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UNINTENDED PREGNANCY PREVENTION IN WOMEN USING PSYCHOACTIVE SUBSTANCES: A SYSTEMATIC REVIEW

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Running title: Contraception among women using psychoactive substances.

Abstract

This systematic review seeks to evaluate the efficacy of interventions aimed at preventing unintended pregnancies in women using psychoactive substances. Seven electronic databases

(Medline, EMBASE, CINAHL, Web of Science Core Collection, PsycINFO, Cochrane CENTRAL database) were searched in October 2017. Twenty-two articles met our inclusion criteria. Interventions based on behavior change theory yielded an increase in the initiation of effective contraception as compared with provision of written information materials. The effect was more pronounced when the intervention provided on-site contraceptive counseling and free access to birth control. Financial incentives also seemed to effectively increase women's contraception intake. Case management interventions including pregnant and postpartum women with heavy levels of substance use showed promising results in terms of initiation of contraception, but rates of unintended pregnancy over long-term follow-up were nevertheless elevated. Finally, some interventions integrated family planning services into specialized centers taking care of pregnant and postpartum women with substance abuse. However, most studies aimed at postpartum and post-abortion contraception used a non-comparative design and had a number of methodological flaws. The risk of bias in most studies is high. All interventions with a primary or secondary focus on the prevention of unintended pregnancy in women using psychoactive substances short-term improvements in contraception intake, but it is unclear if these effects last or have any impact on unintended pregnancy rates in the long-term.

Keywords Systematic review; unintended pregnancy prevention; substance users.

1. INTRODUCTION

Prevention of unintended pregnancy via the provision of universal access to effective contraceptive methods is one of the Millennium Development Goals decided by WHO.¹ The prevalence of unintended (i.e. unwanted, mistimed or ambivalent) pregnancy fluctuates in Western countries between 30-50%.^{2,3} Psychoactive substances use, which is frequent, is associated with a high risk of unintended pregnancy, yet it often goes undetected.⁴ According to Heil et al., in the United States, nearly 86% of pregnancies in women using opioids are unintended.⁵

Regular use of highly effective contraceptive methods could prevent unintended pregnancy, particularly among women who use psychoactive substances. However, developing effective family planning interventions for women who use psychoactive substances is challenging.⁶ Existing evidence suggests that female substance users face many individual and systemic barriers for the use of sexual and reproductive health services.^{7,8} First, compared to their male counterparts, women using psychoactive substances are more likely to have a history of neglect or abuse, mental illness and low self-esteem, all of which can influence self-care and the ability to use preventive health services.⁹ Second, women who use psychoactive substances may avoid general sexual and reproductive health services for reasons, including a) anticipation of drug-related stigma on the part of health professionals, b) emotional difficulties when discussing sexual history, c) challenges related to coping with unfavorable test results and d) perceptions of low anticipated value of sexual health interventions, and e) fear of losing child custody.^{8,10} Such discriminatory practices can have a negative impact on women's contraceptive use, but when they are lifted, women using substances can make choices favoring the regular use of birth control methods.¹¹

In 2018, the United Nations in its annual World Drug Report emphasized the importance of addressing gender-specific needs of women who use substances.¹² This includes the development of interventions aimed at improving access to contraception and lowering levels of unintended pregnancy in this population.

In this review, we synthesize quantitative evidence regarding interventions focused on unintended pregnancy prevention in women using any substance (excluding tobacco alone) or being under substitution treatment, whether or not they are pregnant or have recently undergone pregnancy termination.

Twenty-two studies aimed to prevent unintended pregnancy in substance users were analyzed.

2. METHODS

2.1. Study selection

A systematic review was performed according to the PRISMA consensus statement on the conduct of systematic reviews.¹³ The protocol was registered with PROSPERO (CRD42018094929), an international database for systematic reviews.

2.2. Search strategy

The literature search was conducted in six databases (Medline, EMBASE, CINAHL, Web of Science Core Collection, PsycINFO, Cochrane CENTRAL database) using a specific search strategy for each database (Supplementary materials, S2).

2.3. Types of investigations

Randomized controlled trials (RCTs), cohort, pre- and post-intervention studies, which reported outcomes of interest and were published as full text articles, were eligible for our analysis. The study population had to meet the following criteria: 1) heterosexual or bisexual women aged 15-45 years who used substances (drugs or alcohol) at any dose and frequency at least in the three months preceding the intervention, as documented by self-report or biomarkers, or who were current clients of addiction treatment centers; 2) who had at least one episode of unprotected vaginal sex with men or used reliable contraceptives in an ineffective way during the three preceding months. Ineffective use was defined as inconsistent or not according to the recommendations of the national or international guidelines; 3) who did not desire to get pregnant in the near future. All interventions with a primary or secondary focus on unintended pregnancy prevention that included the above-mentioned population were eligible. Interventions involving exclusive tobacco smokers or centered on condom promotion were out of the scope of this review.

Studies published only as abstracts or in non-peer reviewed sources were not included.

2.4. Outcome measures

The primary outcomes considered were: unintended pregnancy rate or risk, intentional pregnancy termination rate, or repeated pregnancy rate defined as pregnancy within 24 months of a previous pregnancy. Secondary outcomes included: initiation and continuation of effective contraceptive use; initiation and continuation of long acting reversible contraceptives (LARCs) use (intrauterine device (IUD) and implant).

2.5. Study selection

Two investigators (AY and VM) independently reviewed the titles and abstracts of citations identified via the independent search and from reference lists of all included studies. All citations that were assessed as potentially relevant were retrieved for further assessment in the full text. Full text articles were independently evaluated by two reviewers (AY and VM). Disagreements were settled by discussion and consensus, with the third reviewer (MM) available as adjudicator.

