exposed pregnancy, and encouraging access to effective contraception should be prioritized.²³⁹ Brief public health, clinical, and integrated behavioral interventions aimed at screening and educating women in the Obstetrician-Gynecologists, and family planning clinics have impacted improving health outcomes.^{240,241}

The rates of unintended pregnancy vary among the fractions of the population depending upon the individual, environmental, social factors, and health and family planning services-related elements. We also assessed the correlates of unintended pregnancy reported in the included studies to explore this. Studies reported younger maternal age (<20 years) as a significant predictor of unintended pregnancy.^{221,222,225,227} This is consistent with the previously published research where most teen pregnancies have been regarded as unplanned or unwanted.²⁴² Other factors associated with unintended pregnancy in the studies included in this review were low educational achievement,²⁴³ non-Hispanic Black race,²⁴⁴ lack of a partner,²⁴⁵ history of prior pregnancy²⁴⁶ or adverse pregnancy outcome,²⁴⁷ and initiating sexual activities before the age of 16 years²⁴⁸ also reported in other investigations. Poor socioeconomic status is also an established independent risk factor for unintended pregnancy.²⁴⁹ Notably, in the present SR, the study conducted among urban women with low-socioeconomic status reported over 80% of pregnancies to be unintended.²³ Moreover, as reported in the literature,²⁵⁰ women experiencing physical or emotional abuse were more likely to experience unplanned pregnancy outcomes.²⁵¹ In addition, three studies documented significant associations between smoking and alcohol consumption and unintended pregnancy in the adjusted analyses.^{188,221-222} Previously published literature has shown the use of drugs as a cause of risky sexual behaviors, including unprotected sex.²⁵²

Implications

Implications for research

The results of our SR with MA have several implications for future research. First, most of the studies included were cross-sectional in design, precluding determination of causality. Second, seven out of eight studies used retrospective measurement of pregnancy intention.^{220-221,223-227} Pregnancy intention was measured post-partum or even months after the birth, raising the likelihood of recall bias. The pregnancy outcome may affect the accuracy of parental recall and are likely to bias studies toward the null.²⁵³ It is more evident since parents originally not intending the pregnancy are more likely to recall it as intended than the parents planning to become pregnant and recall it as unintended, leading to underestimating the full impact of unintended pregnancy.^{254,255} Third, illicit and recreational drugs may be subjected to under-reporting due to social desirability bias and the stigma of substance use. All the included studies in the current SR with MA used self-reported data, which may lead to underestimating the prevalence of drug use.²⁵⁶ It is challenging to gauge substance use prevalence due to under-reporting, inconsistent screening and drug testing among providers, and inaccurate reporting systems, so findings must be interpreted cautiously. Finally, based on the risk of bias assessment, future studies need to improve their reporting regarding 1- evaluation of potential sources of bias, 2- methods used to handle missing data, 3- reporting response rate, 4- providing a comparison of responders and non-responders to evaluate the risk of selection bias, 5- factors adjusted for in the multivariable analysis.

Implications for practice

The pooled findings of the current SR with MA suggest that illicit and recreational drugs during the preconception period may significantly increase the risk of unintended pregnancy. These findings have important implications for practice if confirmed in future extensive, prospective studies. Given the adverse effects of drugs on maternal and child health^{Error! Bookmark not defined.}, preventing unintended pregnancies among this high-risk group should be recognized as a public health priority. Furthermore, the findings of this study support screening all women of childbearing age for substance use as recommended by the CDC²⁵⁷ and the American College of Obstetricians and Gynecologists (ACOG)²⁵⁸. However, evidence-based and culturally tailored screening interventions are needed due to the personal and institutional stigma of substance use.²⁵⁹

Strength and limitations

To the best of the authors' knowledge, this is the first SR with MA to investigate the association of illicit and recreational drug use to the likelihood of unintended pregnancy among women of childbearing age. This study used the inverse variance model (IVhet) that takes studies' precision, sample size, and within-study heterogeneity into account, producing more precise estimates. Thus, the current results provide more accurate information than the random effect model.²¹² We used the DOI plot and LFK index to assess publication bias. These tests are more precise while examining the small study effects than the traditional tools.²⁶⁰ The influence analysis results indicated modest variation in the effect size depicting a lack of outlier or highly influential study. The findings of cumulative analysis also suggested the consistency of magnitude of risk over two decades, adding to the robustness of current findings.

The present study results should be interpreted with caution due to the following limitations. First, SR with MA is inherently vulnerable to biases in the original studies and cannot make up for the poor quality of original studies.²⁶¹ Second, MA relies heavily on published studies. It is more difficult to publish studies with no statistically significant results, potentially leading to disproportionate reporting of significant findings (publication bias). In our assessment of potential publication bias, evaluation using DOI plots and the LFK index indicated a moderate risk of publication bias. Third, literature search bias (i.e., failure to identify all relevant studies) is a potential problem in all SRs. However, we performed an extensive search following the pre-defined criteria. Thus, we expect this bias to be minimal. Fourth, while inter-rater agreement can be a potential problem during the study selection, data abstraction, and risk of the bias assessment process, the authors reached a consensus in each of these domains in conducting this SR with MA. Fifth, the current study was limited to studies published in the English language, introducing another potential bias. However, any resulting bias is unlikely to have appreciably affected our findings, as published literature has shown meta-analyses restricting studies by language overestimate the magnitude of the association by only 2%.²⁶² Sixth, 75% of the included studies were cross-sectional in design, limiting the assessment of cause-effect relationships. Moreover, most(all) studies relied on self-report, potentially introducing recall and other information bias. Finally, we could not perform a meta-regression for the determinants of unintended pregnancy among women using substances due to the differences in the classifications of variables and lack of data for a few potential predictor variables.

Conclusion

In this SR and MA of eight observational studies, preconception use of illicit and recreational drugs among women of childbearing age was positively and significantly associated with unintended pregnancy. The findings of this SR with MA may have important implications for future research, policy, and practice. Additional rigorous prospective research is needed to address current studies' design and methodological limitations and improve reporting bias. This SR with MA further highlights the need for universal screening among all women of childbearing age, especially in light of the known adverse effects of both illicit and recreational drug use on maternal and child health. Our findings also support evidence-based and culturally sensitive screening and family planning interventions to prevent unintended pregnancy and improve health outcomes.

Chapter 5

Discussion

Summary of Key Findings

Overview

The current studies were aimed to determine the extent and nature of unintended pregnancy risks associated with substance use during the preconception period among women of childbearing age in the US. We looked at the sociodemographic determinants of unintended pregnancy among various substance-using women and continued that exploration among women using polysubstance. Finally, our third study established a systematic review with a meta-analysis of the risk of unintended pregnancy among women using illicit and recreational drugs. Although substance use during pregnancy and its adverse outcomes on the child's health have been focused on over the years. Fewer studies have explored women's pregnancy intentions in the circumstances involving various forms of substance use in the preconception period. Also, only a few studies that have investigated the risk of unintended pregnancy with substance use are limited to small-scaled hospital-based studies. The authors are unaware of any study investigating the risk of unintended pregnancy with polysubstance use and its predictors among women of childbearing age.

We performed a secondary cross-sectional data analysis on sizeable national representative data from PRAMS (phase 8) in the first two aims. PRAMS is a national maternal and child health data providing information on a range of estimates during preconception, pregnancy, and postpartum periods. By using PRAMS data, we met the goal of utilizing a large representative sample. The sample consisted of 74,543 women giving live births during 2016-17. For our third study, we conducted an SR with MA to analyze the risk of unintended pregnancy

associated with the use of illicit and recreational drugs. A total of 4,920 records were screened from various resources based on the predetermined eligibility criteria as follows; (1) observational studies, (2) studies with pregnancy intention as the primary outcome or variable of interest, (3) studies with pregnant women, or women giving live births, (4) exposure variable include illicit and recreational drugs specified by authors, (5) studies conducted in the US, UK, Australia, New Zealand, (6) studies published in the English language, (7) studies published from January 2000 – June 2021, and (8) studies conducted in the general population. The literature search plan utilized numerous resources, including (1) electronic searches in multiple databases PubMed (MEDLINE), Scopus, CINAHL, PsychINFO, and Web of Science in October 2021, (2) citation indices of pertinent review articles and papers identified as potentially eligible (citation tracking). The summaries of the key findings from all three aims are discussed below.

Preconception Substance Use and the Risk of Unintended Pregnancy

Our first study aimed to examine the association of preconception substance use and unintended pregnancy among women of childbearing age in the US. As an association existed, we compared substance use between subtypes of unintended pregnancies, i.e., mistimed, unwanted, and ambivalent. The study also aimed to assess the association between sociodemographic factors and unintended pregnancies among women who use substances. We used data from PRAMS 2016-17 surveys to achieve this aim. The sample comprised 74543 women giving live births during 2016-17 and participated in the PRAMS. In the current sample, about 41% of the pregnancies were unintended. Of those reports, 19.5% were mistimed, 6.2% were unwanted, and 15.3% were described as ambivalent these reports similar to the national prevalence.²⁶³ A higher prevalence of substance use in the preconception was noted. About a half of the women documented alcohol use, while one-third revealed binge drinking.

Cigarette smoking was reported by 17%, tobacco/nicotine products 10.6%, Cannabis 10%, prescription opioids 5.2%, and illicit and recreational drugs 4.2%. The adjusted odds ratios indicated increased likelihood of unintended pregnancy with alcohol consumption (AOR: 1.05, 95%CI: 1.0-1.1), smoking (AOR: 1.5, 95% CI: 1.4-1.6), nicotine/tobacco (AOR: 1.4, 95% CI: 1.3-1.5), cannabis (AOR: 1.9, 95% CI: 1.5-2.3), illicit/recreational drugs (AOR: 1.7, 95% CI: 1.2-2.4). A higher magnitude of risk was noted with heavy smoking (AOR: 1.9, 95%CI: 1.5-2.3), heavy (AOR: 1.9, CI: 1.5-2.2), and binge drinking (AOR:1.2, 95%CI:1.04-1.4). A similar pattern was observed with subtypes of unintended pregnancy, with a higher risk noted for unwanted pregnancies. Many of the associations found in the current study are previously reported in the literature, such as smoking, illicit drugs, tobacco, and cannabis.²⁶⁴⁻²⁶⁵⁻²⁶⁶ The likelihood of unintended pregnancy was significantly elevated with heavy smoking, high alcohol consumption, and binge drinking, similar to what is reported in the literature.²⁶⁷⁻²⁶⁸

The results of the stratified analysis to compare the maternal characteristics showed that women using different substances also vary in their characteristics. A more significant fraction of pregnancies were unintended among the illicit/recreational drugs using women; these women also reported annual income below FPL and inadequate PNC. A higher fraction of opioid-using women reported having depression and anxiety and experiencing physical and emotional abuse than other women. After controlling for other risk factors, the regression analysis results indicated that urban living women who were using prescription opioids were at three times higher risk of unintended pregnancy than women in rural areas, while among illicit and recreational drug users two folds risk was observed. These results align with another study where eight out of ten pregnancies were unintended, and the use of illicit drugs was significantly associated with unintended pregnancy.²⁶⁹ Having an annual income less than FPL was a strong

predictor of unintended pregnancy among all substance users, specifically among prescription opioid users. These findings are consistent with the existing literature showing that less annual income than FPL was independently associated with pregnancy intention.²⁷⁰ It is also reported that women below FPL were five times more likely to experience unintended pregnancies.²⁷¹ Among all substance users, age < 17 was a significant predictor of unintended pregnancy compared to the women aged 35 years and above. These findings are consistent with the existing literature where the proportion of unintended pregnancy decreases with age. The adolescents aged 15-19 had the highest rates of unintended pregnancy than any other age group.²⁷²⁻²⁷³ Our findings that not having a graduate education and marital status other than married increased the risk of unintended pregnancy are consistent with the previous studies. Women from racial and ethnic minorities are at increased risk of experiencing an unintended pregnancy.²⁷⁴ Our study found an increased risk among Black women using alcohol and tobacco/nicotine, opioid using non-Hispanic Whites, and illicit/recreational drugs using women from other races. Various social and economic factors contribute to health disparities. A study based on National Survey of Family Growth data reported age, relationship status, annual income, education, and insurance contributing factors to the higher likelihood of unintended pregnancy.²⁷⁵ The findings of our study provide insight into the factors contributing to poor reproductive health among women with substance use. It is crucial to identify the women at higher risk and ensure that younger women, minorities, and women with poor socioeconomic status have information and access to reproductive and family planning services.²⁷⁶

