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Association of Intrauterine System Use With Depression: Adolescent Risk Revisited

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Abstract

Background

Concerns that the levonorgestrel-releasing intrauterine system increases the risk of depression in adolescent users derive largely from registry data collected when use in young, nulliparous women was not recommended. This raises the possibility of confounding by special indication. We assessed whether current use of the intrauterine system was associated with depressive symptoms in a contemporary sample and whether associations differed by age.

Methods

We conducted a preregistered cross-sectional survey of women aged 14–55 years, comparing associations between younger and older individuals. Participants reported contraceptive use, previous health issues, and executive functioning, and they completed the Patient Health Questionnaire-9. Intrauterine system users were compared with non-users, users of combined oral contraceptives containing levonorgestrel, and users of other hormonal contraceptives. Associations and age moderation (≤ 21 vs >21 years) were examined using hierarchical multiple linear regression. Equivalence between intrauterine system users and non-users was tested with two one-sided tests and prespecified bounds of ±1 point on the Patient Health Questionnaire-9.

Results

Of the 1590 participants included, 523 used an intrauterine system and 514 used no hormonal contraception. Mean Patient Health Questionnaire-9 scores were 6.9 in both intrauterine system users and non-users (mean difference 0.04 points, 95% CI −0.77–0.85), and the 90% CI fell entirely within the prespecified equivalence bounds. There was no evidence of age moderation. Furthermore, intrauterine system users did not differ significantly from users of combined oral contraceptives containing levonorgestrel, whereas other hormonal contraceptive users had higher symptom scores than non-users and intrauterine system users. Sensitivity analyses showed no group differences in antidepressant use or self-reported depression diagnosis.

Conclusions

Our findings challenge the previously reported pattern of greater depression risk in younger intrauterine system users and suggest that historical prescribing patterns may have contributed to earlier associations. Taken together, these results support the intrauterine system as an appropriate option for adolescents and may help inform contraceptive counselling.

Background

The levonorgestrel-releasing intrauterine system (LNG-IUS) has become one of the most popular hormonal contraceptives (HCs) worldwide, and it is increasingly used also by adolescents and young women [1–4]. While effectively preventing pregnancy and providing non-contraceptive benefits such as reduced menstrual bleeding and pain, attenuated symptoms of endometriosis, and decreased risk of ovarian and endometrial cancers [5–8], concerns have been raised that it increases the risk of depression, particularly in adolescent users. These concerns stem from studies that combined data from prescription and psychiatric registries and reported associations between contraceptive prescription history and later adverse mental health outcomes. Central to this discussion is the nationwide Danish study by Skovlund et al. [9] that assessed a range of HCs and found a higher incidence of depression among individuals previously prescribed HCs, across most products examined. One of the highest risk estimates was reported for the LNG-IUS. This comparatively high estimate, however, emerged only when the analysis was restricted to adolescent women. The authors described these associations as reflecting “increased risk” and referred to depression as a “potential adverse effect”, thereby framing the findings in causal terms. This framing is consequential, as the study has become one of the most highly cited investigations of HCs and depression, and it has been cited as representing a “shift” in the research on HCs and mental health [10]. Registry-based studies, however, are vulnerable to confounding by unknown or unmeasured variables, such as the clinical indications underlying a prescription. If these indications reflect conditions or characteristics independently associated with mental health problems, subsequent depressive symptoms may be misattributed to HC use. This potential source of confounding is of particular concern for the adolescent LNG-IUS findings reported by Skovlund et al. [9], as the study used data collected from 1995 to 2013, a period when adolescent use of this method was not supported by medical recommendations.

While approved for contraceptive use in 1990, for the next two decades the 52-mg LNG-IUS was recommended only for adult women who had given birth to at least one child [11] (Danish Medicines Agency, written personal communication, December 2024; Norwegian Medical Products Agency, written personal communication, January 2025). These recommendations were rooted in concerns about infertility, pelvic infections, and insertion pain in younger users [12]. It was not until 2013 and 2016, respectively, that 13.5 and 19.5 mg-LNG-IUSs were approved and specifically marketed towards young, nulliparous women [13–16], followed by a steep rise in adolescent use [2–4]. All three doses can now be used by adolescents [2, 17], and current LNG-IUS users therefore likely represent a broader and more typical adolescent population than those appearing in early registry studies, when prescribing outside medical guidelines may have occurred only under particular clinical circumstances. Support for this possibility comes from a subsequent study by Skovlund et al. [18], using the same Danish registry sources to examine associations between HCs and suicide. In this study, the authors explicitly identified confounding by indication as likely for long-acting reversible contraceptives, including the LNG-IUS, reasoning that these methods were preferentially prescribed to institutionalized women, or women with intellectual disability or severe psychiatric problems. Risk estimates for these products were therefore omitted from the main product-specific figure. Although the authors did not raise this issue regarding the

LNG-IUS in the earlier depression study [9], or consider whether adolescents might have been disproportionately affected by such prescribing practices, we consider it plausible that the adolescent depression findings were influenced by a similar selection bias.