2.6. Data abstraction and risk of bias assessment

Two reviewers (AY and VM) independently extracted the following data from full text articles: study design, years of study, study origin (city, state, country), study setting, study inclusion and exclusion criteria, definition of substance use and how it was measured, age, pregnancy status,

outcomes, follow-up duration and information on risk of bias assessment. Inconsistencies were resolved through the consensus process described earlier.

Study quality was assessed using the RoB 2.0 Cochrane tool (RCTs) or a modified Newcastle-Ottawa Scale (observational studies) (Supplementary materials S1).^{14,15}

2.7. Data synthesis

Significant heterogeneity between population studies, interventions and their multiple versions precluded the conduct of a meta-analysis. Therefore we synthesized the data using a narrative approach and tabulation. The effect size of each intervention was estimated using an intention-to-treat approach and expressed as Hedge's *g* for RCTs or comparative observational studies; and as an event rate for non-comparative studies.¹⁶ All computations were performed with the Comprehensive Meta-Analysis software (version 2).

3. RESULTS

3.1. Article search

Applying the search strategy described in Supplementary materials S2, 5,830 unduplicated titles and abstracts were found (Fig.1).

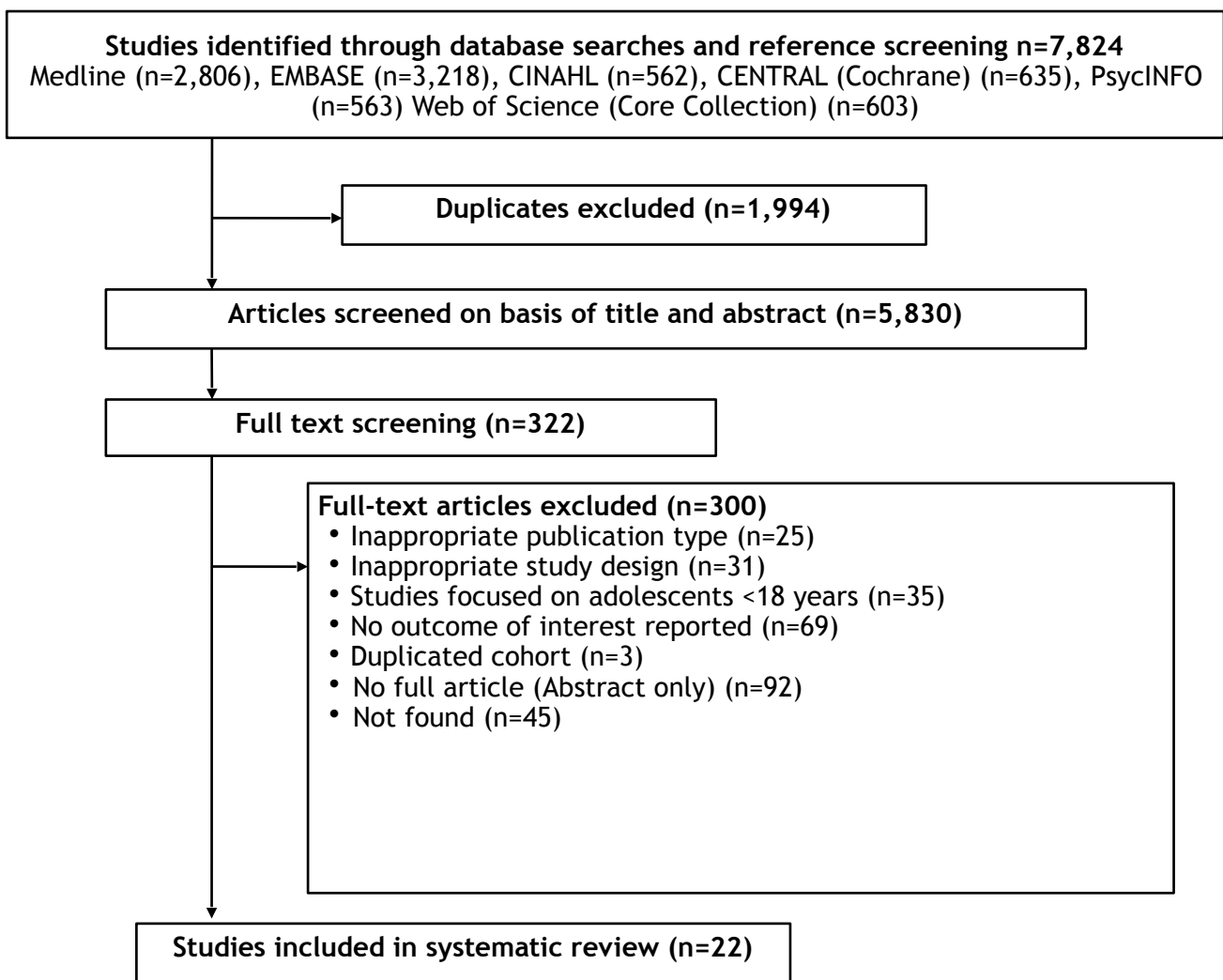


Figure 1 Flow chart of study identification and selection in the systematic review, including reasons for exclusion. A particular study could be excluded for more than one reason. n= number of studies

Using broad inclusion criteria for further screening of full text, 322 articles were identified. Publication type (e.g., conference abstracts, letters to the editor, commentaries), other definitions of effective contraception (including barrier and natural methods), and absence of outcomes of interest were the most frequent reasons for exclusion. Overall, we identified 22 studies as appropriate for further analysis.