Polysubstance Use and the Risk of Unintended Pregnancy

This study aimed to examine the association between polysubstance use and unintended pregnancy among women of childbearing age and to assess the predictors of unintended pregnancy among women co-using substances. The study sample comprised 74543 women delivering live births during 2016-17 and participated in the PRAMS survey. In this sample, about 56.5% of the respondents reported drinking alcohol; of those 33% revealed heavy or binge drinking. About 17% of the sample smoked cigarettes, among those 27.1% were heavy smokers. A higher prevalence of polysubstance use during the preconception period was observed in the current study. Among alcohol drinking women, one quarter (25.3%) were heavy smokers, 13% used cannabis, and 5% used opioids. Among smokers, 25.8% were co-using cannabis, 12.5 % used illicit drugs, 33% used other tobacco/nicotine products, and about 10% used opioids. A higher proportion of women reporting heavy smoking and heavy or binge drinking were co-using other substances. The regression analysis results revealed that alcohol drinking women and co-using other substances were at higher risk of unintended pregnancy. Statistically significant and positive association of unintended pregnancy was observed with heavy smoking (AOR: 1.5, 95%CI:1.4 – 1.6), cannabis (AOR: 2.0, 95%CI:1.6 – 2.4), tobacco/nicotine (AOR: 1.6, 95%CI:1.4 – 1.7), and illicit/recreational drugs (AOR: 1.8, 95%CI: 1.1 – 2.7). Higher odds of unintended pregnancy were noted among heavy or binge drinkers with smoking (AOR: 1.9, 95%CI: 1.5 – 2.4), cannabis use (AOR: 2.1, 95%CI: 1.4 – 3.1), tobacco/nicotine (AOR: 2.3, 95%CI: 1.7 – 3.1). The risk of unintended pregnancy was not statistically significant with co-use of opioids with alcohol (AOR: 1.3, 95%CI: 0.9 – 1.9) and heavy or binge drinking (AOR: 1.4: 95%CI: 0.6 – 3.6) after adjusting for potential confounders. To identify the predictors of unintended pregnancy among women co-using alcohol with other substances. Four highly

prevalent patterns of polysubstance use were identified, including alcohol and smoking (N=9,145), alcohol and cannabis (N=1511), alcohol and illicit/recreational drugs (N=346), and smoking and cannabis (N=1091).

The logistic regression analysis revealed urban living, income below FPL, and marital status other than married were significant predictors of unintended pregnancy among polysubstance users. Women older than 35 years (AOR: 2.0, 95%CI: 1.3 – 3.0) and Black race (AOR: 1.4, 95%CI: 1.1 – 1.7) increased the odds of unintended pregnancy among women co-using alcohol and smoking. Education less than or equal to high school was significantly associated with unintended pregnancy among alcohol and smoking (AOR: 2.8, 95%CI: 2.3 – 3.6) and alcohol and cannabis users (AOR: 2.6, 95%CI: 1.6 – 4.6). Marital status other than married had higher odds of unintended pregnancy among alcohol only (AOR: 3.2, AOR: 3.0 -3.5), alcohol and smoking (AOR: 2.4, 95%CI: 2.0 -2.8), and alcohol and cannabis users (AOR: 2.8, 95%CI: 1.8 – 4.4).

Our findings from the current population-based sample of US women demonstrated a positive and statistically significant association between polysubstance use during the preconception period and the risk of unintended pregnancy. The prevalence of unintended pregnancy was 39% for alcohol consumers and the highest for heavy smokers (62.5%). However, co-using alcohol with smoking, illicit substances, or cannabis led to a higher prevalence of unintended pregnancy (60%). Cannabis was the most commonly co-used substance among smokers and alcohol drinkers. Compared to moderate drinking and smoking, women with heavy/binge drinking and heavy smoking had a high prevalence of polysubstance use. These findings suggest a potential sequel that starts with the initiation of substance use with the legal substances, particularly tobacco and alcohol, and progressing towards heavy smoking/drinking

and proceeding to co-using other substances. This pattern is in alignment with the gateway drug hypothesis. This hypothesis suggests the beginning of substance use with alcohol, tobacco, and cannabis that escalates to using more addictive substances, including illicit drugs.^{277,278}

Our study noted the most frequent polysubstance use patterns, including alcohol, cannabis, and tobacco, which is similar to the findings of another study.²⁷⁹ The results showed that most women reporting polysubstance use resided in urban areas, were 20-34 years of age, were non-Hispanic White, had education \leq high school, were not married, and their annual income was below the FPL. Polysubstance use among women of childbearing age is common and leads to maternal and child health risks. Our study's findings suggest the need for interventions addressing polysubstance use in women of childbearing age. The United States Preventive Services Task Force (USPSTF)²⁸⁰, CDC²⁸¹, and American College of Obstetricians and Gynecologists (ACOG)²⁸² recommend universal screening of women of childbearing age and pregnant women. There is evidence suggesting the benefits of screening and brief interventions leading to a reduction in alcohol use, smoking, and illicit drug use^{283,284,285}.

Unintended Pregnancy Among Women of Substance Use: A Systematic Review with Meta-Analysis

The purpose of our third study was to conduct a systematic review with meta-analysis to assess the relation of illicit and recreational drugs use and the likelihood of unintended pregnancy among women of childbearing age.

We included eight studies that met our review's inclusion criteria (N=38,520 women). The findings suggest a statistically significant and positive association between preconception illicit or recreational drugs use and unintended pregnancy (Pooled OR=1.84, 95%CI=1.4 – 2.4).

A moderate heterogeneity ($I^2=66\%$) across studies, with significant Cochran Q statistics ($Q=20.41$, $p\text{-value} = 0.00$) was also noted. The influence analysis results after deleting each study one by one yielded pooled ORs ranging from 1.65 – 2.1 (Table 6). All ORs remained significant; the very modest variation in ES across studies suggests a lack of outliers or highly influential studies among the investigations included in the MA. The cumulative analysis comparing ORs by year of publication did not show significant changes in the magnitude of risk over the two decades. The DOI plot was asymmetrical, and the LFK index was 2.66 indicating a positive asymmetry that might happen due to a small study effect or fewer studies in the review.

The prevalence of reported illicit and recreational drug use in our studies ranged from 4.0-21.0%, which is in the range of the prevalence reported in the other studies.^{286,287} The prevalence of unintended pregnancies varied from 5.3%²²⁵ to 82%.²²⁰ Average crude prevalence in the seven studies using nationally representative samples was 44%. In the systematic review, determinants of unintended pregnancy included age <20 years,^{220-221,225,227} non-Hispanic White²²⁰ and Black race,²²¹ not married or not having a partner,^{220,224} having one or more previous pregnancies,²²⁴ previous adverse pregnancy outcomes,²²¹ lower educational attainment,^{224,227} and abusive relationship.²²⁴ Use of substances in addition to illicit and recreational drugs included smoking^{221,224-227} and alcohol consumption.^{223,225,227}

Preconception substance has been shown to increase the risk for substance use during pregnancy.¹⁸² These exposures have known adverse effects on fetal growth, development, and birth outcomes.²⁸⁸ Moreover, women with unintended or unwanted pregnancies are more likely to continue substance use during pregnancy than are those with planned pregnancies.²⁸⁹ Substance exposed pregnancies are at risk for poor pregnancy and perinatal outcomes,²⁹⁰

including but not limited to low birth weight (LBW), preterm birth, stillbirth, and Neonatal Abstinence Syndrome (NAS).^{291,292}

To improve birth outcomes, women and child health advocates suggest implementing programs to improve preconception health for all women of childbearing age.²⁹³ The Center for Disease Control and Prevention (CDC) has identified evidence-based interventions promoting preconception care and pregnancy-related outcomes, including risk screening and health promotion.²⁹⁴ An essential aspect of preconception care is pregnancy planning associated with health behaviors influencing birth outcomes.²⁹⁵ Promoting public awareness of the effects of substance-exposed pregnancy might strengthen the efforts to prevent substance use among women of childbearing age. Brief interventions to screen and educate women and provide access to effective contraception in the Obstetrician-Gynecologists and family planning clinics have improved health outcomes.^{296,297}

To the author's knowledge, this is the first SR with MA to assess the relation of illicit and recreational drugs use and the likelihood of unintended pregnancy among women of childbearing age. Our findings suggest that the preconception use of illicit and recreational drugs among women of childbearing age was positively and significantly associated with unintended pregnancy. The findings of this SR with MA may have important implications for future research, policy, and practice. Our results indicate the need for a more rigorous methodology to improve the study quality. The risk of bias assessment regarding the precise gauge of the prevalence of substance use and pregnancy intention suggested that future studies need to improve their reporting regarding the study design and evaluation of potential sources of bias. Given the high prevalence of both unintended pregnancy and illicit and recreational drugs in the preconception period preventing unintended pregnancies among this high-risk group should be recognized as a public health priority.

Strengths of the dissertation

The primary strength of our study is using a large, population-based, representative sample of US women of childbearing age. For the first two studies, we used national data from PRAMS 2016-17, providing information on a range of social, demographic, mental health, and substance use variables. The study used a granular approach and provided an in-depth analysis of the significant determinants of unintended pregnancy among types of substance use. To the best of our knowledge, this is the first study examining the association between substance/polysubstance use and unintended pregnancy among US women of childbearing age. We also performed a stratified analysis to compare the characteristics of groups with highly prevalent patterns of substance use and co-using substances. The study also provided a breakdown of sub-types of unintended pregnancy, i.e., mistimed, unwanted, and ambivalent pregnancies, and their risk with a range of substance and polysubstance use.

For our third aim, to our knowledge, this is the first SR with MA to investigate the association of illicit and recreational drug use to the likelihood of unintended pregnancy among women of childbearing age. This study used the inverse variance model (IVhet) that takes studies' precision, sample size, and within-study heterogeneity into account, producing more precise estimates. Thus the current results provide more accurate information than the random effect model.²¹² Using the DOI plot and LFK index to assess publication bias is another advantage over previous studies. These tests are more precise while examining the small study effects than the traditional tools.²⁹⁸ Another merit of our research was the influence analysis indicating a lack of an outlier or highly influential study and modest variation in the effect size.

The results of the cumulative analysis also suggested the consistency of magnitude of risk over two decades, adding to the robustness of current findings.

Limitations of the dissertation

Despite the strengths, the study has a few limitations that should be considered while interpreting the findings. For our first two aims, the analysis is limited to women delivering live births, leading to underreporting adverse outcomes (miscarriage or stillbirth) associated with unintended pregnancy and substance use. Secondly, this cross-sectional study cannot predict polysubstance use patterns over time. However, estimating preconception substance use might provide a temporal relationship to measure the risk associated with unintended pregnancy. Third, due to retrospective measurement, recall bias may influence pregnancy intention. Fourth, PRAMS questionnaires are self-reported and may be subjected to under-reporting of behaviors perceived to be unhealthy. Substance use is prone to underreporting owing to social desirability bias and the stigma of illicit drug use.