A related concern applies to a more recent registry study by Skovlund and colleagues, focusing on depression exclusively related to LNG-IUS use [19]. It compared the three available doses and reported lower risk with the two lower-dose systems than with the high-dose LNG-IUS. Although dose may play a role, historical confounding could have influenced these findings as well, as the high-dose group included women from 2001 onwards, again overlapping with a period when adolescent LNG-IUS use was generally not recommended. By contrast, the low-dose groups were drawn from 2014 and 2017 onwards, respectively, when adolescent LNG-IUS use was becoming more common. Moreover, if dose is related to risk, the substantially lower systemic hormonal exposure resulting from the LNG-IUS's predominantly local mechanism of action warrants attention. In contrast to hormones in combined oral contraceptives (COCs), which are absorbed from the gastrointestinal tract into the systemic circulation and act primarily through centrally mediated suppression of ovulation, the LNG-IUS delivers levonorgestrel directly to the uterus. Here it acts mainly locally, thickening cervical mucus and exerting antiproliferative effects on the endometrium [20]. Although some levonorgestrel enters the systemic circulation and may reach the brain and affect mental health, plasma levonorgestrel concentrations at one year with the highest-dose LNG-IUS are estimated to be 38–46-fold lower than mean peak concentrations and 18–22-fold lower than average steady-state concentrations observed with different levonorgestrel-containing COCs [21–23]. Compared to levonorgestrel-only pills, concentrations observed with LNG-IUSs are approximately fivefold lower than peak concentrations and 1.2–2.4-fold lower than average concentrations [24]. From a systemic exposure perspective, the higher risk estimates for the LNG-IUS than for levonorgestrel-containing COCs reported by Skovlund et al. [9] thus appear counterintuitive. This adds weight to the possibility that these findings stem from historically rooted confounding rather than representing a causal effect. Consistent with this interpretation, subsequent Swedish registry studies using data from 2010–2017 [25, 26] found a weaker association between the IUS and depression among adolescents than that reported by Skovlund et al. [9], potentially reflecting changes in adolescent HC practices. Stenhammar et al. also noted that the risk declined towards the end of the study period, as adolescent LNG-IUS use became more common, and both studies suggested that residual confounding from factors influencing both subsequent depressive outcomes and IUS prescription or choice could inflate the risk estimate [25, 26].

Given these concerns, associations between LNG-IUS use and depressive symptoms in adolescents warrant revisiting using contemporary data. We thus investigated these associations comparing current LNG-IUS users with users of levonorgestrel-containing COCs, users of other HCs, and non-users. Although prescribing guidelines have changed, and LNG-IUS use is widespread across diverse adolescent backgrounds, real-world prescribing patterns may still influence the user population. We therefore initially conducted an exploratory study of factors potentially affecting adolescent contraceptive prescribing and choice, to identify possible residual confounders [27]. Findings were used to inform the present study. As previous registry studies suggested that associations between LNG-IUS

use and depression are particularly pronounced in adolescent users, we included participants across reproductive ages to test whether symptoms differ between younger and older users, with older participants serving as a developmental comparison group. Furthermore, as registry data cannot establish actual or ongoing LNG-IUS use, only that the LNG-IUS was prescribed/redeemed, we sampled confirmed current users. Our main, preregistered research question [28] was whether LNG-IUS use is differently associated with depressed mood than no HC use or use of an oral contraceptive containing levonorgestrel and ethinyl estradiol [28]. We further asked whether LNG-IUS use differs from other HCs, including other pills, implants, patches, or injections, in its association with depressive symptoms, and whether any differences are moderated by age. Our preregistered hypotheses [28] were that IUS use would not be associated with depressed mood (H1), that COC use would be associated with depressed mood (H2), and that any effects would be less pronounced in older subjects (H3) [28].

