

## CoSRH Statement: Effect of Hormonal Contraception in Individuals with Anxiety and Mood (Affective) Disorders

### Introduction

Studies included in previous CoSRH guidelines<sup>1–4</sup> show no clear evidence that hormonal contraception worsens or improves mood, with different forms of hormonal contraception being undistinguishable in this regard. The main body of evidence came from observational studies which are subject to confounding factors, with few randomised controlled studies reported. In addition, most studies focused on women without pre-existing mental health conditions.

It is important to acknowledge that some individuals report mood change during use of hormonal contraception whether the hormonal contraception is the cause of these changes or not. Current guidance is that health care professionals should ensure an individualised approach to managing signs and symptoms of depression and explore other possible contributing factors whilst considering offering alternative contraception if an individual considers that their mood has been adversely affected by use of their contraceptive method.<sup>2</sup>

This statement focuses on the effect of hormonal contraception (HC) in those with pre-existing anxiety and mood (affective) disorders. Very limited evidence from 11 studies (2015-2025) shows that overall, there is not consistent evidence that hormonal contraceptives (HCs) worsen or improve anxiety or mood (affective) disorders in those with pre-existing conditions.

### Recommendation

When starting hormonal contraception in those with pre-existing anxiety or mood (affective) disorders, clinicians should provide individualised counselling and advise patients to monitor their mood, seeking follow-up with their healthcare provider if they notice a deterioration.

### Summary of evidence

- **Combined oral contraception (COC):** There is not clear consistent evidence that COC improves or worsens mood in those with pre-existing anxiety and mood disorders. Moderate to low quality evidence is mixed, showing either no effect on mood or a small negative effect on anxiety and mood (affective) disorder symptoms over time. No evidence was found for non-oral combined methods.
- **Progestogen only pill (POP):** There is no evidence looking at the effect of desogestrel or traditional POPs on mood in those with pre-existing anxiety or mood disorders. One small observational study has shown that drospirenone (DRSP) may reduce postpartum depressive symptoms over time.

- **Levonorgestrel intrauterine device (LNG-IUD):** Moderate quality evidence from one observational study found no significant difference in depression or anxiety recurrence in LNG-IUD users, when compared with copper IUD (Cu-IUD) users, in women with mood or anxiety disorders.
- **Medroxyprogesterone acetate (DMPA):** There is not clear consistent evidence that DMPA improves or worsens mood in those with pre-existing anxiety and mood disorders.

## The Evidence

### Population

This statement focuses on women with clinically diagnosed or self-reported anxiety and mood (affective) disorders and does not cover the development of new disorders whilst using hormonal contraception. Diagnostic grouping in this statement was guided by the Diagnostic and Statistical Manual of Mental Disorders (both *DSM-IV* and *DSM-5*) frameworks<sup>5</sup>. Accordingly, anxiety disorders include generalised anxiety disorder (GAD), panic disorder, obsessive-compulsive disorder (OCD) and separation anxiety disorder. Mood (affective) disorders include major depressive disorder (MDD), dysthymia, postpartum depression, mood changes and bipolar disorder. In some studies, the definition of mental health conditions included a mixed set of disorders beyond anxiety and mood (affective) disorder, with other disorders representing only a small proportion of participants.

### Overview of included studies

Studies included >900,000 participants across Europe, North and South America and Africa. Study designs included randomised controlled trials (RCTs),<sup>6,7</sup> observational studies<sup>8–15</sup> and a non-randomised experimental study.<sup>16</sup> Investigated outcomes included change in depression (including postpartum),<sup>6–9,12,13,16</sup> broader mood or psychiatric symptoms,<sup>10,14,15</sup> anxiety,<sup>6,13</sup> and antidepressant use.<sup>11</sup> Follow-up durations varied from 24 weeks<sup>9</sup> to 12 years.<sup>12</sup> Populations included adults,<sup>6,8,14–16</sup> adolescents,<sup>10–12</sup> postpartum,<sup>9</sup> and mixed aggregated adolescent–adult samples.<sup>7,13</sup> Most studies recruited mixed populations of women with and without prior mental health histories.<sup>6–8,12–16</sup> Two studies enrolled women with diagnosed mental health conditions.<sup>9,10</sup>

### Results by contraceptive method

#### Combined oral contraceptives

Evidence from four studies<sup>6,8,14,16</sup> showed neutral to small negative effects on anxiety and mood (affective) disorders in users of COC. These studies are limited by relatively small sample sizes, cross-sectional or observational designs, heterogeneity in OC formulations and outcome measurement.