The results should be interpreted with caution for our third aim due to the following limitations. First, SR with MA is inherently vulnerable to biases in the original studies and cannot make up for the poor quality of original studies.²⁹⁹ Second, MA relies heavily on published studies. It is more difficult to publish studies with no statistically significant results, potentially leading to disproportionate reporting of significant findings (publication bias). In our assessment of potential publication bias, evaluation using DOI plots and the LFK index indicated a moderate risk of publication bias. Third, literature search bias (i.e., failure to identify all relevant studies) is a potential problem in all SRs. Although, we performed an extensive search according to the eligibility criteria. Thus, we expect this bias to be minimal. Fourth, while inter-

rater agreement can be a potential problem during the study selection, data abstraction, and risk of the bias assessment process, the authors reached a consensus in each of these domains in conducting this SR with MA. Fifth, the current study was limited to studies published in the English language, introducing another potential bias. However, any resulting bias is unlikely to have appreciably affected our findings. Previous literature has revealed that meta-analyses restricting studies by language overestimate the magnitude of the association by only 2%.³⁰⁰ Sixth, 75% of the included studies were cross-sectional in design, limiting the assessment of cause-effect relationships. Moreover, most(all) studies relied on self-report, potentially introducing recall and other information bias. Finally, we could not perform a meta-regression for the determinants of unintended pregnancy among women using substances due to the differences in the classifications of variables and lack of data for a few potential predictor variables.

Public Health Implications and Future Recommendations

Rates of unintended pregnancy have remained high in the US during the past decade. Unintended pregnancy is associated with poor well-being of women and their families and substantial economic, health care, and individual costs.³ Among women of childbearing age, substance use has increased the risk for unintended pregnancy and poor health outcomes.^{Error!} **Bookmark not defined.** Given the high prevalence of substance use and the risk of unintended pregnancy among women of childbearing age, it is crucial to identify the prevalence and patterns of substance and polysubstance use and their association with unintended pregnancy.¹⁵

Our studies explored the association between unintended pregnancy and substance and polysubstance use. A high prevalence of substance use and unintended pregnancy was found with an increased likelihood of unintended pregnancy among substance users. Women with

substance use suffer from poor sexual and reproductive health. They encounter individual and systemic challenges, including medical and psychological comorbidities, neglect and abuse, mistrust of healthcare services, guilt, denial, and embarrassment regarding substance use, fear of losing child custody, and poor access to family planning services.^{301,302} These high-risk situations indicate the significance of recognizing and reducing substance use among women of childbearing age and facilitating effective contraceptive use among women tending to avoid pregnancy. Healthcare providers must be aware of the women's unique needs and implications surrounding substance use.³⁰³

The current study's findings revealed inadequate PNC and low contraception use among all substance-using women, specifically illicit and recreational drug users, thus supporting the evidence of poor reproductive health among substance-using women.³⁰⁴ The preconception period is a critical time in women's life to promote healthy behavior that can significantly improve maternal and child health outcomes.³⁰⁵ Implementing interventions to educate them on the harmful effects of the substance, screening women for substance use, and encouraging substance users for effective contraception use can significantly improve maternal and child health outcomes.³⁰⁶

Our study also noted a high prevalence of polysubstance use among women of childbearing age and suggested the need for interventions addressing this serious concern. The advocates of maternal and child, including the United States Preventive Services Task Force (USPSTF)³⁰⁷, CDC³⁰⁸, and American College of Obstetricians and Gynecologists (ACOG)³⁰⁹ recommend universal screening of women of childbearing age. There is evidence suggesting the benefits of screening and brief interventions leading to a reduction in alcohol use, smoking, and illicit drug use^{310,311,312}.

Current studies also looked into the sociodemographic and mental health determinants of unintended pregnancy among substance-using women. It was found that younger women, urban living, lower education levels, poverty, marital status other than married, abuse, depression, and anxiety were significantly and positively associated with unintended pregnancy. These findings indicate the need for appropriate educational, screening and treatment efforts to identify the women in need and provide treatment services integrated with family planning services.³¹³ Prevention and treatment efforts should consider the significant determinants of health. These include social-economic factors, social support, family structure, and cultural norms.³¹⁴ Effective screening plays a vital role in providing data regarding these factors and information on mental health,³¹⁵ physical or emotional abuse,³¹⁶ childhood adversity³¹⁷ that are known determinants of substance use, and poor reproductive health among women. Screening and assessment from a perspective affirming the cultural values and beliefs facilitate the women's engagement in the screening leading to the treatment process.³¹⁸ In addition to cultural differences, women from minorities, racial/ethnic groups, living in rural areas, and not speaking English experience unique challenges while pursuing substance use treatment.³¹⁹ A customized supportive therapy aimed to address the barriers identified in the screening and assessment process may help women contact and stay in the treatment services.³²⁰

The substance-using women often report poor access to healthcare and family planning services.³²¹ One of the barriers to accessing health care and family planning services is the social stigma of substance use.³²² Women with substance use experience social and structural stigma.³²³ Other barriers reported in the literature include misconceptions about contraceptive use, limited social support, health insurance, lack of transportation, intimate partner violence, and trauma. A qualitative study conducted among physicians suggested patient-centered

communication and shared decision-making to improve contraception access and use among substance use women to address these issues.³²⁴

The results of SR with MA also have implications for future research. Our findings recommend a more rigorous methodology to improve the study quality for future research. It is also suggested that future studies focus on improving the reporting regarding potential sources of bias. There is also a need for a precise gauge for variables prone to reporting bias like substance use and pregnancy intention to the recall bias. Additional rigorous prospective research is needed to address current studies' design and methodological limitations and improve reporting bias. Given the high prevalence of illicit and recreational drug use among women of childbearing age, the risk of unintended pregnancy, and their impact on maternal and child health, it is necessary to prioritize this pressing public health concern. Our findings also support the need for evidence-based and culturally sensitive intervention to prevent unintended pregnancy and improve maternal and child health outcomes.

Conclusion

Our findings from the large population-based sample of the US women of childbearing age substantiated that preconception substance and polysubstance use are significantly and positively associated with unintended pregnancy. Our investigations also found that younger age, urban living, lower educational attainment, marital status other than married, annual income <FPL, physical or emotional abuse, poor mental health, i.e., having depression or anxiety, were significant determinants of unintended pregnancy among substance-using women. The results of SR with MA suggest that the use of illicit and recreational drugs increases the likelihood of unintended pregnancy. This study's findings highlight the need to address preconception substance use among women of childbearing age, screening and counseling for substance use,

and provision of effective contraception methods among women at risk to reduce unintended pregnancy and associated adverse effects on maternal and child health.

Tables

Chapter 2

Table 1(a). Background, demographics, and preconception substance use among the women of childbearing age, PRAMS, 2016-17 (N=74,543)

Maternal Characteristics	Unweighted count	Weighted %	(95 % CI)	SE	p-value
Rurality					<.001
Urban	58954	78.3	77.8 - 78.7	0.2	
Rural	14535	21.7	21.3 – 22.12	0.2	
Race					<.001
Asian	4976	5.9	5.7 – 6.2	0.1	
White	42695	69.6	69.1 – 70.1	0.3	
Black	13581	14.8	14.4 – 15.2	0.2	
Others	10747	9.7	9.3 - 10.0	0.2	
Ethnicity					<.001
Hispanic	13423	19.7	19.2 – 20.1	0.2	
Non-Hispanic	58781	80.3	79.9 – 80.8	0.2	
Age					<.001
<=17	1004	1.3	1.2 – 1.5	0.1	
18-24	16806	22.0	21.5 – 22.5	0.2	
25-35	43373	58.9	58.3 – 59.4	0.3	
35+	13358	17.8	17.4 – 18.3	0.2	
Mean Age (SD)yrs.	23.48(5.8)				
Range yrs.	12-46				
Education					<.001
Less than high school	9848	12.9	12.5 – 13.3	0.2	
High school only	17947	24.1	23.6 – 27.3	0.3	
Some college	21083	26.8	26.3 – 27.3	0.3	
Graduate	73784	36.2	35.6 – 36.7	0.3	
Marital status					<.001
Married	44393	62.1	61.6 – 62.6	0.2	
Others	30077	37.9	37.4 – 38.4	0.2	
Income to Need Ratio					<.001
Below FPL	18078	27.7	27.2 – 28.3	0.3	
At/ above FPL	41999	72.3	71.7 – 72.8	0.3	
Insurance					<.001
Medicaid	20894	23.3	22.8 – 23.7	0.2	
Others	44311	62.7	62.2 – 63.3	0.2	
No insurance	9338	14.1	13.7 – 14.5	0.3	
Kessner Index					<.001
Adequate PNC	50298	68.5	68.0 – 69.1	0.3	
Intermediate PNC	14350	19.1	18.6 – 19.6	0.2	
Inadequate PNC	4472	5.8	5.6 – 6.1	0.1	

Unknown PNC	5423	6.6	6.3 – 6.8	0.1	
Pregnancy Intention					<.001
Intended	42302	59.0	58.5 – 59.6	0.3	
Unintended	30997	41.0	40.0 – 41.5	0.3	
Mistimed	14196	19.5	19.0 – 20.0	0.2	
Unwanted	4722	6.2	5.9 – 6.5	0.1	
Ambivalent	12079	15.3	14.9 – 15.7	0.2	
Preconception contraception Use					<.001
Yes	10254	41.0	40.0 – 41.9	0.5	
No	14985	59.0	58.1 – 60.0	0.5	
Depression/Anxiety					<.001
Yes	13559	17.3	16.9 – 17.7	0.2	
No	60383	82.7	82.3 – 83.1	0.2	
Prior Live Births					<.001
Yes	45291	61.5	61.0 - 62.1	0.3	
No	29072	38.5	37.9 – 39.0	0.3	
Abuse					<.001
Yes	24315	45.9	45.2 – 46.6	0.4	
No	23724	54.1	53.4 – 54.8	0.4	
ACE scores					<.001
0	3282	51.6	49.8 – 53.4	0.9	
1-3	2851	41.8	40.0 – 43.6	0.9	
4+	439	6.6	5.8 - 7.6	0.5	
Smoking					<.001
Yes	13976	17.4	17.0 - 17.8	0.2	
No	59445	82.6	82.2 – 83.0	0.2	
Alcohol consumption					<.001
Yes	39831	56.6	56 – 57.1	0.3	
No	33392	43.4	42.9 – 44.0	0.3	
Binge drinking					<.001
Yes	3811	31.8	30.6 – 33.0	0.6	
No	8258	68.2	67.0 – 69.4	0.6	
Nicotine/Tobacco					<.001
Yes	7955	10.6	10.2 – 11.0	0.2	
No	65465	89.4	89.0 – 89.8	0.2	
Cannabis					<.001
Yes	1986	10.0	9.4 – 10.7	0.3	
No	15022	90.0	89.3 – 90.6	0.3	
Illicit/recreational Drugs					<.001
Yes	563	4.2	3.7 – 4.8	0.3	
No	15920	95.8	95.2 – 96.3	0.3	
OTC pain relief					<.001
Yes	9741	70.1	68.9 – 71.2	0.6	
No	4544	29.9	28.8 – 31.1	0.6	
Prescription opioids					<.001

Yes	848	5.2	4.7 – 5.8	0.3	
No	15612	94.8	94.2 – 95.3	0.3	
Prescription antidepressants					<.001
Yes	165	7.1	6.1 – 8.2	0.5	
No	2156	92.9	91.8 – 93.9	0.5	

P-value based on chi-square test statistics. SE=standard error. FPL=Federal Poverty Level.

Adverse Childhood Experiences (ACE) scores were calculated from maternal childhood experiences. Binge drinking defined as ≥ 4 drinks in 2 hours; Over the Counter (OTC) pain relief included aspirin, Tylenol, Advil, or Aleve; prescription opioids defined as hydrocodone, oxycodone, or codeine; prescription antidepressants defined as prescribed antidepressants and anti-anxiety medications.