Methods

Study design

We conducted a cross-sectional study using the online questionnaire platform “Nettskjema” [29], following the STROBE reporting guidelines (see supplementary materials). We assessed background variables including age, years of education (parental education for school-aged participants), previous mental and physical health diagnoses, use of medication, the Plan/Organize scale of the Behavior Rating Inventory of Executive Function (BRIEF) [30], along with current HC use and product choice (see supplementary materials). Depressive symptoms were measured with the Patient Health Questionnaire-9 (PHQ-9), a short, validated, and widely used self-report tool. PHQ-9 scores of 5–9 indicate mild depressive symptoms, 10–14 moderate, 15–19 moderately severe, and 20–27 severe symptoms [31]. All questions were mandatory, resulting in no missing data.

Recruitment, data collection and setting

To recruit women aged 13–55 from varied backgrounds, including users of any HC available in Norway, and non-users, we chose multichannel purposive convenience and snowball sampling with no specific exclusion criteria. We distributed QR-coded information cards at universities, high schools, and regional adolescent health centers, and we shared survey links publicly on Facebook, in national and regional Facebook groups for women, and on Snapchat. The different recruitment channels were selected to ensure we reached participants across a broad age range and users of different contraceptive methods. Data were collected from May 6 to July 25, 2025. We performed an a priori power analysis for the preregistered main regression analysis, based on a full model having 17 predictor variables of which three were the tested variables. In order to reach 95% power with an alpha of 0.05 and a small effect-size of $f^2 = 0.2$ [32], we needed a minimum of 95 subjects with balanced groups. However, data collection was continued after reaching this number, to enable sensitivity analyses.

The study was conducted in accordance with the Declaration of Helsinki and assessed by the Western branch of the Norwegian Regional Ethics Committees and deemed to be in accordance with national guidelines for health research (reference #806938, December 11, 2024).

Statistical analysis

Depressive symptoms were operationalized as total PHQ-9 score and analysed as a continuous outcome. HC exposure was coded as a four-level categorical variable: no HC, LNG-IUS, levonorgestrel/ethinyl estradiol-containing combined oral contraceptives (LNG/EE-COC), and other HCs, including other oral products, vaginal rings, patches, injections, and implants. Age was analysed as a binary moderator (≤ 21 versus > 21 years). This cutoff was chosen to distinguish younger women still undergoing development from those considered to have reached adult brain maturity [33], to test the age-dependent association suggested by previous registry studies.

Following the preregistered analysis plan, we fitted three models in a hierarchical multiple linear regression analysis with total PHQ-9 score as outcome. In the first model we entered dummy variables representing LNG-IUS, LNG/EE-COC, and other HC use. In the second model we added the binary variable age ≤ 21 years, and the interaction terms with the HC groups. In the third model, we further added self-reported diagnoses (severe anxiety disorder, schizophrenia or other psychotic disorder, attention-deficit hyperactivity disorder, eating disorder, autism spectrum disorder, bipolar disorder and obsessive-compulsive disorder), use of antipsychotic or anxiolytic drugs, and BRIEF. These adjustment variables were prespecified rather than selected according to observed between-group differences. We report standardized coefficients, $R^{2,}$ changes, and p-values for model changes individual coefficients.

Because the main hypothesis concerned no difference in depressive symptoms between LNG-IUS users and non-users, we conducted a secondary equivalence analysis using two one-sided tests (TOST). Equivalence bounds were set at −1 to + 1 PHQ-9 points, representing the largest difference considered clinically irrelevant for this analysis, also being a more conservative threshold than the 1.9–2.0-point margins used in previous PHQ-9 non-inferiority studies [34, 35]. The comparison used Welch's independent-samples t-test. Equivalence was concluded when both one-sided tests were significant at α = 0.05, equivalent to a 90% confidence interval (CI) entirely within the prespecified bounds.

Sensitivity analyses used separate logistic regression models with antidepressant use and self-reported diagnosis of depression as binary outcomes. Both models included HC group, age group, and the HC group × age group interaction as predictors.

Regression model assumptions were assessed by inspecting residual distributions and plots for the regression models, and model-fit indices and influential observations for the logistic regression models. Multicollinearity was assessed by inspecting tolerances and variance inflation factors. Analyses were performed using SPSS version 31.0.2.0 and jamovi 2.7.37 with TOSTER 0.8.4.

Results

Participant characteristics

A total of 1590 women aged 14–55 participated in the study. Of these, 1076 reported current HC use and 514 reported no current HC use. Descriptive statistics are reported in Table 1.