3.2. Study characteristics

Among the twenty-two studies that met inclusion criteria, ten were RCTs, three were prospective cohort studies and nine before-after comparisons. Nineteen studies were based in the USA. Four studied focused on women using drugs, thirteen on women using alcohol, five on women using alcohol with other addictive substances.

Women's pregnancy status can influenced the choice of intervention and predict contraceptive outcomes independently of the intervention. We therefore separately analysed data from: non-pregnant women (fifteen studies); women seeking intentional pregnancy termination (one study); pregnant or postpartum women (six studies). The maximum duration of follow-up was 36 months.

The total number of participants pooled in the analysis was 4,989. Fifteen studies involved non-pregnant women (pooled sample size n=3,819), one study included women after induced pregnancy termination (sample size n=12) and six studies recruited pregnant and postpartum women (pooled sample size n=1158). Characteristics of studies included in the analysis are reported in **Table 1**.

Table 1 Key characteristics of studies included in the systematic review

First author, year, cohort origin	Study design	Inclusion criteria			Recruitment settings	Financial incentives provided	Race/ ethnic group, %				Follow-up		Index intervention sample size	Reference intervention sample size
		General conditions	Related to psychoactive substance use	Related to unintended pregnancy risk			White	African-American	Hispanic	Others	Duration, months	Method		
Ernst et al., 1999, Seattle, US ³⁴	RCT	Pregnant women with little connection with community service providers, and little or no prenatal care.	Heavy alcohol (≥ 5 SDs on 1 occasion) and/or illicit drug use	-	Community, hospitals	no	32 %	44 %	-	-	36	In-person	60	25
Ingersoll et al., 2005, Virginia, US ²³	RCT	Non-pregnant 18 - 24 years old; sexually active*	Risky alcohol use, defined as ≥ 5 standard drinks (SDs) per occasion at least once in the past 90 days or ≥ 8 SDs per week on average	Ineffective contraception use (none, incorrect use of an effective method, or exclusive use of an ineffective method)	College	NR	70 %	16 %	4 %	10 %	1	By mail	114	114
Floyd et al., 2007, Multiple cities across US ¹⁹	RCT	Non-pregnant 18 -44 years old; sexually active women	Risky alcohol use (i.e., average of ≥ 8 SDs per week) or binge drinking (i.e., ≥ 5 SDs on at least one occasion) or both	No or inappropriate contraception use	Hospitals, Community, Addiction treatment services, Family planning services, jails	yes	-	48 %	-	-	9	In-person, by phone	414	416

Ceperich et al., 2011, Virginia, US ¹⁷	RCT	Non-pregnant 18-44 years old; sexually active	Risky alcohol use (i.e., average of ≥ 7 SDs per week) or binge drinking (i.e., ≥ 5 SDs on at least one occasion) or both	Ineffective contraception use (defined as any or all of the following: (a) no use, (b) incorrect or inconsistent use of an effective method, or (c) exclusive use of an ineffective method).	Mid-Atlantic urban university	years										114	114	
							72%	15%	-	12%	4	Mail, email						
Ingersoll et al., 2013, Virginia, US ²⁴	RCT	Non-pregnant 18-44 years old; sexually active women	Alcohol use of ≥ 7 SDs on average per week and/or ≥ 3 SDs on at least one occasion in the preceding 90 days		Community	years										73	74	70
							38%	48%	1%	13%	6	In-person						
Rendall-Mkosi et al., 2013, Western Cape, South Africa ²⁶	RCT	Non-pregnant 18-44 years; sexually active	Risky alcohol use (defined by Alcohol Use Disorders Identification Test)	Ineffective or no contraceptive use (defined under Measures)	Hospitals, Community	years				98%						82	83	
							-	-	-	12		In-person						
Wilton et al., 2013, Wisconsin, US ³⁰	RCT	Non-pregnant 18-44 years; sexually active.	Alcohol use of ≥ 7 SDs per week on average and/or ≥ 3 SDs on at least one occasion in the preceding 90 days	No effective contraception in preceding 90 days; (c) not pregnant. Contraception effectiveness was ascertained by identifying all methods of birth control used in the preceding 90 days.	Community	NR										63	68	
							63%	20%	5%	12%	6	In-person, by phone						
Heil et al., 2016, Burlington, VT, US ³³	RCT	Non-pregnant 18-44 years old	Opioid maintenance treatment in the preceding 30 days.	No use of birth control pills, patch, ring, implants, or IUDs in the preceding 7 days or no depot injections in the preceding 3 months	Addiction treatment services	years										16	15	
							90%	NR	NR	NR	6	In-person						

Sobell et al., 2017, Florida, US ²⁷	RCT	Non-pregnant 18-44 years	Alcohol use of ≥ 8 SDs per week on average and/or binge drinking (≥ 5 SDs on 1 occasion)	Ineffective contraception (i.e., participants' self-reported deviations from published guidelines for different birth control methods)	Community	yes	50%	N	N	N	6	By mail	72	108	73	101
Velasquez et al., 2017, Harris County, Texas, US ²⁹	RCT	Non-pregnant 18-44 years old; sexually active	Risky alcohol use (≥ 3 SDs per day or ≥ 7 SDs per week, on average)	Vaginal intercourse without effective contraception in the preceding 3 months	Hospitals	yes	10%	42%	47%	1%	9	In-person, by phone	131			130
Grant et al., 2004, Washington, US ³⁵	Non-comparative	Women with diagnosed or suspected fetal alcohol damage	Alcohol drinking during the index pregnancy	-	Hospitals	no	63%	4%	-	-	12	In-person	19			no
Grant et al., 2005, 3 sites in Washington state, US ³⁶	Non-comparative	Pregnant or post-partum	Alcohol use ≥ 5 SDs per occasion once per month and/or use of any illicit substance ≥ 1 per week during pregnancy	-	Community, hospitals	no	30 / 38 / 56%	45 / 42 / 31%	-	-	36	In-person	60	76	80	
Ip et al., 2008, Hong Kong ³⁸	Non-comparative	Pregnant women who decided to terminate their pregnancy	Methadone clinic clients	-	Addiction center	no	N	R	N	N	N	N	In-person	12		
Elko and Jansson, 2011, Maryland, US ³⁹	Non-comparative	Women delivering an infant or having a pregnancy termination	Care at the Center for Addiction and Pregnancy	-	Center for Addiction and Pregnancy	N	R	55%	42%	-	2, 1%	-	-	671		-