Table 2(a). Association between pregnancy intention and preconception substance use, PRAMS, 2016-17 (N=74,543)

Substance Use types	Odd ratios (95% CI)	
	Unadjusted	Adjusted*
Smoking	2.3 (2.2 – 2.5)	1.5 ^a (1.4 – 1.6)
No Smoking	Ref	Ref
Cigarettes /day		
No smoking	Ref	Ref
Moderate smoking	1.8 (1.5 – 2.1)	1.5 ^b (1.3 – 1.8)
Heavy smoking	2.3 (1.9 – 2.8)	1.9 (1.5 – 2.3)
Alcohol Consumption	0.8 (0.8 – 0.9)	1.05 ^c (1.0 – 1.1)
No drinking	Ref	Ref
Drinks/Week		
No drinking	Ref	Ref
Moderate	1.01 (1.0 – 1.1)	1.2 ^d (1.1 – 1.2)
Heavy	1.5 (1.2 – 1.8)	1.5 (1.2 – 1.8)
Binge Drinking	1.4 (1.3 – 1.6)	1.2 ^e (1.04 – 1.4)
No	Ref	Ref
Nicotine/tobacco	2.0 (1.9 – 2.2)	1.4 ^f (1.3 – 1.5)
No	Ref	Ref
Cannabis	2.4 (1.6 – 2.8)	1.9 ^g (1.5 – 2.3)
No	Ref	Ref
Illicit/recreational drugs	2.6 (2.3 – 3.2)	1.7 ^h (1.2 – 2.4)
No	Ref	Ref
OTC Pain relief	0.88 (0.8 – 0.99)	1.0 ⁱ (0.9 – 1.1)
No	Ref	Ref
Prescription opioids	1.7 (1.3 – 2.1)	1.4 ^j (1.02 – 1.9)
No	Ref	Ref
Prescription antidepressants	1.3 (1.0 – 1.8)	1.8 ^k (1.1 – 3.0)
No	Ref	Ref

Moderate smoking= <10 cigarettes/day; Heavy smoking= \geq 10 cigarettes/day; moderate drinking= up to 7 drinks/week, heavy drinking= 8-14 drinks/week; Binge drinking = \geq 4 drinks in 2 hours.

^{a,b,k,f} Adjusted for maternal age, race, education, marital status, rurality, income to need ratio and depression/anxiety

^c adjusted for maternal age, race, income to need ratio and smoking

^{d,e,g,h,j} Adjusted for maternal age, race, education, marital status, rurality, income to need ratio

ⁱ adjusted for maternal age and race

Table 3(a): Distribution of pregnancy intention subtypes by preconception substance use, PRAMS, 2016-17 (N=74,543)

Substance use	Pregnancy Intention weighted %				p-value
	Intended	Ambivalent	Mistimed	Unwanted	
Smoking					<.001
Yes	42.0	24.0	24.0	10.0	
No	62.8	13.4	18.5	5.3	
Number of cigs. /day					<.001
No smoking	58.3	15.2	20.5	6.0	
Moderate	44.0	22.3	24.6	9.2	
Heavy	37.5	28.0	22.3	12.3	
Alcohol consumption					<.001
Yes	60.6	14.5	19.1	5.8	
No drinking	57.3	16.1	20.0	6.7	
Drinks /week					<.001
No drinking	62.0	13.4	18.7	6.0	
Moderate	61.0	14.4	19.0	5.7	
Heavy drinking	52.2	17.5	22.6	7.7	
Binge drinking					<.001
Yes	54.9	16.7	22.4	5.9	
No	64.2	14.0	17.0	4.8	
Nicotine/Tobacco					<.001
Yes	43.6	19.3	27.6	9.5	
No	61.0	14.7	18.5	5.8	
Cannabis					<.001
Yes	38.3	22.4	28.6	10.7	
No	59.6	15.0	19.4	6.0	
Illicit/recreational drugs					<.001
Yes	34.0	26.4	26.8	12.7	
No	57.7	15.6	20.3	6.4	
OTC Pain relief					0.195
Yes	57.4	15.7	20.3	6.6	
No	54.5	16.5	22.0	7.0	
Prescription opioids					<.001
Yes	44.2	19.1	24.0	12.8	
No	57.5	16.0	20.4	6.2	
Prescription antidepressants					0.054
Yes	50.0	27.3	19.2	3.5	
No	56.5	19.7	17.4	6.3	

P-values based on chi-square statistics. Percentages presented in table as row percentages; individual percentages may not total 100 due to rounding. Bold text indicates a statistical significance with a p-value<0.05.

Moderate smoking= <10 cigarettes/day; Heavy smoking= \geq 10 cigarettes/day; moderate drinking= up to 7 drinks/week, heavy drinking= 8-14 drinks/week; Binge drinking = \geq 4 drinks in 2 hours.

Table 4(a). Unadjusted and adjusted ORs (95%CI) for pregnancy intention subtypes and preconception substance use, PRAMS, 2016-17 (N=74,543)

Substance Use	Unadjusted OR (95% CI)			Adjusted* OR (95%CI)		
	Ambivalent	Mistimed	Unwanted	Ambivalent	Mistimed	Unwanted
Smoking	2.7	1.9	2.8	1.7	1.2	1.8
	(2.5 – 2.9)	(1.7 – 2.1)	(2.5 – 3.2)	(1.6 – 1.9)	(1.1 – 1.4)	(1.6 – 2.1)
No smoking	Ref	Ref	Ref	Ref	Ref	Ref
Moderate smoking	1.9	1.6	2.0	1.6	1.4	1.5
	(1.5 – 2.5)	(1.3 – 2.0)	(1.4 – 2.9)	(1.2 – 2.1)	(1.1 – 1.8)	(1.0 – 2.3)
Heavy smoking	2.8	1.7	3.1	2.2	1.4	2.1
	(2.2 – 3.6)	(1.3 – 2.1)	(2.1 – 4.7)	(1.7 – 3.0)	(1.1 – 1.8)	(1.3 – 3.2)
Alcohol	0.85	0.9	0.8	1.0	1.2	0.9
	(0.8 – 0.9)	(0.8 – 1.0)	(0.7 – 0.9)	(0.9 – 1.1)	(1.1 – 1.3)	(0.8 – 0.9)
No drinking	Ref	Ref	Ref	Ref	Ref	Ref
Moderate	1.1	1.0	0.9	1.5	1.4	1.4
	(1.0 – 1.2)	(0.9 – 1.6)	(0.8 – 1.2)	(1.2 – 1.7)	(1.2 – 1.6)	(1.3 – 2.7)
Heavy	1.5	1.4	1.5 (1.1 –	2.0 (1.5 –	1.8 (1.4 –	1.9 (1.3 –
	(1.3 – 1.9)	(1.1 – 1.7)	2.1)	2.6)	2.3)	2.7)
Binge Drinking	1.4	1.5	1.4	1.1	1.3	1.1
	(1.2 – 1.6)	(1.3 – 1.8)	(1.1 – 1.8)	(1.0 – 1.4)	(1.0 – 1.5)	(0.9 – 1.5)
No	Ref	Ref	Ref	Ref	Ref	Ref
Nicotine or tobacco	1.8	2.1	2.3	1.3	1.4	1.3
	(1.6 – 2.0)	(1.9 – 2.3)	(2.0 – 2.6)	(1.2 – 1.5)	(1.3 – 1.6)	(1.2 – 1.5)
No	Ref	Ref	Ref	Ref	Ref	Ref
Cannabis	2.3	2.3	2.8	1.8	1.7	2.3
	(1.9 – 2.8)	(1.9 – 2.7)	(2.2 – 3.7)	(1.4 – 2.2)	(1.3 – 2.1)	(1.7 – 3.2)
No	Ref	Ref	Ref	Ref	Ref	Ref
Illicit/recreational drugs	2.9	2.2	3.4	1.7	1.5	1.9
	(2.0 – 4.1)	(1.6 – 3.1)	(2.2 – 5.3)	(1.1 – 2.6)	(1.01 – 2.3)	(1.1 – 2.3)
No	Ref	Ref	Ref	Ref	Ref	Ref
OTC Pain relief	0.9	0.9	0.9	1.5	1.4	1.4
	(0.7 – 1.1)	(0.8 – 1.0)	(0.7 – 1.1)	(1.2 – 1.8)	(1.2 – 1.7)	(1.1 – 1.9)
No	Ref	Ref	Ref	Ref	Ref	Ref
Prescription opioids	1.6	1.5	2.7	1.2	1.3	2.1
	(1.1 – 2.1)	(1.1 – 2.1)	(1.8 – 4.0)	(0.8 – 1.8)	(0.9 – 2.0)	(1.3 – 3.2)
No	Ref	Ref	Ref	Ref	Ref	Ref
Prescription antidepressants	1.6	1.2	0.6	2.1	1.7	0.7
	(1.1 – 2.3)	(0.8 – 1.9)	(0.3 – 1.4)	(1.2 – 3.7)	(1.0 – 3.1)	(0.2 – 1.9)
No	Ref	Ref	Ref	Ref	Ref	Ref

*Adjusted for maternal age, race, ethnicity, education, marital status, rurality, income to need ratio, and substance use

Moderate smoking= <10 cigarettes/day; Heavy smoking= ≥10 cigarettes/day; moderate drinking= up to 7 drinks/week, heavy drinking= 8-14 drinks/week; Binge drinking = ≥4 drinks in 2 hours

Table 1(b) Maternal sociodemographic characteristics stratified by preconception substance use PRAMS 2016-17

Characteristics	All women	Alcohol	Tobacco/Nicotine	Prescription Opioids	Illicit/Recreational Drugs
	N (Wt.%)	N (Wt.%)	N (Wt. %)	N (Wt. %)	N (Wt. %)
	N=74543	N=39831 (56.6)	N=17535 (22.1)	N=848 (5.2)	N=1886 (10.8)
Rurality					
Urban	58954 (78.3)	31307 (78.2)	13830 (78.6)	575 (76.7)	1290 (76.2)
Rural	14535 (21.7)	7968 (21.8)	3431 (21.4)	198 (22.9)	476 (23.8)
Race/Ethnicity					
Asian	4976 (5.9)	154 (3.3)	359 (1.9)	14 (1.0)	10 (0.8)
Non-Hispanic White	34367 (56.9)	22413 (68.3)	8746 (64.0)	352 (68.3)	888 (73.1)
Hispanic White	8124 (12.7)	3299 (9.3)	1169 (8.1)	30 (2.8)	43 (2.5)
Black	13581 (14.8)	6004 (11.9)	3480 (16.9)	164 (18.2)	303 (15.3)
Others	10747 (9.7)	4842 (7.2)	3139 (9.1)	214 (9.6)	363 (8.4)
Age					
≤17	1004 (1.3)	153 (0.3)	224 (1.4)	16 (2.0)	43 (2.1)
18-24	16806 (22.0)	7628 (18.4)	5623 (31.7)	219 (23.3)	680 (35.0)
25-35	43373 (58.9)	24814 (63.1)	9615 (55.3)	485 (60.4)	975 (52.3)
35+	13358 (17.8)	7234 (18.2)	2071 (11.5)	128 (14.3)	188 (10.5)
Education					
≤HS	9848 (12.9)	2656 (5.9)	3006 (16.0)	147 (15.4)	312 (15.1)
Only HS	17947 (24.1)	7764 (19.3)	6072 (34.1)	297 (34.3)	675 (39.2)
Some College	21083 (26.8)	12349 (29.2)	5882 (33.3)	279 (33.9)	621 (33.0)
Graduate	24906 (36.2)	16740 (45.6)	2416 (16.6)	116 (16.5)	262 (12.7)
Income to Need ratio					
<FPL	18078 (27.7)	7520 (19.6)	6569 (41.6)	337 (46.4) *	914 (53.3) *
At/above FPL	41999 (72.3)	26136 (80.4)	7667 (58.6)	332 (53.6)	744 (46.7)
Marital status					
Married	44393 (62.1)	24978 (65.6)	6177 (38.6)	314 (40.6)	503 (31.4)
Others	30077 (37.9)	14815 (34.4)	11320 (61.4)	533 (59.4)	1379 (68.6)
Depression/Anxiety					
No	60383 (82.7)	31688 (81.0)	11682 (69.0)	526 (61.5)	1141 (62.5)
Yes	13559 (17.3)	7943 (19.0)	5737 (31.0)	318 (38.5)	734 (37.5)
Abuse					
No	23724 (54.1)	14491 (55.4)	4410 (47.2)	174 (31.4)	397 (41.8)
Yes	24315 (45.9)	14433 (44.6)	6107 (52.8)	420 (68.8)	755 (58.2)
Pregnancy Intention					
Intended	42302 (59.0)	23212 (60.6)	7218 (43.1)	371 (44.2)	652 (34.9)

Unintended	30997 (41.0)	16100 (39.4)	10030 (56.9)	460 (55.8)	1195 (65.1)
Contraception use					
No	14985 (59.0)	7610 (58.7)	5281(63.3)	162 (58.8)	437 (74.2)
Yes	10254 (41.0)	5357 (41.3)	2999 (36.7)	105 (41.2)	194 (25.8)
Kessner Index					
Adequate PNC	50298 (68.5)	28670 (73.5)	4960 (64.5)	529 (63.2)	307 (55.7)
Intermediate PNC	14350 (19.1)	6516 (15.7)	1728 (19.8)	194 (22.1)	137 (23.6)
Inadequate PNC	4472 (5.8)	1790 (4.2)	615 (7.4)	78 (7.2)	80 (11.0)
Unknown PNC	5423 (6.6)	2855 (6.6)	652 (8.2)	47 (8.4)	39 (9.8)

*Chi-squared p-value NS (>.05). HS= High school, FPL = Federal Poverty Level, Abuse status was defined as physical/emotional abuse. Tobacco/Nicotine included smoking, hookah, electronic cigarettes, cigars, cigarillos, nicotine, and betel nut. Prescription opioids included Hydrocodone, and Oxycodone, Codeine. Illicit/Recreational drugs included Adderall, Marijuana, synthetic marijuana, Methadone, Heroin, Amphetamine, Cocaine, Tranquillizers, and Hallucinogens.