Table 1
Descriptive Statistics for the Sample

Variable	No use (n = 514)	LNG-IUS (n = 523)	LNG/EE-COC (n = 157)	Other (n = 396)	Total (N = 1590)
Age, years, M (SD)**	30.1 (10.8)	31.3 (11.1)	24.3 (7.2)	24.3 (8.0)	28.5 (10.4)
≤ 21 years of age, n (%)**	146 (28.4%)	149 (28.5%)	69 (43.9%)	202 (51%)	566 (35.6%)
Education parents[b]	16.3 (2.3)	16.5 (2.5)	16.2 (2.9)	15.9 (2.4)	16.2 (2.5)
Education self[c]*	15.8 (3.4)	15.1 (3.2)	15.6 (2.9)	15 (2.4)	15.4 (3.1)
Duration of HC use, months, Median (IQR)**	NA	36 (60)	36 (72)	24 (41)	24 (61)
PHQ-9, M (SD)**	6.9 (6.7)	6.9 (6.6)	7.3 (6.3)	8.6 (6.9)	7.4 (6.7)
Severe depression, n (%)	33 (6.4%)	29 (5.5%)	6 (3.8%)	31 (7.8%)	99 (6.2%)
Antidepressants, n (%)	42 (8.2%)	43 (8.2%)	10 (6.4%)	28 (7.1%)	123 (7.7%)
BRIEF, M (SD)	1.7 (0.5)	1.7 (0.5)	1.7 (0.4)	1.8 (0.5)	1.7 (0.5)
Severe anxiety disorder, n (%)	28 (5.4%)	22 (4.2%)	5 (3.2%)	25 (6.3%)	80 (5%)
Obsessive-compulsive disorder, n (%)	22 (4.3%)	12 (2.3%)	2 (1.3%)	9 (2.3%)	45 (2.8%)
Eating disorder, n (%)	36 (7%)	25 (4.8%)	11 (7.0%)	33 (8.3%)	105 (6.6%)
Attention-deficit hyperactivity disorder, n (%)	62 (12.1%)	50 (9.6%)	14 (8.9%)	44 (11.1%)	170 (10.7%)
Autism spectrum disorder, n (%)	9 (1.8%)	11 (2.1%)	5 (3.2%)	8 (2.0%)	33 (2.1%)
Bipolar disorder, n (%)	7 (1.4%)	10 (1.9%)	3 (1.9%)	6 (1.5%)	26 (1.6%)
Psychotic disorder, n (%)	2 (0.4%)	2 (0.4%)	1 (0.6%)	2 (0.5%)	7 (0.4%)
Anxiolytics, n (%)	12 (2.3%)	15 (2.9%)	5 (3.2%)	11 (2.8%)	43 (2.7%)

* $p < 0.05$ (unadjusted for multiple comparisons); ** $p < 0.0027$ (Bonferroni-adjusted for 18 comparisons). Categorical p-values estimated using Chi-square and continuous p-values estimated using one-way ANOVA. Other = other pills/patch/injection/implant/ring. LNG-IUS = levonorgestrel intrauterine system; LNG/EE-COC = levonorgestrel/ethinyl estradiol combined oral contraceptives; [b] Highest completed education in years for any parent as reported by subjects aged < 20 years; [c] Education years for subjects of age 20 or higher; IQR = interquartile range; PHQ-9 = Patient Health Questionnaire-9; NA = not applicable; “Severe” depression or anxiety disorder was self-reported.

Variable	No use (n = 514)	LNG-IUS (n = 523)	LNG/EE-COC (n = 157)	Other (n = 396)	Total (N = 1590)
Antipsychotics, n (%)	9 (1.8%)	13 (2.5%)	3 (1.9%)	12 (3.0%)	37 (2.3%)

* p < 0.05 (unadjusted for multiple comparisons); ** p < 0.0027 (Bonferroni-adjusted for 18 comparisons). Categorical p-values estimated using Chi-square and continuous p-values estimated using one-way ANOVA. Other = other pills/patch/injection/implant/ring. LNG-IUS = levonorgestrel intrauterine system; LNG/EE-COC = levonorgestrel/ethinyl estradiol combined oral contraceptives; [b] Highest completed education in years for any parent as reported by subjects aged < 20 years; [c] Education years for subjects of age 20 or higher; IQR = interquartile range; PHQ-9 = Patient Health Questionnaire-9; NA = not applicable; “Severe” depression or anxiety disorder was self-reported.