15.	Rasmussen et al., 2012, Edmonton, Canada ³⁷	Non-comparative	Pregnant or up to 6 months postpartum	Self-reported heavy alcohol and/or illicit drug use during the index pregnancy	-	Community	yes				Aboriginal 49%, 4%	12-36	In-person	70	
	Wright et al., 2012, Hawaii, US ⁴⁰	Non-comparative	Post-partum women	Past or present history of drug addiction	NR	Hospitals, Addiction treatment centers	yes				Native Hawaiian 50%	NR	In-person	97	
	Farrell-Carnahan et al., 2013, Virginia, US ¹⁸	Non-comparative	Non-pregnant 18-44 years old; sexually active	Alcohol use ≥ 7 SDs per week on average and/or more than ≥ 3 SDs on at least one occasion in the preceding 90 days	No or unreliable contraception	Community	yes						Phone, mail	46	-
	Hanson et al., 2013, Northern Plains, US ²⁰	Non-comparative	Non-pregnant 18-44 years old; sexually active women	Alcohol use at any one time in the preceding 90 days	Unprotected sexual intercourse in the preceding 90 days	Community	NR				100% American Indians	12	by phone	162*	-
	Hanson et al., 2017, South Dakota, US ²¹	Non-comparative	Non-pregnant American Indians aged >18 years	Risk for alcohol exposed pregnancy, defined based on preexisting CHOICES studies	Unprotected sexual intercourse in the preceding 90 days	Hospitals, Community	yes				100% American Indians	6	In-person, by phone	193	
	Hutton et al., 2014, Denver and Baltimore, US ²²	Cohort prospective	Non-pregnant 18-44 years	Binge drinking (≥ 5 SDs on 1 occasion) or heavy alcohol use (≥ 4 SDs per day and/or ≥ 8 SDs per week)	Ineffective contraceptive use defined as failure to use condoms or a hormonal or intrauterine device as directed for every episode of vaginal sex	STI clinic	NR						In-person, by phone	221	205
							NR								

Letourneau et al., 2017 Florida, US ²⁵	Cohort prospective	Non-pregnant 18-44 years old; heterosexual vaginal intercourse	Risky alcohol use (i.e., an average of ≥ 8 SDs per week) or binge drinking (i.e., ≥ 5 SDs on at least one occasion) or both	No or ineffective contraceptive methods	Community	yes	-	-	100%	-	6	By mail	67	22
Tenkku et al., 2011 (27), St Louis, USA ²⁸	Cohort prospective	Non-pregnant 18-44 years; reported one or more male sexual partners in the preceding 4 months,	Any alcohol use in the past 30 days	No birth control or ineffective birth control methods, including (a) rhythm; (b) male withdrawal; (c) birth control pill or emergency contraception, if two or more pills were missed in the preceding 4 months; (d) irregular condom or diaphragm; and (e) spermicidal foam or jelly without associating a condom.	Community	yes	66%	17%	3%	14%	4	Internet, mail	84	374

*Sexually active women was defined as having at least one instance of sexual intercourse with a man in the last 90 days

3.3. Risk of bias assessment

According to our assessment, only three studies were characterized by a low risk of bias, outcomes reported from eight studies were characterized by a high risk of bias and for eleven studies the risk of bias was unclear. The most common problems were: sample size too small to detect outcomes of interest (n=5), non-blinding of participants, intervention providers and assessors (n=22), follow-up period of less than 6 months (n=6), loss to follow-up of more than 30% of participants (n=5), or self-reported psychoactive substance use and study outcomes (n=22).

3.4. Intervention outcomes

For an overall description of the interventions reviewed, please see **Table 2**.

Table 2 Characteristics of interventions, risk of bias assessment and outcomes measured

Author, years	Index intervention	Reference intervention/Comparator	Characteristics of the contraceptive component of interventions				Risk of bias assessment	Outcome measured	Results, event/total number of participant in intervention group (ITT)		Effect size	P value		
			Contraceptive counselling	Motivational information for contraceptive use	Mode of delivery	Contraception supply								
Intervention based on behavioral change theories														
Ingersoll et al., 2005 ²³	BALANCE	Information only	No, but referral provided	Yes, integrated in one session	In-person	NR	Unclear	Initiation of contraception	58/114	50/114	0.154	0.289		
Ceperich et al., 2011 ¹⁷	BALANCE	Information only	No, but referral provided	Yes, integrated in one session	In-person	NR	Unclear	Effective contraception use over 4 months	68/114	59/114	0.176	0.230		
Floyd et al., 2007 ¹⁹	CHOICES	Information only	Yes	Yes, stand-alone session	In-person	Yes	Unclear	Reliable contraception over 3 months	2.12 (1.54, 2.92) unadj 1.69 (1.22, 2.32) adj		0.363	0.000		
								Reliable contraception over 6 months	1.84 (1.33, 2.54) unadj 1.55 (1.12, 2.14) adj				0.274	0.001
								Reliable contraception over 9 months	2.10 (1.52, 2.91) unadj 1.46 (1.06, 2.01) adj					
Rendall-Mkosi et al., 2013 ²⁶	CHOICES	Information only	No, but referral provided	Yes, integrated to 5 sessions	In-person	NR	Low	Ineffective contraception at 3 months	63/82	76/83	0.650	0.012		
								Ineffective contraception at 12 months	56/82	67/83			0.364	0.069
Hutton et al., 2013 ²²	CHOICES with onsite contraceptive counselling	CHOICES with contraceptive counselling as add-on service	yes	Yes, integrated to 4 sessions	2 in-person and 2 by phone	yes	High	Reliable contraception over 3 months	41/221	23/205	0.324	0.036		
								Reliable contraception over 6 months	36/221	14/205			0.537	0.003
Hanson et al., 2013 ²⁰	OST CHOICES	-	No, but referral provided	Yes, workbook based on motivational interviewing	By mail	NR	High	No contraception use over 3 months	16/49		0.327	0.017		