Table 2(b) Association of sociodemographic characters with pregnancy intention among women using Alcohol PRAMS 2016-17 (N=74,543)

Characters	Pregnancy Intention N (Weighted %)		p-value	Odds Ratios (95% CI)	
	Unintended	Intended		Unadjusted	Adjusted*
Rurality			<.001		
Urban	13221 (40.5)	17649 (59.5)		1.2 (1.1 – 1.3)	1.2 (1.1 – 1.3)
Rural	2877 (36.6)	5009 (63.4)		ref	ref
Race/Ethnicity			<.001		
Asian	489 (33.4)	1027 (66.6)		ref	ref
Non-Hispanic White	7332 (33.5)	14814 (66.5)		1.00 (.84 - 1.12)	0.8 (0.7 – 1.0)
Hispanic White	1533 (45.9)	1730 (54.1)		1.7 (1.4 – 2.1)	0.9 (0.7 – 1.0)
Black	3746 (63.4)	2165 (36.6)		3.4 (2.9 – 4.2)	2.1 (1.7 – 2.6)
Others	2416 (50.3)	2356 (49.7)		2.02 (1.7 – 2.4)	1.1 (0.9 – 1.4)
Age (Years)			<.001		
≤17	130 (89.6)	19 (10.4)		20.4 (8.4 – 49.3)	7.0 (1.9 – 25.3)
18-24	4786 (63.0)	2745 (37.0)		4.04 (3.6 – 4.5)	2.1 (1.8 – 2.3)
25-35	8985 (35.1)	15502 (64.9)		1.3 (1.2 – 1.4)	1.1 (1.01 – 1.2)
35+	2197 (29.7)	4946 (70.3)			
Education			<.001		
<High School	1569 (61.4)	1033 (38.6)		5.0 (4.3 – 5.8)	2.1 (1.7 – 2.5)
High School only	4345 (56.0)	3297 (44.0)		4.0 (3.7 – 4.4)	2.3 (2.0 – 2.6)
Some college	5918 (48.5)	6243 (51.5)		3.0 (2.8 – 3.2)	2.1 (1.9 – 2.3)
Graduate	4138 (24.0)	12450 (76.0)		ref	ref
Income to need ratio			<.001		
<FPL	4925 (66.0)	2479 (34.0)		4.0 (3.7 – 4.4)	2.2 (1.9 – 2.4)
At/above FPL	8580 (32.5)	17262 (67.5)		ref	ref

Marital status			<.001		
Married	6594 (26.2)	18089 (73.8)		ref	ref
Others	9485 (64.8)	5107 (35.2)		5.18	3.2
				(4.8 – 5.6)	(2.9 – 3.5)
Depression/anxiety			<.001		
No	11948 (37.3)	19297 (62.5)		ref	ref
Yes	4026 (48.4)	3809 (51.6)		1.6	1.3
				(1.5 – 1.7)	(1.2 – 1.4)
Abuse			<.001		
No	4903 (32.8)	9460 (67.2)		ref	ref
Yes	5534 (37.8)	8757 (62.2)		1.2	0.96
				(1.2 – 1.3)	(0.9 – 1.04)

FPL=Federal Poverty Level.

Weighted percentages presented in tables as row percentages. P-value based on chi-square. Bold text indicates a statistically significant with a p-values <0.05. *Adjusted for Rurality, age, income, marital status, education and having depression/anxiety.

Table 3(b) Association of socio-demographic characters with pregnancy intention among women using Tobacco/ Nicotine products, PRAMS 2016-17 (N=17,535)

Characters	Pregnancy Intention N (Weighted %)		p-value	Odd Ratios (95% CI)	
	Unintended	Intended		Unadjusted	Adjusted
Rurality			.033		
Urban	8150 (57.9)	5426 (42.1)		1.1 (1.01 – 1.3)	1.2^a (1.02 – 1.3)
Rural	1880 (54.9)	1518 (45.1)		ref	ref
Race/Ethnicity			<.001		
Asian	173 (48.2)	179 (51.8)		ref	ref
Non-Hispanic White	4600 (53.3)	4023 (46.7)		1.2 (0.9 – 1.7)	0.8 ^b (0.6 – 1.2)
Hispanic White	672 (58.0)	484 (42.0)		1.5 (1.03 – 2.1)	0.9 (0.6 – 1.3)
Black	2331 (68.0)	1080 (32.0)		2.3 (1.6 – 3.2)	1.5 (1.02 – 2.1)
Others	1919 (62.2)	1169 (37.8)		1.7 (.2 – 2.5)	1.03 (0.7 – 1.5)
Age			<.001		
≤17	193 (87.7)	30 (12.3)		8.4 (4.1 – 17.0)	5.2^c (2.1 – 12.6)
18-24	375 (67.0)	1788 (33.0)		2.4 (2.03 – 2.8)	1.8 (1.5 – 2.2)
25-35	5089 (52.6)	4364 (47.4)		1.3 (1.1 – 1.5)	1.2 (1.01 – 1.4)
35+	989 (45.8)	1036 (54.2)		ref	ref
Education			<.001		
<HS	1909 (65.3)	1040 (34.7)		3.6 (2.9 – 4.3)	1.7^d (1.4 – 2.1)
HS only	3748 (62.7)	2215 (37.3)		3.2 (2.7 – 3.7)	2.1 (1.7 – 2.5)
Some college	3391 (58.2)	2407 (41.8)		2.6 (2.3 – 3.1)	2.0 (1.7 – 2.3)
Graduate	887 (34.4)	1500 (65.6)		Ref	Ref
Income to need ratio			<.001		
<FPL	4434 (69.4)	2033 (30.6)		2.5 (2.2 – 2.8)	1.9^e (1.7 – 2.1)
At/above FPL	3706 (47.6)	3856 (52.4)		ref	ref
Marital status			<.001		
Married	2434 (39.4)	3643 (60.6)		ref	ref

Others	7575 (67.9)	3559 (32.1)		3.2 (2.9 – 3.6)	2.4^f (2.1 – 2.7)
Depression/anxiety			<.001		
No	6402 (54.9)	5092 (45.1)		ref	ref
Yes	3561 (61.5)	2079 (38.5)		1.3 (1.2 – 1.5)	1.1^g (1.01 – 1.3)
Abuse			.005		
No	2266 (51.0)	2089 (49.0)		ref	ref
Yes	2448 (55.6)	2578 (44.4)		1.2 (1.01 – 1.4)	0.9^h (0.8 – 1.05)

FPL=Federal Poverty Level, HS=High School

Weighted percentages presented in tables as row percentages. P-value based on chi-square. Bold text indicates a statistically significant with a p-values <0.05.

A, b, g, h Adjusted for rurality, age, income, education, depression/anxiety

f adjusted for age, race/ethnicity, income, rurality, education

c adjusted for age, income, race/ethnicity

d e adjusted for age, income, education, depression/anxiety

Table 4(b) Association of sociodemographic characters with pregnancy intention among women using prescription opioids, PRAMS 2016 (N=848).

Characters	Pregnancy Intention Weighted %		p-value	Odd Ratios (95% CI)	
	Unintended	Intended		Unadjusted	Adjusted*
Rurality			<.001		
Urban	382 (66.8)	177 (33.2)		3.6 (1.9 – 6.4)	3.5 (1.8 – 6.8)
Rural	78 (35.9)	119 (64.1)		ref	ref
Race/Ethnicity			0.042		
Asian	07 (62.1)	07 (37.9)		1.5 (0.3 – 7.8)	5.6 (0.8 – 39)
Non-Hispanic White	180 (51.4)	166 (48.6)		ref	ref
Hispanic White	17 (59.3)	13 (40.7)		1.3 (0.5 – 3.7)	2.8 (1.00 - 7.7)
Black	100 (66.9)	60 (33.1)		1.9 (1.1 – 3.2)	1.5 (0.8 – 3.2)
Others	121 (64.6)	87 (35.4)		1.7 (1.02 – 2.9)	4.0 (1.9 – 8.5)
Age			.015		
≤17	12 (85.9)	04 (14.1)		5.1 (1.2 – 21.6)	NAC**
18-24	150 (68.0)	66 (32.0)		1.8 (0.8 – 3.9)	1.2 (0.4 – 3.5)
25-35	232 (50.4)	243 (49.6)		0.86 (0.43 – 1.7)	0.74 (0.3 – 1.6)
35+	66 (54.1)	58 (45.9)		ref	ref
Education			0.054		
<HS	82 (55.3)	58 (44.7)		2.0 (0.9 – 4.9)	1.2 (0.3 – 4.2)
HS only	185 (62.1)	111 (37.9)		2.7 (1.3 – 5.8)	1.7 (0.6 – 4.7)
Some college	150 (57.1)	124 (42.9)		2.2 (1.1 – 4.6)	2.0 (0.8 – 5.2)
Graduate	37 (37.3)	75 (62.7)		ref	
Income to need ratio			<.001		
<FPL	233 (71.2)	99 (28.8)		3.2 (1.9– 5.4)	3.0 (1.6 – 5.7)
At/above FPL	143 (43.5)	182 (56.5)		ref	ref

Marital status			<.001		
Married	111 (41.3)	196 (58.7)		ref	ref
Others	348 (65.5)	175 (34.5)		2.6	1.8
				(1.6 – 4.4)	(1.01-3.4)
Depression/anxiety			<.006		
No	263 (49.3)	251 (50.7)		ref	ref
Yes	194 (65.6)	119 (34.4)		1.9	2.0
				(1.2 – 3.2)	(1.05 - 3.9)
Abuse			.131		
No	91 (61.6)	82 (38.4)		-	-
Yes	225 (50.8)	190 (49.2)		-	-

FPL=Federal Poverty Level, HS=High School

Abuse was not significantly associated with other SD variables so was not included in further analysis. Weighted percentages presented in tables as row percentages. P-value based on chi-square. Bold text indicates a statistically significant with a p-values <0.05.* Adjusted for rurality, income, race/ethnicity, and depression/anxiety. Marital status adjusted for income and rurality.

**NAC= Not able to calculate

Table 5(b) Association of sociodemographic characters with pregnancy intention among women using Illicit and recreational drugs, PRAMS 2016-17 (N=1886).