In Table 2 we report the results of the sequential regression analysis with PHQ-9 as outcome.

Table 2
Sequential regression with total PHQ-9 as the outcome

Model	Variable	R^2	R^2change	b	β	p
1	**Model fit**	**.012**	**.012**			**< .001**
	No use vs LNG-IUS			0.040	.003	.923
	No use vs LNG/EE-COC			0.373	.017	.539
	No use vs Other HC			1.733	.112	< .001
2	**Model fit**	**.015**	**.003**			**.244**
	No use vs LNG-IUS			-0.097	− .007	.843
	No use vs LNG/EE-COC			1.046	.047	.186
	No use vs Other HC			1.946	.126	.001
	Age*			0.693	.050	.287
	(No use vs LNG-IUS) x Age			0.478	.021	.602
	(No use vs LNG/EE-COC) x Age			-1.777	− .054	.156
	(No use vs Other HC) x Age			-0.724	− .036	.438
3	**Model fit**	**.350**	**.334**			**< .001**
	No use vs LNG-IUS			.042	.003	.917
	No use vs LNG/EE-COC			.871	.039	.177
	No use vs Other HC			1.553	.100	.001
	Age*			− .105	− .008	.844
	(No use vs LNG-IUS) x Age			.525	.023	.483
	(No use vs LNG/EE-COC) x Age			-1.263	− .038	.218
	(No use vs Other HC) x Age			− .833	− .041	.275
	Anxiolytics			2.183	.053	.017
	Antipsychotics			1.111	.025	.276
	Anxiety disorder			3.610	.118	< .001
	Obsessive-compulsive disorder			.369	.009	.671
	Eating disorder			1.622	.060	.004

b: Unstandardized regression coefficients.; β: Standardized regression coefficients; Age: ≤21 years = 1; >21 years = 0

Model	Variable	R^2	R^2change	b	β	p
1	**Model fit**	**.012**	**.012**			**< .001**
	Attention-deficit hyperactivity disorder			-1.102	− .051	.019
	Autism spectrum disorder			1.876	.040	.055
	Bipolar disorder			− .105	− .002	.929
	Psychotic disorder			.028	.000	.990
	BRIEF			7.805	.536	< .001
b: Unstandardized regression coefficients.; β: Standardized regression coefficients; Age: ≤21 years = 1; >21 years = 0						

All three models show that LNG-IUS users do not differ in PHQ-9 scores compared to the non-use group, thus supporting H1. H2 was not supported, as LNG/EE-COC users did not show elevated PHQ-9 scores as compared to the non-use group. Age did not have a main effect or interaction effect, hence not supporting H3. Means and confidence intervals are presented in Fig. 1.

We observe that the “other HC” groups had higher PHQ-9 scores in all three models compared to no use, but this was not related to a prespecified hypothesis.

A post-hoc power analysis with a sample size of 1590 with an alpha of 0.05 and three tested predictors among a total of 17 predictor variables revealed a power of > 99% for a small effect size of f^2[32].

Table 3 shows TOST results demonstrating statistical equivalence of LNG-IUS versus No use, but not versus LNG/EE-COC, with equivalence bounds of ± 1 PHQ-9 points.

Table 3
TOST Results. LNG-IUS versus No use and LNG/EE-COC

LNG-IUS vs:	***t***	***df***	***p***
No Use: PHQ-9 t-test	-0.10	1034	.923
No Use: TOST lower	2.33	1034	.010
No Use: TOST upper	-2.52	1034	.006
LNG/EE-COC: PHQ-9 t-test	0.58	268	.564
LNG/EE-COC: TOST lower	2.31	268	.011
LNG/EE-COC: TOST upper	-1.16	268	.124
TOST: Two one-sided tests			

Finally, logistic regression sensitivity analyses showed no differences between HC groups and non-users in antidepressant use or self-reported diagnosis of depression, and there were no significant correlations between duration of use and PHQ-9 when controlling for age.

Discussion

The study's main finding was statistically equivalent depression scores in LNG-IUS users and HC non-users. Importantly, there was no evidence that this association differed by age, providing no support for the previously reported pattern of greater risk among young and adolescent users. Correspondingly, neither antidepressant use nor self-reported diagnosis of depression was more common among LNG-IUS users than non-users. Additional findings were that levonorgestrel-containing COC users did not show higher depressive symptoms than non-users, but users of other HCs reported higher depressive symptom scores than non-users. Also for this comparison, there was no evidence that differences were moderated by age. H1 was thus supported, but not H2 and H3.