Wilton et al., 2013 ³⁰	Healthy CHOICES phone-based	Healthy CHOICES in-person	NR	Yes, integrated to 4 sessions	By phone or in-person	NR	Unclear	Risk of pregnancy over 6 months	42/68	32/63	-0.453	0.101
Letourneau et al., 2017 ²⁵	Healthy CHOICES English language materials	Healthy CHOICES Spanish language materials	No, but referral provided	Yes, motivational materials containing embedded messages about birth control	By mail	NR	Unclear	Reliable contraception over 6 months	38/67	8/22	0.453	0.101
Velasquez et al., 2017 ²⁹	CHOICES plus	Brief Advises informational and referral brochure	yes	Yes, integrated in 2 sessions	In-person	yes	Low	Pregnancy over 3 months	83/128	99/128	0.338	0.024
								Pregnancy in 6 months	73/128	100/128	0.544	0.000
								Pregnancy over 9 months	67/128	94/128	0.507	0.000
Hanson et al., 2017 ²¹	OST CHOICES	-	No, but referral provided	Yes, integrated to 4 sessions	In-person	NR	High	Unintended pregnancy	16/193		0.083	0.000
								Reliable contraception over 3 months	69/193		0.327	0.017
								Reliable contraception over 6 months	40/193		0.207	0.000
Sobell et al., 2017 ²⁷	Healthy CHOICES	Information only	No, but list of local birth control services was provided	Yes, motivational feedback materials including messages about contraception. Brochure on birth control practices.	By mail	NR	Unclear	Reliable contraception over 6 months	49/72 41/108	38/73 42/101	0.684 0.231	0.000 0.172
Ingersoll et al., 2013 ²⁴	EARLY	Informational video or informational brochure	No, but referral provided	Yes, integrated in one session	In-person	NR	Low	Ineffective contraception over 3 months	60/73	62/74 55/70	0.203	0.380

								Ineffective contraception over 6 months	49/73	67/74 46/70	0.490	0.017
Farrell-Carnahan et al., 2013 ¹⁸	EARLY remote	-	No, but referral provided	Yes, integrated in one session	Phone-based	NR	High	Reliable contraception over 3 months	7/46		0.152	0.000
								Reliable contraception over 6 months	8/46		0.173	0.000
Tenkku et al., 2011 ²⁸	Web-based motivational intervention	Mail-based motivational intervention	NR	Yes, integrated in the first module	Web-based or mail-based	NR	High	Reliable contraception over 4 months	154/374	43/84	-0.222	0.095
Heil et al., 2016 ³³	Intervention using behavioral economic theory	Informational booklet about birth control methods and list of nearby providers of contraceptive services.	Yes	Yes	In-person			Unintended pregnancy	0/16	3/15	-1.196	0.153
								Initiation of contraception use	16/16	4/15	2.385	0.004
								Reliable contraception over 1 month	10/16	2/15	1.279	0.009
								Reliable contraception over 3 months	14/16	3/15	1.789	0.000
								Reliable contraception over 6 months	15/16	2/15	2.459	0.000
								LARCs over 1 month	3/16	0/15	0.217	0.683
								LARCs over 3 months	7/16	1/15	1.282	0.038
								LARCs over 6 months	9/16	1/15	1.551	0.012
<i>Interventions based on psychosocial support</i>												
Ip et al., 2008 ³⁸	Early Intervention programme	-	Yes	Immediately	Social worker	Yes	Unclear	Initiation of LARCs	12/12		0.962	0.048
Rasmussen et al., 2012 ³⁷	Parent-Child Assistance	-	No, but access to community	NR	Peer	NR	High	Unintended pregnancy	21/68		0.308	0.002

	Program		ity family planning service provided					Induced pregnancy termination	4/21		0.059	0.000
								Tubal ligation	14/68		0.206	0.000
								Regular use of family planning method over 12 months	38/68		0.599	0.333
Ernst et al., 1999 ³⁴	Parent-Child Assistance Program	No intervention	No, but access to community family planning service provided	NR	Peer	NR	Unclear	Regular contraception use over 36 months	44/60	13/25	0.508	0.060
								LARCs	26/60	8/25	0.265	0.333
Grant et al., 2004 ³⁵	Parent-Child Assistance Program	-	No, but access to community family planning service provided	NR	Peer	NR	Unclear	Unintended pregnancy	1/19		0.053	0.005
Grant et al., 2005 ³⁶	Parent-Child Assistance Program	-	No, but access to community family planning service provided	NR	Peer	NR	Unclear	Regular contraception use over 36 months	57/80 56/76		0.737 0.712	0.000 0.000
								LARCs	42/80 37/76		0.487 0.525	0.819 0.655
								Reliable contraception over 12 months	14/19		0.737	0.048
								LARCs	12/19		0.632	0.257
Integrative interventions												
Elko and Jansson, 2011 ³⁹	The Family Planning Initiative Services	-	Yes	Immediately or in 6-8 weeks	Healthcare provider	Yes	High	Initiation of contraception use	576/671		0.858	0.000
								Initiation of LARCs	214/671		0.319	0.000
Wright et al., 2012 ⁴⁰	Perinatal addictions	-	Probably yes	Immediately or in late postpartum	Healthcare provider	Yes	High	Initiation of LARCs	28/97		0.289	0.000

	on clinic			postpart um	provid er			Sterilisa tion	14/97	0.144	0. 00 0
								Repeate d pregnan cy	13/97	0.134	0. 00 0