Characters	Pregnancy Intention N (Weighted %)		p-value	Odd Ratios (95% CI)	
	Unintended	Intended		Unadjusted	Adjusted*
Rurality			<.001		
Urban	943 (73.5)	315 (26.5)		2.8 (1.8 – 4.3)	2.7 (1.7 – 4.1)
Rural	252 (52.2)	217 (47.8)		ref	ref
Race/ethnicity			.005		
Non-Hispanic White	542 (62.2)	331 (37.8)		ref	ref
Hispanic White	31 (76.0)	11 (24.0)		1.9 (0.7 – 5.0)	2.1 (0.4 – 11.3)
Black	214 (73.6)	80 (26.4)		1.7 (1.1 – 2.5)	1.4 (0.8 – 2.3)
Others	286 (75.1)	97 (24.9)		1.8 (1.1 – 2.9)	3.3 (1.9 – 5.8)
Age			<.001		
≤17	38 (97.0)	4 (3.0)		15.1 (2.0 – 112.4)	11.3 (1.7 – 76.2)
18-24	486 (74.2)	182 (25.8)		1.9 (0.9 – 3.06)	1.8 (0.9 – 3.7)
25-35	569 (58.6)	386 (41.4)		1.1 (0.5 – 2.2)	1.05 (0.5 – 2.0)
35+	102 (60.8)	80 (39.2)		ref	ref
Education			<.001		
<HS	218 (71.2)	85 (28.8)		1.5 (0.7 – 3.5)	1.5 (0.7 – 3.6)
HS only	452 (68.4)	207 (31.6)		1.8 (1.0 – 3.5)	1.7 (0.9 – 3.3)
Some college	398 (68.2)	213 (31.8)		2.5 (1.3 – 4.7)	2.3 (1.2 – 4.4)
Graduate	116 (41.6)	142 (58.4)		ref	ref
Income to Need ratio			<.001		
<FPL	656 (74.0)	237 (26.0)		1.9 (1.2 – 3.1)	2.2 (1.4 – 3.4)
At/above FPL	393 (54.3)	340 (45.7)		ref	ref

Marital status			<.001		
Married	212 (47.6)	281 (52.4)		ref	ref
Others	981 (73.2)	370 (26.8)		3.0	2.4
				(2.1 -4.3)	(1.4 – 3.9)
Depression/anxiety			.241	-	-
Yes	514 (68.1)	207 (31.9)			
No	675 (63.3)	440 (36.7)			
Abuse			.764	-	-
Yes	483 (61.7)	263 (38.3)			
No	220 (60.1)	173 (39.9)			

FPL=Federal Poverty Level, HS=High School

Weighted percentages presented in tables as row percentages. P-value based on chi-square. Bold text indicates a statistically significant with a p-values <0.05. Due to small number of women in Asian category, it was combined with Others in Race/Ethnicity variable. *Adjusted for Rurality, age, income, marital status, race/ethnicity.

Chapter 3

Table 1 Maternal sociodemographic characteristics of women delivering a live birth, stratified by Alcohol use and Smoking during preconception period; PRAMS 2016-17

Characteristics	All women	Alcohol	Heavy Binge Drinking	Smoking	Heavy Smoking
	N (Wt.%)	N (Wt.%)	N (Wt. %)	N (Wt. %)	N (Wt. %)
	N=74543	N=39831 (56.6)	N=3,937	N=13,976 (17.4)	N=4,303
Rurality					
Urban	58954 (78.3)	31307 (78.2)	3081 (74.8)	11052 (78.8)	3408 (77.6)
Rural	14535 (21.7)	7968 (21.8)	854 (25.2)	2709 (21.2)	857 (22.4)
Race/Ethnicity					
Asian	4976 (5.9)	154 (3.3)	138 (3.2)	224 (1.4)	29 (0.5)
Non-Hispanic White	34367 (56.9)	22413 (68.3)	1842 (67.4)	7411 (68.9)	2906 (82.5)
Hispanic White	8124 (12.7)	3299 (9.3)	326 (10.4)	798 (6.8)	126 (3.1)
Black	13581 (14.8)	6004 (11.9)	364 (7.8)	2490 (14.4)	455 (8.0)
Others	10747 (9.7)	4842 (7.2)	833 (11.1)	2507 (8.4)	560 (6.0)
Marital Status					
Married	44393 (62.1)	24978 (65.6)	2259 (63.4)	4613 (36.4)	1340 (33.0)
Others	30077 (37.9)	14815 (34.4)	1671 (36.6)	9330 (63.6)	2942 (67.0)
Age (in years)					
≤17	1004 (1.3)	153 (0.3)	14 (0.4)	168 (1.3)	36 (0.8)
18-24	16806 (22.0)	7628 (18.4)	939 (21.0)	4352 (30.8)	1265 (29.8)
25-35	43373 (58.9)	24814 (63.1)	2431 (63.1)	7747 (56.0)	2454 (56.4)
35+	13358 (17.8)	7234 (18.2)	553 (15.5)	1707 (12.0)	547 (13.1)
Education					
<HS	9848 (12.9)	2656 (5.9)	323 (7.4)	2687 (18.1)	906 (20.8)
Only HS	17947 (24.1)	7764 (19.3)	879 (20.5)	5154 (36.0)	1693 (38.0)
Some College	21083 (26.8)	12349 (29.2)	1236 (27.7)	4576 (33.0)	1422 (34.8)
Graduate	24906 (36.2)	16740 (45.6)	1484 (44.4)	1437 (12.8)	234 (6.5)
Income to Need ratio					
<FPL	18078 (27.7)	7520 (19.6)	720 (20.0)	5656 (45.0) *	1957 (50.4) *
At/above FPL	41999 (72.3)	26136 (80.4)	2315 (80.0)	5695 (55.0)	1639 (49.6)
Depressive symptoms					
No	60383 (82.7)	31688 (81.0)	1309 (45.0)	2949 (41.0)	815 (36.6)

Yes	13559 (17.3)	7943 (19.0)	1415 (55.0)	5185 (59.0)	1649 (63.4)
Kessner Index					
Adequate PNC	50298 (68.5)	28670 (73.5)	2789 (70.2)	8321 (62.1)	2461 (59.8)
Intermediate PNC	14350 (19.1)	6516 (15.7)	759 (20.3)	3305 (22.0)	1036 (23.1)
Inadequate PNC	4472 (5.8)	1790 (4.2)	202 (4.8)	1267 (8.2)	435 (8.5)
Unknown PNC	5423 (6.6)	2855 (6.6)	187 (4.7)	1083 (7.7)	371 (8.6)
Abuse					
No	23724 (54.1)	14491 (55.4)	1357 (57.9)	3284 (46.0)	971 (43.0)
Yes	24315 (45.9)	14433 (44.6)	1364 (42.1)	4834 (54.0)	1490 (57.0)
Birth control					
No	14985 (59.0)	7610 (58.7)	930 (57.7)	4419 (64.4)	1557 (70.0)
Yes	24315 (41.0)	5357 (41.3)	680 (42.3)	2430 (35.6)	703 (30.0)
Pregnancy Intention					
Intended	42302 (59.0)	23212 (60.6)	2035 (55.0)	5550 (42.0)	1584 (37.5)
Unintended	30997 (41.0)	16100 (39.4)	1848 (45.0)	8193 (58.0)	2647 (62.5)
Mistimed	14196 (19.5)	7441 (19.1)	875 (22.4)	3186 (23.9)	906 (22.3)
Unwanted	4722 (6.2)	2505 (5.8)	275 (5.8)	1451 (10.1)	538 (12.3)
Ambivalent	12079 (15.3)	6154 (14.5)	699 (16.8)	3556 (24.1)	1203 (27.9)
Alcohol Consumption					
No	33392 (43.4)	-	-	4657 (30.1)	1692 (35.0)
Yes	39831 (56.6)	-	-	9149 (69.9)	2565 (65.0)
Heavy/Binge drinking					
No	8042 (67.1)	8042 (67.1)	-	1515 (50.7)	393 (50.7)
Yes	3938 (32.9)	3938 (32.9)	-	1339 (49.3)	371 (49.3)
Smoking					
No	59445 (82.6)	30400 (78.5)	2568 (69.1)	-	-
Yes	13976 (17.4)	9149 (21.5)	1339 (30.9)	-	-
Heavy Smoking					
No	11466 (72.9)	7790 (74.7)	1123 (77.0)	9673 (69.0)	-
Yes	4303 (27.1)	2565 (25.3)	371 (23.0)	4303 (31.0)	-
Cannabis					
No	15022 (90.0)	8732 (87.1)	1056 (70.5)	2609 (74.2)	745 (68.2)
Yes	1986 (10.0)	1511 (12.9)	393 (29.5)	1091 (25.8)	416 (31.8)

Illicit Drugs					
No	15920 (95.8)	9276 (95.4)	1200 (95.6)	3504 (87.5)	1001 (82.2)
Yes	563 (4.2)	346 (94.6)	68 (4.4)	378 (12.5)	183 (17.8)
Tobacco/Nicotine					
No	65465 (89.4)	33902 (86.0)	3123 (80.5)	9511 (67.0)	2747 (63.1)
Yes	7955 (10.6)	5748 (14.0)	788 (19.5)	4396 (33.0)	1535 (36.9)
Opioids					
No	15612 (94.8)	9130 (95.0)	1196 (94.1)	3477 (89.6)	1018 (86.4)
Yes	848 (5.2)	480 (5.0)	69 (5.9)	393 (10.4)	163 (13.6)

HS=High School, FPL= Federal Poverty Level, PNC=Prenatal Care

*Chi-squared p-value (>.05). HS= High school, FPL = Federal Poverty Level, Abuse status was defined as physical/emotional abuse. Depressive symptoms were defined as feeling depressed or sad before pregnancy. Tobacco/Nicotine included smoking, hookah, electronic cigarettes, cigars, cigarillos, nicotine, and betel nut. Prescription opioids included Hydrocodone, and Oxycodone, Codeine. Illicit/Recreational drugs included Adderall, Marijuana, synthetic marijuana, Methadone, Heroin, Amphetamine, Cocaine, Tranquillizers, and Hallucinogens.

Table 2: Association of unintended pregnancy to co-use of alcohol and other substances in a representative sample of US women of childbearing age, PRAMS 2016-17 (N=39,831)

Other substance	Alcohol		Heavy Binge Drinking	
	Odds Ratios	Adjusted Odds Ratios*	Odds Ratios	Adjusted Odds Ratios*
Smoking (Yes vs. No)	2.36 (2.18 – 2.55)	1.5 (1.4 – 1.6)	2.6 (2.1 – 3.1)	1.9 (1.5 – 2.4)
Heavy smoking (Yes vs. No)	1.47 (1.3 – 1.7)	1.3 (1.1 – 1.5)	1.6 (1.01 – 2.3)	1.6 (1.0 – 2.5)
Cannabis (Yes vs. No)	2.4 (1.9 – 3.0)	2.0 (1.6 – 2.4)	2.4 (1.7 – 3.5)	2.1 (1.4 – 3.1)
Tobacco/Nicotine (Yes vs. No)	1.8 (1.4 – 2.2)	1.6 (1.4 – 1.7)	2.6 (2.1 – 3.3)	2.3 (1.7 – 3.1)
Illicit drugs (Yes vs. No)	3.04 (2.1 – 4.4)	1.8 (1.1 – 2.7)	2.2 (1.1 – 4.4)	1.6 (0.6 – 3.9)
Opioids (Yes vs. No)	1.4 (1.01 – 1.9)	1.3 (0.9 – 1.9)	2.4 (1.2 – 4.7)	1.4 (0.6 – 3.6)

*Adjusted for maternal age, race/ethnicity, education, income to need ratio, rurality.

Bold text indicates statistically significant effect size at alpha 0.05

Table 3: Association of unintended pregnancy sub-types to preconception use of alcohol in concert with other substances in a representative sample of US women of childbearing age, PRAMS 2016-17 (N=39,831); multivariable logistic regression.