Our findings contradict the adolescent LNG-IUS findings by Skovlund et al. [9], but are consistent with reported associations of other products in that study, namely elevated depressive symptom scores in a group of users of patches, rings, implants, injections, and non-levonorgestrel pills. The fact that our study detected an association for these products while finding none for the LNG-IUS suggests that this null finding cannot simply be attributed to a design that was insensitive to contraceptive-mood associations. However, the "other" group was heterogeneous, younger than the LNG-IUS and non-use groups, and may itself be subject to confounding by indication. These secondary findings should therefore be interpreted cautiously.

We propose that a plausible explanation for the discrepancy with early registry findings is particular selection into LNG-IUS use and thus confounding by indication. The registry-based studies were conducted during a time when clinical guidelines discouraged LNG-IUS use in young, nulliparous women. Consequently, the adolescents receiving an LNG-IUS may have differed systematically from their peers in behavioral, cognitive, or psychological vulnerabilities that were seen as warranting particularly reliable and user-friendly contraception. These vulnerabilities may themselves be associated with later mental health outcomes.

Several aspects of the present study support this interpretation. Most importantly, it was conducted in a contemporary context in which LNG-IUS use is common across reproductive ages [2], and LNG-IUS users and non-users were similar in age and educational attainment/parental education (Table 1). This suggests that current LNG-IUS users are less selected on characteristics that likely distinguished adolescent LNG-IUS users two to three decades ago. Moreover, the study was conducted in Norway, where contraception is subsidized for all young women and may be prescribed by public health nurses and midwives, facilitating broad access and further reducing barriers that could otherwise contribute to selective prescribing. At the same time, our previous exploratory study of Norwegian prescribing practices indicated that the LNG-IUS may still be particularly promoted to adolescents perceived as

vulnerable [27]. Such residual selection would thus be expected to increase symptom scores among LNG-IUS users, shifting the comparison toward poorer outcomes for this group. Finding equivalence despite this possibility therefore strengthens the null finding. The comparison with levonorgestrel-COC users adds a further control, as women who choose any hormonal method may differ from those who avoid such products. The absence of a difference suggests that the decision to use an HC does not account for the result.

Several design features also strengthen our findings. The equivalence margin of ± 1 PHQ-9 point is well below commonly used minimal clinically important differences for this instrument [34, 35], making the equivalence test stringent. Preregistration of the hypotheses strengthens its interpretation as a prospective test rather than a post-hoc reading of nonsignificant results. The sample provided high power to detect small group differences. Although the design is cross-sectional and temporality cannot be established, the equivalence of current symptom levels, the null findings in sensitivity analyses, and the lack of any relationship between duration of use and symptom scores together suggest that any association between LNG-IUS use and depressed mood is small, context-dependent, or limited to subgroups not identified here. Moreover, self-selection may have favored participation by those with more symptoms, but the lack of higher scores among IUS users than non-use controls despite this possibility supports the equivalence findings. The absence of age moderation is particularly relevant given that the strongest previous LNG-IUS association was reported in adolescents.

Implications

Our findings suggest that concerns about depression should not, by themselves, discourage clinicians from prescribing the LNG-IUS to adolescents and young women. The LNG-IUS is a highly effective contraceptive method with established non-contraceptive benefits [7], and unnecessary reluctance to prescribe it may limit access to a valuable contraceptive option. Ensuring access to effective contraception for adolescents is important both on an individual and a societal level, as teenage pregnancies are associated with several adverse socioeconomic and health outcomes. These include increased likelihood of poverty, lack of employment and educational attainment, as well as obstetric complications, adverse neonatal outcomes, and in some parts of the world, also unsafe abortions [36, 37]. While contraceptive counselling should remain individualised, with attention to medical history and individual preference, our findings may strengthen clinician confidence in prescribing the LNG-IUS to young and adult women alike.

The findings also underline the importance of considering historical prescribing practices when interpreting earlier registry associations, particularly for contraceptive methods that were only restrictively used in younger population. Additional studies using complementary designs are needed to strengthen the evidence, and future studies should recruit participants before initiation, then follow both continuers and discontinuers, so that discontinuation bias can be examined directly and transient effects distinguished from persistent ones. Such studies should record LNG-IUS dose, reasons for contraceptive choice and discontinuation, and baseline mental health. Linking registry data to prescribing indications

and prior mood symptoms would also help clarify confounding by indication. Randomized allocation to contraceptive methods, although ethically challenging in adolescents, would provide the strongest causal evidence.