The most frequent study outcome was the initiation of contraception. It was reported in two different ways: initiation of effective contraception (i.e. following the CDC classification,⁴¹ which distinguishes a) tier 2 contraceptive methods including hormonal injection, the pill, patch, vaginal ring and diaphragm; b) tier 3 methods including a intrauterine device and implant - so called LARCs; c) irreversible methods) or initiation of effective use (that is use of a contraceptive method chosen by the person following national or international guidelines). Despite these differences, we considered both outcomes as valid measures of initiation of contraception. Adherence to the contraceptive method of choice during the follow-up period was assessed by all 22 interventions. Results regarding initiation and continuation of LARCs were presented in five publications. Only three studies addressed the rate of unintended pregnancy, rapid repeated pregnancy (occurring less than 24 months after the index birth) or pregnancy termination.

To report outcomes of interest, we grouped interventions according to the pregnancy status of targeted populations (women who were not recently pregnant and did not intend to get pregnant, abortion seekers, pregnant and postpartum women).

3.4.1. Interventions focused on women who did not desire to get pregnant (excluding postpartum and post-abortion periods)

Among the 15 studies that tested interventions in non-pregnant women using substances who did not desire to get pregnant, eight examined the effectiveness of motivational approaches vs. standard written information on contraceptive methods recommended by the CDC or WHO.^{41,42} Only one study reported a consistent and significant effect of financial incentives on LARC use during a 6-month follow-up ($g=1.282-2.385$, $p<0.05$), but the effect on unintended pregnancy rate was comparable to usual practice ($g=-1.196$, $p=0.153$).³³ Three motivational interventions had a moderate but significant effect on adherence to regular contraceptive use at 3-month follow-up.^{19,26,29} The effect of motivational interventions on contraceptive use was quite stable and moderate (g ranged between 0.274 and 0.684, $p<0.05$) at 6 and 9 months post-intervention.^{19,24,29} Only one study reported contraceptive coverage at a 12-month follow-up, with no sustained effect of the intervention.²⁶ The methods used to deliver motivational materials to women had different effects on contraceptive use; in-person interviewing seemed to be most reliable ($p<0.05$).^{25,28,30} However, non-comparative studies that explored alternative methods of delivering motivational interventions, for instance via the Internet or mail,¹⁸ with cultural adaptations for women belonging to different ethnic groups found some positive changes in contraceptive use at three and six months post-intervention.^{20,21}

3.4.2. Interventions focused on women seeking abortion

A one arm study from Hong Kong observed a very strong effect of collaboration between a methadone clinic and a public hospital with regard to LARC selection.³⁸ It showed that eleven out of twelve women included in the protocol chose LARCs immediately after undergoing pregnancy termination.

3. Interventions focused on pregnant and postpartum women

Four out of six studies evaluated interventions based on peer case management models.³⁴⁻³⁷ In a study conducted by Ernst et al, the effect size of the intervention on women's contraceptive use was not statistically significant after three years of observation compared with usual care ($g=0.265$, $p=0.333$).³⁴ Other one-arm studies that examined the same intervention reported a decrease in the risk of unintended pregnancy^{35,37} and induced pregnancy termination at a 12-month follow-up.³⁷ In general, all studies reported a positive tendency in terms of contraceptive use.

Two integrative interventions found that this approach was highly effective to encourage LARCs use in postpartum women with substance use problems.^{39,40} Wright *et al.* showed a significant reduction in the risk of rapid repeated pregnancy.⁴⁰

4. DISCUSSION

4.1. Main findings

To the best of our knowledge, this systematic review is the first to examine the efficacy of interventions aiming to address the risk of unintended pregnancy among female substance users. Among 22 examined articles more than half had unclear or high risk of bias for outcomes related to unintended pregnancy prevention that particularly may be explained by the privileged focus of analyzed interventions on the reduction in alcohol and substance use.

Several limitations to our study should be noted. First, our systematic review mostly identified interventions conducted in the US, where universal contraceptive coverage was only introduced in 2012 and is currently offered by approximately 90% of health insurance companies.^{43,44} Because of the specificity of the American context, the generalizability of interventions to promote family planning among women with substance use problems in other countries with different cultural, social and healthcare contexts is needed. Second, we found no interventions focused on access to emergency contraception, indicating the need to evaluate its use among substance users. Third, the growing population of women who use and abuse prescription drugs were not included in the family planning interventions which we examined.