	Crude ORs with 95%CI			Adjusted* ORs with 95% CI		
	Mistimed	Unwanted	Ambivalent	Mistimed	Unwanted	Ambivalent
Other Substances						
Smoking (Yes vs. No)	2.0 (1.8 – 2.2)	2.9 (2.5 – 3.4)	2.7 (2.4 – 2.96)	1.3 (1.1 – 1.4)	1.8 (1.5 – 2.1)	1.7 (1.5 – 1.9)
Heavy smoking (Yes vs. No)	1.8 (1.4 – 2.4)	3.1 (1.9 – 4.8)	2.6 (1.9 – 3.5)	1.6 (1.2 – 3.9)	2.3 (1.4 – 3.9)	2.2 (1.6 – 3.1)
Cannabis (Yes vs. No)	2.3 (1.8 – 2.9)	3.3 (2.5 – 4.6)	2.4 (1.9 – 3.1)	1.7 (1.4 – 2.2)	2.8 (2.0 – 3.8)	2.0 (1.5 – 2.6)
Tobacco/Nicotine (Yes vs. No)	2.2 (1.9 – 2.5)	2.5 (2.1 – 3.0)	1.9 (1.7 – 2.2)	1.6 (1.4 – 1.8)	1.8 (1.5 – 2.3)	1.4 (1.3 – 1.7)
Illicit drugs (Yes vs. No)	2.5 (1.6 – 4.0)	4.7 (2.7 – 8.2)	3.06 (1.9 – 4.8)	1.6 (1.0 – 2.6)	2.7 (1.4 – 5.1)	1.8 (1.04 – 3.1)
Opioids (Yes vs. No)	1.4 (0.9 – 2.1)	3.1 (1.9 -5.1)	1.5 (1.0 – 2.2)	1.2 (0.7 – 2.0)	2.3 (1.3 – 4.0)	1.01 (0.6 – 1.7)

*Adjusted for maternal age, race/ethnicity, education, income to need ratio, rurality. Bold text indicates statistically significant effect size at alpha 0.05

Table 4: Demographic characteristics of women delivering a live birth, stratified by patterns of polysubstance use during the preconception period (PRAMS 2016-17)

Characteristics	Alcohol only	Alcohol and Smoking	Alcohol & Cannabis	Alcohol & Illicit/recreational drugs
	N = 39,831	N = 9,149	N = 1,511	N = 346
	N (Wt. %)	N (Wt. %)	N (Wt. %)	N (Wt. %)
Rurality				
Urban	31307 (78.2)	7210 (78.8)	1069 (75.8)	261 (86.5)
Rural	7968 (21.8)	1788 (21.2)	372 (24.2)	75 (13.5)
Age				
≤19	975 (2.2)	478 (4.5)	103 (5.9)	24 (3.8)
20-34	31620 (79.6)	7059 (77.7)	1160 (76.7)	254 (77.2)
35+	7234 (18.2)	1612 (17.8)	248 (17.4)	68 (19.0)
Race/Ethnicity				
Non-Hispanic White	22413 (68.3)	4962 (70.4)	805 (70.5)	173 (81.3)
Hispanic White	3299 (9.3)	577 (7.4)	71 (7.9)	10 (2.2)
Black	6004 (11.9)	1552 (12.7)	201 (10.8)	29 (7.4)
Others	6388 (10.5)	1707 (9.5)	231 (10.8)	90 (9.2)
Education				
≤High School	10418 (25.2)	4477 (46.8)	638 (45.4)	169 (47.4)
Some college	12349 (29.2)	3347(36.6)	524 (30.9)	120 (35.3)
Graduate	16740 (45.6)	1258 (16.6)	333 (23.7)	50 (17.3)
Income				
Below FPL	7520 (19.6)	3256 (37.2)	620 (39.8)	162 (46.0)
At/Above FPL	26136 (80.4)	4399 (62.8)	770 (60.2)	135 (54.0)
Marital status				
Married	24978 (65.6)	3331 (40.1)	562 (43.9)	91 (37.8)
Others	14815 (34.4)	5799 (59.9)	943 (56.1)	255 (62.2)
Pregnancy Intention				
Intended	23212 (60.6)	3768 (37.2)	590 (40.4)	103 (33.8)
Unintended	16100 (39.4)	4399 (62.8)	892 (59.6)	232 (66.2)
Depressive symptoms				
No	14065 (53.0)	2187 (44.3)	329 (38.8)	71 (36.4)
Yes	14896 (47.0)	3451 (55.7)	647 (61.2)	149 (63.6)

Chi-squared p-value ($<.05$). FPL=Federal poverty level, Depressive symptom=feeling sad or depressed before pregnancy, Rurality=based on rural-urban codes by NCHS

Table 5: Association of maternal sociodemographic factors to likelihood of unintended pregnancy, stratified by preconception substance use pattern, PRAMS 2016-17 (N=39,831).

Characteristics	Alcohol Only	Alcohol and smoking (n=9149)	Alcohol & Cannabis (n=1511)	Alcohol & Illicit/recreational drugs (n=346)
	AOR* (95%CI)	AOR* (95%CI)	AOR* (95%CI)	AOR* (95%CI)
Rurality				
Rural	Ref	Ref	Ref	Ref
Urban	1.2 (1.1 – 1.3)	1.2 (1.1 – 1.5)	2.5 (1.6 – 3.9)	1.6 (0.6 – 4.4)
Age				
≤19	Ref	Ref	Ref	Ref
20-34	0.4 (0.3 – 0.6)	1.5 (1.0 – 2.2)	1.3 (0.6 – 2.8)	3.6 (0.4 – 33.5)
35+	0.4 (0.2 – 0.5)	2.0 (1.3 – 3.0)	1.7 (0.7 – 4.1)	7.5 (0.7 – 78.1)
Race/Ethnicity				
Non-Hispanic White	Ref	Ref	Ref	Ref
Hispanic White	1.1 (0.9 – 1.2)	0.8 (0.6 – 1.2)	1.3 (0.6 – 2.8)	-
Black	2.3 (2.1 – 2.7)	1.4 (1.1 – 1.7)	1.6 (0.9 – 2.9)	1.02 (0.3 – 3.6)
Others	1.3 (1.1 – 1.4)	1.3 (1.0 – 1.7)	1.6 (0.8 – 3.3)	1.9 (0.6 – 6.0)
Education				
≤High School	2.6 (2.4 – 2.9)	2.8 (2.3 – 3.6)	2.6 (1.6 – 4.6)	2.3 (0.8 – 7.0)
Some college	2.3 (2.1 – 2.5)	2.6 (2.0 – 3.2)	2.9 (1.7 – 4.9)	7.2 (2.1 – 23.7)
Graduate	Ref	Ref	Ref	Ref
Income				
Below FPL	2.3 (2.1 – 2.6)	2.0 (1.6 – 2.3)	2.1 (1.3 – 3.4)	3.7 (1.6 – 9.0)
At/Above FPL	Ref	Ref	Ref	Ref
Marital status				
Married	Ref	Ref	Ref	Ref
Others	3.2 (3.0 – 3.5)	2.4 (2.0 – 2.8)	2.8 (1.8 – 4.4)	1.7 (0.6 – 4.9)
Depressive Symptoms				
No	1.2 (1.1 – 1.3)	1.4(1.1 – 1.6)	1.1 (0.6 – 1.8)	0.6 (0.2 – 1.6)
	Ref	Ref	Ref	Ref

*Adjusted for maternal age, race, ethnicity, income, rurality, and level of education. Bold text indicates statistically significant Odds Ratio

Chapter 4

Table 1: Risk of bias assessment by domain using Newcastle-Ottawa Scale for cross-sectional, case-control, and cohort studies

Study	Study design	Selection (Maxim. 5 stars)	Comparability (Maxim. 2 stars)	Outcome/exposure (Maxim. 3stars)
Besculides et al., 2004	Cross-sectional	****	*	**
Dott et al., 2009	Case-control	***	**	**
Lundsberg et al., 2018	Prospective cohort	****	*	**
Lundsberg et al., 2020	Cross-sectional	**	*	**
Oulman et al., 2015	Cross-sectional	****	**	**
Paquette et al., 2017	Cross-sectional	****	*	**
Short et al., 2020	Cross-sectional	***	*	**
Wellings et al., 2013	Cross-sectional	***	*	**
		3.4	1.25	2.0

Table 2. Characteristics of eligible studies (N=8 studies). SR with MA regarding the association between maternal illicit and recreational drug use and the likelihood of unintended pregnancy.

First author (Publication years)	Region	Study design	Data collection period	Sample size	Population	Data source
Besculides et al., 2004	NYC/US	Cross-sectional	1998-2001	8886	Pregnant women	Office of family health, NYC, Dept. of Health & Mental Hygiene
Dott et al., 2009	US	Case-control	1997-2002	4094	Women who gave live births	National Birth Defects Prevention study
Lundsberg et al., 2018	MA, CT/US	Cohort	2005-09	2654	Pregnant women	Hospital based research study
Lundsberg et al., 2020	CT/US	Cross-sectional	2014-15	123	Pregnant women	Questionnaire
Oulman et al., 2015	Canada	Cross-sectional	2005-2006	6421	Women of childbearing age	Maternity experience survey
Paquette et al., 2017	Britain	Cross-sectional	2010-12	4980	Women of childbearing age	Natsal-3
Short et al., 2020	US	Cross-sectional	2016	5676	Women who gave live births	PRAMS
Wellings et al., 2013	Britain (England, Scotland, Wales)	Cross-sectional	2010-12	5686	Women of childbearing age	Natsal-3

Table 3. Description of the exposure and outcome variables from the eligible studies (N=8). SR with MA regarding the association between maternal illicit and recreational drug use and the likelihood of unintended pregnancy.

First author (Publication years)	Exposure/ Exposure assessment	Prevalence of illicit/recreational drug use	Outcome/ outcome assessment	Prevalence of unintended pregnancy	Determinants of unintended pregnancy
Besculides et al., 2004	Smoking, alcohol, drug use/ Self-reported	Drug use = 4%	Pregnancy intention/ Question about current pregnancy' intention	82.10%	10-19yrs, OR:2.2), white-non-Hispanic (OR:1.67), Unmarried (OR:3.4)
Dott et al., 2009	Smoking, alcohol, illicit drugs, vitamin intake / Self-reported	Illicit drugs = 5.3%	Pregnancy intention/ Question about current pregnancy' intention	40.00%	Age:<20years, Non-Hispanic Black race, <HS education, Prev. adverse pregnancy outcome, smoking (OR: 1.69)
Lundsberg et al., 2018	Marijuana, cocaine, smoking, alcohol/ Self-reported	Marijuana = 6.5%, cocaine = 1%	Pregnancy intention/ Question about current pregnancy' intention	37.20%	Preconception substance use
Lundsberg et al., 2020	Tobacco, alcohol, cannabis, illicit drugs/ Self-reported	Cannabis = 21%, illicit drugs = 12%	Pregnancy intention & perception/ LMUP	67.50%	substance use including alcohol (OR: 3.2) and tobacco
Oulman et al., 2015	Smoking, alcohol, drugs/ Self-reported	Drug use = 6.7%	Pregnancy intention/ Question about current pregnancy' intention	27.00%	Age:<20years (OR: 4.4), Immigrants (OR:1.5), ≤HS education (OR:1.7), no partner (OR: 3.2), abuse (OR:1.3), 1 or more Prev. pregnancies, Substance use
Paquette et al., 2017	Illicit drugs (Amphetamines, cocaine, crack, Ecstasy, Heroin,	Illicit drugs and cannabis = 12.5%	Risky sexual behaviors & Pregnancy intention/LMUP	5.30% among those using drugs	Not reported since primary outcome of the study was different

	LSD, Crystal meth, other non-prescribed drugs)				
Short et al., 2020	Alcohol, tobacco, marijuana/ Self-reported	Marijuana = 8%	Pregnancy intention/PRAMS questions on pregnancy intention	42.60%	Not reported since the primary outcome of the study was different
Wellings et al., 2013	Smoking, alcohol, drugs, cannabis/ Self-reported	Cannabis = 7.3%, Illicit drugs = 5.8%	Unplanned pregnancy/LMUP	45.20%	Age:<20, First intercourse before age 16 (OR:2.8), lower educational attainment (OR:1.98), Substance use

Table 4: Findings of included studies in SR and MA regarding the association between illicit and recreational drug use during the preconception period and the likelihood of unintended pregnancy (N=8 studies).