Limitations

The non-randomized, cross-sectional design limits causal inference, and effects in specific subgroups or during periods following contraceptive initiation cannot be excluded. Moreover, despite the fact that duration of use was unrelated to symptom scores, and LNG-IUS user scores did not differ from LNG/EE-COC user scores even though COCs can be discontinued more easily, discontinuation bias remains a potential limitation. Although LNG-IUS users and non-users were comparable on measured characteristics, representativeness cannot be fully assessed because recruitment was anonymous and convenience-based, and no response rate was available. Self-selection may also have reduced participation among individuals with lower health literacy or digital competence but is unlikely to differentially affect HC groups. All data were self-reported. We did not record LNG-IUS dose, so dose-specific effects cannot be excluded. Finally, the PHQ-9 is a validated measure of symptom severity but not a clinical diagnostic assessment.

Conclusions

This study found no evidence of higher depressive symptom scores among LNG-IUS users, including adolescents and young women. These findings challenge suggestions that LNG-IUS use increases depression risk in younger users and are consistent with the interpretation that previously reported registry associations reflect confounding by indication or selection effects. While longitudinal studies are needed to confirm these findings and assess possible effects in specific subgroups, our results provide reassurance regarding LNG-IUS use in all reproductive ages.

Abbreviations

LNG-IUS
levonorgestrel-releasing intrauterine system
HC
hormonal contraceptives
COC
combined oral contraceptive
BRIEF
Behavior Rating Inventory of Executive Function
PHQ-9
Patient Health Questionnaire-9
LNG/EE-COC
levonorgestrel/ethinyl estradiol-containing combined oral contraceptives

TOST
Two one-sided tests

Declarations

Ethics approval and consent to participate:

This research was carried out in compliance with the Declaration of Helsinki and assessed by the Western branch of the Norwegian Regional Ethics Committees (REK) and found to be in accordance with national guidelines for health research (reference #806938, December 11, 2024). Digital information sheets were provided to participants prior to data collection, through which participants were thoroughly informed about the project's purpose and what would be required of them if they chose to take part. Participants were informed about potential benefits and risks, as well as data management. They were also informed that it would not be possible to withdraw their answers once submitted, as the data collection was completely anonymous and individual responses could therefore not be identified. To preserve anonymity, signed consent forms identifying participants were not collected. Instead, participants had to tick a box confirming their consent before accessing the survey. The general expectation of verified parental consent was weighed against the minors' rights to privacy and to be heard in research, with particular attention to protecting their anonymity and the confidentiality of information concerning contraceptive use and mental health. This assessment was informed by the Norwegian Guidelines for Research Ethics in the Social Sciences and Humanities (https://www.forskningsetikk.no/en/guidelines/social-sciences-and-humanities/guidelines-for-research-ethics-in-the-social-sciences-and-the-humanities), which emphasize minors' best interests and acknowledge that participation without parental consent may be ethically justifiable in particular circumstances. Furthermore, the Declaration of Helsinki does not specify an age below which parental consent is invariably required. Finally, the Norwegian Patient and User Rights Act recognizes that minors aged 12–16 may consent independently to healthcare where parents are not informed in accordance with the act. Informing parents about contraceptive use may not always be desirable for minors, and requiring parental involvement may, in some cases, create a barrier to accessing contraceptive care. These considerations, along with the anonymous nature of our data collection, informed the decision not independently collect parental consent not for minor participants. REK's guidance that research using anonymous data falls outside the Norwegian Health Research Act also informed the decision not to collect participant-identifying consent forms for either adult or minor participants.

Consent for publication:

Not applicable

Competing interests:

The authors declare that they have no competing interests.

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Author Contribution

Study idea: MKB. Study design and conception: MKB and KKB. Data collection: MKB. Initial analysis: MKB and KKB. Further analysis: All authors (MKB, KKB, DAL). Drafting the manuscript: MKB. Directly accessing and verifying underlying participant-level data, reviewing results, contributing to and approving the final version of the manuscript: All authors (MKB, KKB, DAL).

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Data Availability

All data will be made available to reviewers upon request to the corresponding author and then made publicly available by August 2027.