4.2. Interpretation of findings

4.2.1. Interventions focused on women who did not desire to get pregnant (excluding postpartum and post-abortion periods)

The group of general population women with occasional substance use included subjects with addictive behaviors who never sought medical attention for their substance use. Participants were recruited from the community,^{26-28,30} sometimes over-representing certain ethnic or social groups in which psychoactive substance consumption is high (ex. in the United States African American or Native American women),^{20,21,25} youths,^{17,23} or women seeing services to reduce risks associated with risky sexual behaviors.²² In general, women who fell in this category were young (below age 30) and had occasional episodes of addictive drug use or heavy drinking. Indeed, in

the United States approximately 13% of female college students are regularly involved in heavy level alcohol drinking and do not use effective contraception.⁴⁵ The numerous motivational interventions centered on users with substance use disorders or heavy episodic drinkers were based on the CHOICES intervention developed by the CDC.¹⁹ These CHOICES-like interventions (EARLY; BALANCE; Healthy CHOICES; CHOICES plus) implemented a varying number of motivational sessions, integrated discussions regarding contraception to other existing interventions, and replaced on-site contraception counseling with referral to local family planning centers. Despite promising results with regard to the initiation of contraception, these studies were often characterized by a high or unclear risk of bias. These studies faced several challenges: a) difficulties with participant recruitment, which could introduce volunteer bias and result in limited generalizability of the results; b) phone or Internet-based brief screening of substance use and current contraceptive practices, which may be imprecise; c) systematic use of financial incentives to recruit and follow-up participants that may enhance contraceptive use shortly after intervention but is not sustainable over the long term; d) significant attrition which can induce bias;²⁸ e) open-label randomization; f) short follow-up making it impossible to assess extended adherence to the contraceptive of choice. Nevertheless, the positive effect of motivational messages on the initiation of contraception intake was consistent across all studies.

The second category of women consisted of participants identified as women who are clients of addiction treatment centers. This population was more vulnerable and often experienced socio-economic difficulties, psychiatric co-morbidities, used several different kinds of substances, provided sexual services in exchange for money or drugs, had experienced incarceration, and had lost custody of their children.¹⁹ Participants were recruited in addiction treatment centers and hospitals, or upon referral from a general practitioner. We found that motivational interviewing and financial incentives both seemed effective to prevent unintended pregnancy in this group. A study conducted by Heil *et al.* found that financial incentives had the most pronounced effect on unintended pregnancy prevention, compared with dissemination of written information.³³ However, participants were not randomly assigned to the intervention group and the sample size was relatively small (n=31). In recent decades, there have been many debates regarding the ethics of providing financial incentives to women with addiction problems to start LARCs or accept sterilization.⁴⁶ It is worth noting that the intervention conducted by Heil *et al.* preserved the reproductive autonomy of women using substances and should not be confused with interventions exchanging money for contraception.³³ Free contraceptive choice is one of the fundamental reproductive rights of all women that must be respected by family planning programs, especially among vulnerable and underserved women.⁴⁷ Another important element is onsite contraceptive counseling with free provision of contraceptives included in the intervention.^{19,33} In fact, studies that proposed individual counseling showed a significant increase in reliable contraceptive use compared to studies that provided referral to the local family planning centers. The survey conducted by Poulton *et al.* showed that the cost of contraception was identified by women using drugs as one of the main barriers to use.⁴⁸ Thus, it is not clear which component of the intervention (motivational interviewing or free access to

contraceptive methods) is more important. Furthermore, interventions that focused on unintended pregnancy prevention may only be effective when coupled with a reduction of substance use in parallel.⁴⁹

Besides financial barriers, the literature review conducted by Black and Day described other obstacles to regular contraceptive use that should be addressed by interventions, such as multiple referrals, stigma, and concerns about the loss of child custody.⁷ Edelman demonstrated that the initiation and adherence to contraception in substance users is mediated by beliefs, prior experiences and attitudes regarding sexuality and pregnancy risk.⁸

4.2.2. Interventions focused on women seeking abortion or in the postpartum period

Case management appears as another innovative approach extensively implemented in pregnant and postpartum women using psychoactive substances. Being accompanied by a social worker or a peer to the public hospital or family planning center is reassuring and promotes adequate contraceptive care for women with addiction problems. According to Grant *et al.*, home visiting programs for pregnant and postpartum women aiming to prevent alcohol-exposed pregnancies brought, over the course of three years, more than 6.000\$ benefits per case.³⁶ Case managers in this study were trained peers who provided a connection with the local family planning services.³⁴⁻³⁶ Nearly 50% of the cohort in this study chose a reliable contraceptive method; yet about 50% of women became pregnant again and 30% subsequently gave birth. A first look at participants' contraceptive use revealed a non-significant effect size; however, this negative result should not undermine the potential benefits of case management. It is worth noting that this intervention mainly targeted underserved women with a high level of addiction,^{34,36,37} and those who gave birth to babies with fetal alcohol syndrome.³⁵ More recent studies found that only 18.1% of postpartum women with substance use problems use effective contraception and only 7.4% use LARCs.⁵⁰ Another case management intervention focusing on contraception post-pregnancy termination showed that women under methadone treatment who decided to interrupt a pregnancy gave preference to LARCs (event rate 0.926; $p < 0.05$).³⁸ Methadone treatment normalizes ovulation, increasing the chance of getting pregnant.⁵¹ Performing a pregnancy test at each visit to the addiction center allowed women to be aware of their pregnancy status early on. The collaboration between methadone clinics and public hospital services was mediated by social workers and showed promising results, but the non-comparative design of this study; the small sample size and the absence of follow-up limit our ability to draw a reliable conclusion.