Study	ORs	AORs	LCI95%	HCI95%	AORs adjusted for
Besculides et al., 2004	2.13	1.4	0.96	2.05	Age, race/ethnicity, marital status, contraceptive use, number of previous pregnancies, alcohol, and smoking.
Dott et al., 2009	-	3.2	2.26	4.53	Age, race, ethnicity, parity, education, income, history of pregnancy complications
Lundsberg et al., 2018	-	1.6	1.05	2.43	Age, race/ethnicity, education, relationship status, parity, medical history
Lundsberg et al 2020	2.63	1.42	0.27	7.41	Demographics, pregnancy history, mental health, substance use
Oulman et al., 2015	1.69	1.37	1.05	1.79	Predictors of pregnancy intention including demographics, reproductive history
Paquette et al., 2017	2.61	2.39	1.39	6.17	Age, sexual identity, number of sexual partners
Short et al., 2020	-	2.00	1.5	2.8	Demographics
Wellings et al., 2013	-	3.41	1.64	7.11	Age

Table 5: Individual and pooled effect size: Meta-analysis of the association of illicit and recreational drug use during the preconception period and likelihood of unintended pregnancy (N=8 studies).

Study	ES	LCI 95%	HCI 95%	weight (%)
Besculides et al., 2004	1.4	0.96	2.05	14.11003
Dott et al., 2009	3.2	2.26	4.53	16.7961
Lundsberg et al., 2018	1.6	1.05	2.43	11.53442
Lundsberg et al., 2020	1.42	0.27	7.41	0.740288
Oulman et al., 2015	1.37	1.05	1.79	28.54151
Paquette et al., 2017	2.39	1.39	6.17	3.656129
Short et al., 2020	2	1.5	2.8	20.84685
Wellings et al., 2013	3.41	1.64	7.11	3.77467
Pooled	1.84441	1.380783	2.463709	100
Statistics				
I-squared	65.70116	27.13366	83.85523	
Cochran's Q	20.40886			
Chi2, p	0.004751			

Table 6: Influence analysis showing pooled effect size following removal of each eligible study from the meta-analysis (Association of illicit and recreational drug use during the preconception period and likelihood of unintended pregnancy, N=8 studies).

Excluded study	Pooled ES	LCI 95%	HCI 95%	Cochran Q	p	I²	I² LCI 95%	I² HCI 95%
Besculides et al., 2004	1.929864	1.388428	2.68244	18.04647	0.006117	66.7525	25.8576	85.0908
Dott et al., 2009	1.65026	1.334204	2.04118	8.813442	0.184345	31.92217	0	71.0375
Lundsberg et al., 2018	1.878914	1.337595	2.63930	19.91034	0.002873	69.8649	33.9127	86.2587
Lundsberg et al., 2020	1.848011	1.369058	2.49452	20.31236	0.002436	70.46133	35.44496	86.4838
Oulman et al., 2015	2.077	1.546207	2.79001	13.72716	0.032837	56.29102	0	81.1962
Paquette et al., 2017	1.826361	1.34078	2.48780	19.92671	0.002854	69.88966	33.9764	86.2680
Short et al., 2020	1.805485	1.250144	2.60752	20.08201	0.002678	70.12251	34.5750	86.3559
Wellings et al., 2013	1.800478	1.348917	2.40320	17.60575	0.007297	65.92022	23.6892	84.7802

Table 7: Cumulative meta-analysis for the association of illicit and recreational drug use during the preconception period and likelihood of unintended pregnancy, N=8 studies).

Study	ES	LCI 95%	HCI 95%	Cumulative Weight (%)
Lundsberg et al., 2020	1.42	0.271057	7.439017	0.74028811
Short et al., 2020	1.976647	1.454588	2.686077	21.58713753
Lundsberg et al., 2018	1.836357	1.433612	2.352245	33.12155862
Paquette et al., 2017	1.885098	1.490366	2.384376	36.77768797
Oulman et al., 2015	1.639707	1.356379	1.982217	65.31919509
Wellings et al., 2013	1.706625	1.320853	2.205068	69.09386535
Dott et al., 2009	1.929864	1.388428	2.682441	85.8899694
Besculides et al., 2004	1.84441	1.380783	2.463709	100

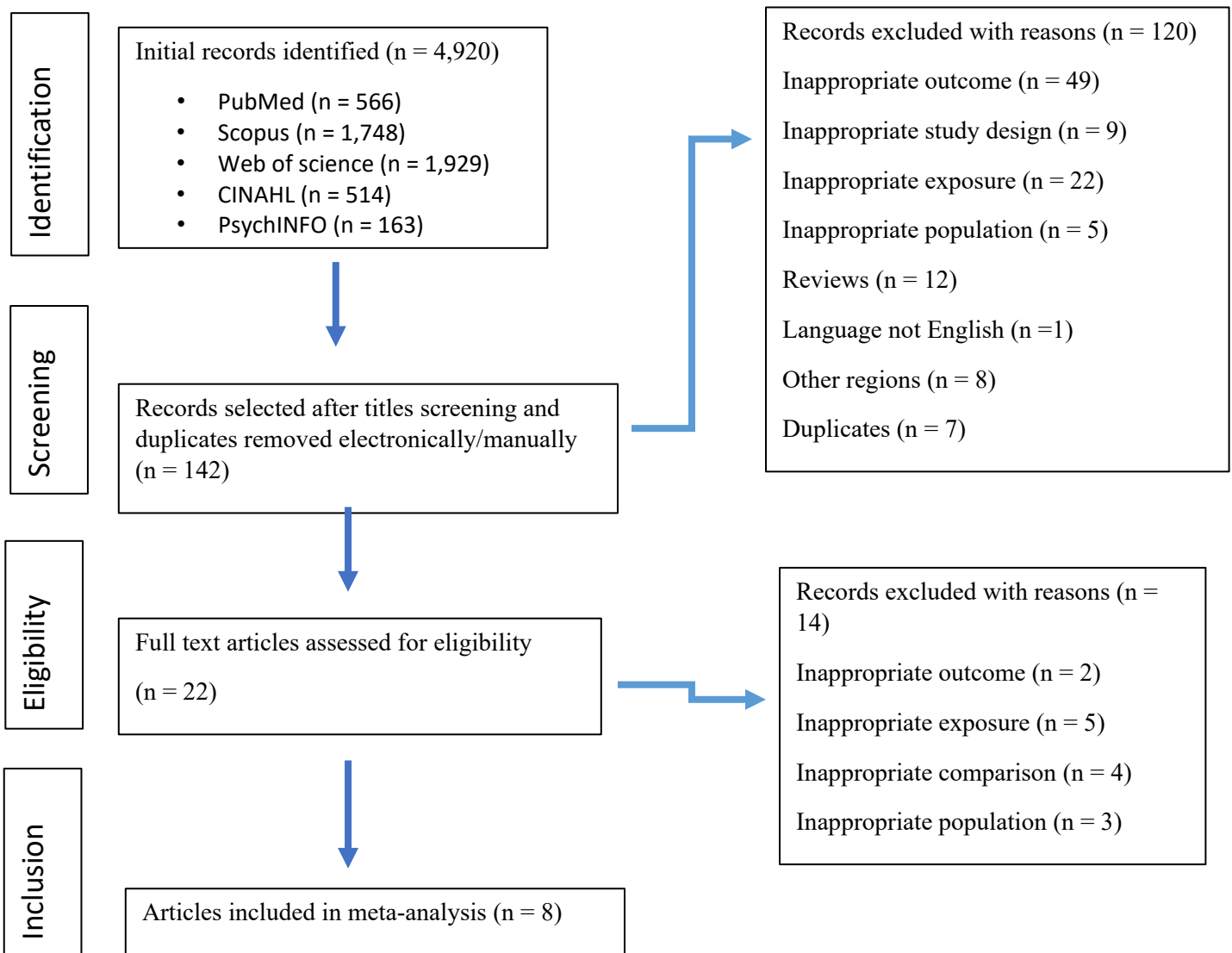


Figure1: Flow chart diagram describing the selection of studies included in the systematic review and meta-analysis (SR and MA) for the association of illicit and recreational drug use during the preconception period and likelihood of unintended pregnancy, N=8 studies).

Figure 2: Forest Plot for the association of illicit and recreational drug use during the preconception period and the likelihood of unintended pregnancy, (N=8 studies).

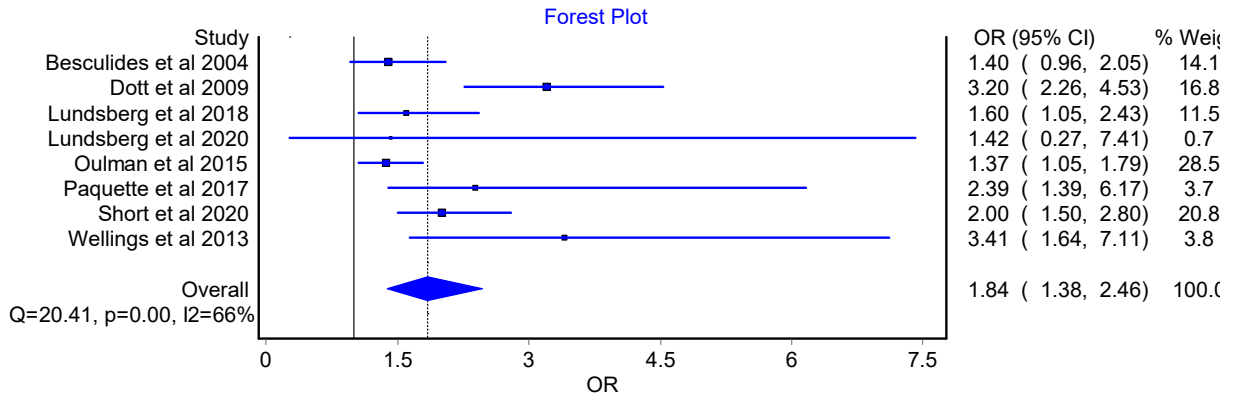
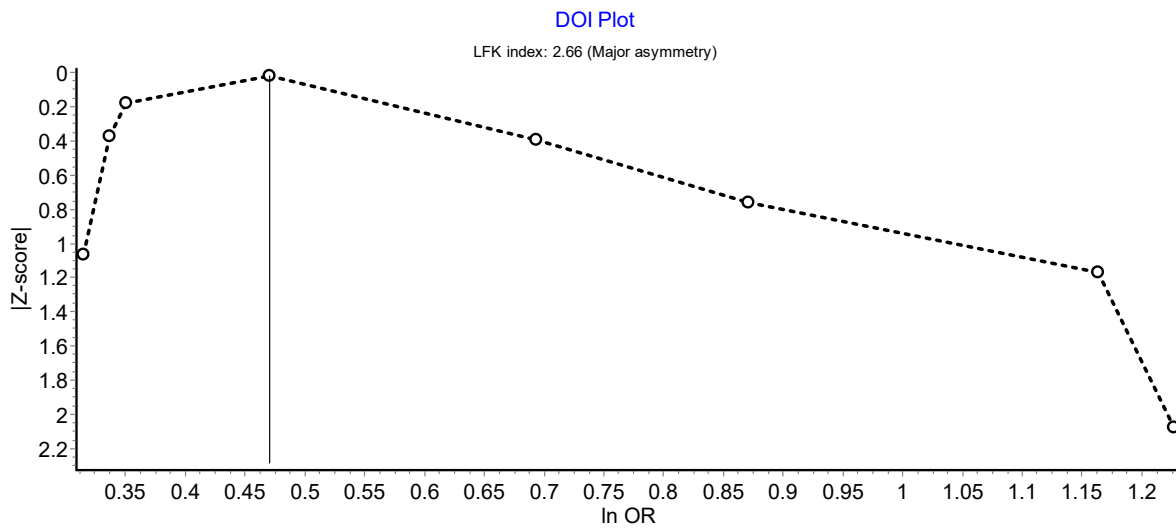


Figure 3: DOI Plot using the logarithm of Odds Ratio as the effect measure to examine the association between illicit and recreational drug use during the preconception period and the likelihood of unintended pregnancy, N=8 studies).

(LFK index = 2.66)



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