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Figures

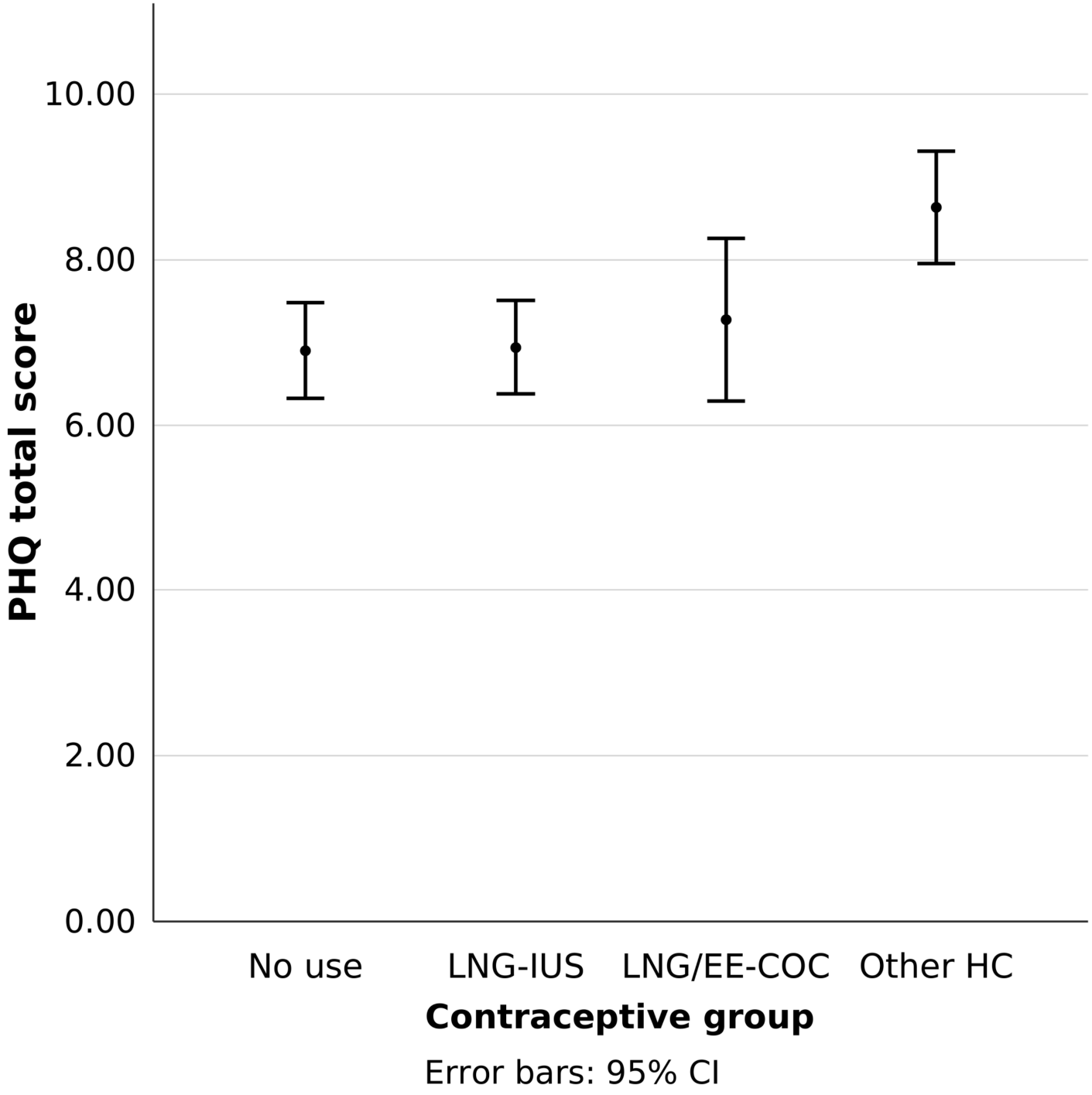

Figure 1

Depressive symptoms by contraceptive group

Points show mean Patient Health Questionnaire-9 (PHQ-9) scores; error bars show 95% CIs. Groups comprise no current hormonal contraceptive (HC) use (n=514), levonorgestrel-releasing intrauterine

system (LNG-IUS; n=523), combined oral contraceptives containing levonorgestrel and ethinylestradiol (LNG/EE-COC; n=157), and other HCs (n=396). Other HCs include other oral contraceptives, vaginal rings, patches, injections, and implants. Total sample: 1590 participants.