Two studies assessed the integration of family planning services with centers for mothers with addictive behavior and their children.^{39,40} Two single-arm studies provided on-site contraceptive counseling and free birth control including LARCs for women who had recently given birth. The results were similar for both interventions. Although nearly 30% of participants chose LARCs in the postnatal period, the rate of rapid repeated pregnancy during 6-month follow-up remained quite high (17%). Loree *et al.* found that approximately 70% of women who use substances initiate the use of contraceptive methods in the postpartum period, which is comparable with the general population.⁵² Immediate postpartum LARCs initiation may be a suited response for

women using psychoactive substances. A postnatal survey of opiate users held by Sinha *et al.* showed that the continuation rate for implants over an 11-month follow-up is 95%.⁵³ The authors suggest that implants may be the best-suited contraception for women who exchange sex for drugs. Another survey among pregnant or recently pregnant opioid users showed that hormonal injections and IUDs were the methods of choice if they were available free of charge.⁵⁴ According to the ACOG, 10-40% of women in the general population do not visit their healthcare practitioner for a postnatal consultation focusing on contraceptive counseling.⁵⁵ Thus, access to LARCs in the immediate postpartum could reduce the number of rapid repeated pregnancies. Female substance users who chose LARCs in the postpartum period had a significantly lower hazard of rapid repeated pregnancy compared to those who received other effective methods or no contraception.⁵⁰ In addition, some studies found that both the staff and clients of addiction treatment centers preferred integrated services.^{49,56,57}

4.3. Future directions

The interventions which we evaluated neither involved male partners nor addressed the role of partner violence with regard to women's ability to access birth control, or their choice of a contraceptive method.⁹ Another potential avenue to prevent unintended pregnancy is to train healthcare practitioners and social workers in ways to provide contraceptive counseling to women using psychoactive substances in a non-judgmental manner.⁴³ In fact, discussions about pregnancy intention should occur not only in the context of reproductive health services but in other social or clinical encounters with women using psychoactive substances. The screening for the pregnancy should become a routine practice for all healthcare practitioners who have patients with addictive behavior, thus the tool for this screening (i.e. the One Key Question®) should be validated in populations with different cultural background.⁵⁸

5. CONCLUSION

In this review, we evaluated the efficacy of interventions with a primary or secondary focus on unintended pregnancy prevention in women using psychoactive substances. We found that population of women who uses substances are very diverse, which imply that interventions helping them access effective contraception vary widely. No single type of intervention appeared especially efficacious, however depending on women's prior reproductive characteristics, motivational, peer-support or integrative approaches may be effective.

It is noteworthy that most of interventions were characterized by methodological concerns, calling for additional rigorous research in this area.

CONTRIBUTORS

Authors AY, VM, FEKL and MM designed study and wrote protocol. AY and VM selected relevant articles and extracted the data. Authors AY, VM, EA, VCD, FEKL, MT, MJR , MM wrote the first draft of the manuscript and all authors contributed to and have approved the final manuscript.

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CONFLICT OF INTEREST

None

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Supplementary materials_S1 Modified Newcastle-Ottawa scale

Selection (Maximum 4 stars)			Comparability (Maximum 2 stars)	Outcome (Maximum 4 stars)		
Representativeness of the exposed cohort	Sample size	Ascertainment of exposure	Confounding factors are controlled	Assessment of outcome	Was follow-up long enough for outcome to occur	Adequacy of follow up of cohorts
*a- truly representative of the psychoactive substance users in the community (all subjects or random sampling)	*a-Justified and satisfactory	**a-contraceptive counseling with contraceptive prescription is a part of intervention	*a-The study controls for the most important factor (select one).	**a-assessment by healthcare practitioner	*a-yes	*a-complete follow-up - all subjects accounted for
*b-somewhat representative of the psychoactive substance users in the community (non-random sampling)	b-Not justified	*b-referral letter to FP service	*b- The study control for any additional factor.	**b-record linkage	b- no	*b-subjects lost to follow-up unlikely to introduce bias (small number <15% or description of lost to follow up provided)
c-selected group of users		c-No description or other options	c-No description of confounding control	*c-self report		c-follow-up rate <30% and no description of the lost

d-no description of the derivation of the cohort				d-no description		d-no statement
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Supplementary materials_S2 Search strategy

((("women"[MeSH Terms] OR "women"[All Fields]) AND ("middle aged"[MeSH Terms] OR "adult"[MeSH Terms])) AND ("drug users"[MeSH Terms] OR "drug users"[MeSH Terms] OR "drug users"[All Fields] OR "drug abusers"[All Fields] OR "drug misusers"[All Fields] OR "substance-related disorders"[MeSH Terms] OR "substance use"[All Fields] OR "analgesics, opioid"[MeSH Terms] OR "opioid"[All Fields] OR "ethanol"[MeSH Terms] OR "ethanol"[All Fields] OR "alcohol"[All Fields] OR "alcohols"[MeSH Terms] OR "alcohols"[All Fields] OR "cocaine"[MeSH Terms] OR "cannabis"[MeSH Terms] OR "cannabis"[All Fields] OR "marihuana"[All Fields] OR "cannabis"[MeSH Terms] OR "cannabis"[All Fields] OR "opioid-related disorders"[MeSH Terms] OR "methadone"[MeSH Terms] OR "methadone"[MeSH Terms] OR "methadone"[All Fields]) OR "mental disorders"[MeSH Terms] OR "risk-taking"[MeSH Terms]) AND (("contraceptive agents"[MeSH Terms] OR "contraception"[MeSH Terms] OR "contraception"[All Fields] OR "contraceptives"[All Fields]) AND ("education"[Subheading] OR "education"[All Fields] OR "counseling"[All Fields] OR "counseling"[MeSH Terms] OR "counseling"[All Fields] OR "counseling"[MeSH Terms] OR program[All Fields] OR service[All Fields] OR "motivation"[MeSH Terms] OR "motivation"[All Fields] OR "incentive"[All Fields] OR "interviews as topic"[MeSH Terms] OR "interview"[All Fields]))))