In a double-blind RCT<sup>6</sup> women with both current or past mental health disorders<sup>a</sup> using norgestrel + estradiol reported modest increases in mood swings, irritability, and anxiety compared with placebo ( $p < 0.05$ ,  $n = 84$ ). Those with current disorders showed increases in irritability only ( $p = 0.017$ ,  $n = 19$ ). Similarly, a cross-sectional study<sup>14</sup> ( $N = 302$ ) found that women with prior MH disorders were nearly twice as likely to report COC-related mood effects (aOR 1.90; 95% CI 1.01–3.59;  $p = 0.047$ ,  $n = 179$ ).

In contrast, one long-term observational study<sup>8</sup> reported limited impact of unspecified COC use on depressive outcomes. Among women with current MDD or dysthymia ( $n = 929$ ), OC use was not associated with differences in depressive symptom severity compared with non-use ( $p = 0.55$ ). COC use was also not associated with higher prevalence of MDD (or dysthymia) within the prior six months (adjusted OR for MDD: 0.99, 95% CI 0.77–1.27,  $p = 0.93$ ; adjusted OR for dysthymia: 0.65, 95% CI: 0.32–1.27,  $p = 0.21$ ). However, additional analysis suggested starting COCs may increase MDD risk (OR 1.70, 95% CI 1.16–2.49,  $p = 0.006$ ).

Non-randomised experimental evidence<sup>16</sup> shows that women with mild to moderate depressive symptoms ( $n = 15$ ; 29% of total participants) reported intensified negative mood when responding to various tasks during COC pill taking when compared to the pill free interval. For example, they took longer to recognise sad and angry faces during COC use compared to the inactive pill week ( $p = 0.015$ ) and showed weaker emotional responses to positive and negative stimuli in a priming task ( $p = 0.010$ ). Additionally, negative emotions interfered more strongly with their ability to classify words during COC use, indicating heightened sensitivity to negative stimuli ( $p = 0.012$ ).

### **Progestogen-only methods**

Evidence is limited to three studies looking at the effects of DRSP<sup>9</sup> and DMPA-IM<sup>7,10</sup> on depressive symptoms in those with pre-existing anxiety and mood disorders. Evidence is constrained by small sample sizes,<sup>10</sup> observational designs,<sup>9</sup> limited statistical adjustment,<sup>7,10</sup> and heterogeneous or mixed mental health assessments.<sup>10</sup>

A prospective study<sup>9</sup> shows that in postpartum women with mild depressive symptoms ( $n = 149$ ),<sup>9</sup> DRSP use was associated with lower mean depression scores at 12 weeks (8.7 vs 10.1;  $p < 0.001$ ) and at 24 weeks (7.7 vs 9.9;  $p < 0.001$ ) compared with non-hormonal methods, suggesting possible beneficial effects. Given that these findings reflect women with mild antenatal depressive symptoms, they may not be generalisable to those with moderate or severe depression.

In an RCT of adolescent and adult women with and without depression ( $n = 605$ ),<sup>7</sup> moderate/severe depression decreased among DMPA-IM users from 17.0% to 9.6%

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<sup>a</sup> Besides anxiety and mood (affective) disorders, it included small subgroups with eating disorders or social phobia.

between 3 to 12 months. At 12 months, DMPA-IM users reported fewer instances of moderate/severe depression (9.6%) than Cu-IUD users (17.7%,  $p = 0.032$ ). In addition, median depression scores were lower for DMPA-IM than for LNG-implant users ( $p = 0.036$ ). Conversely, among adolescents with existing mental or developmental disorders<sup>b</sup> ( $n=69$ ),<sup>10</sup> 15.9% reported mood changes as a complaint related to DMPA-IM use, but attribution was uncertain due to psychiatric comorbidities and psychotropic medication use.

### **LNG-IUD**

Only one study specifically assessed the impact of LNG-IUD use compared with Cu-IUD use on anxiety and mood (affective) disorders in women with prior diagnoses. In a cohort study ( $n = 17,743$ ),<sup>13</sup> among women with clinically diagnosed anxiety or mood (affective) disorders recorded one year before study entry, using LNG-IUD showed no significant difference in anxiety or depression recurrence compared with Cu-IUD users.

Certainty is moderate, limited by reliance on clinical coding, baseline group differences, and residual confounding, but strengthened by the large, representative UK dataset and inclusion of both intention-to-treat and as-treated analyses.

### **Mixed hormonal contraceptives**

Three studies reported on various or unspecified HC methods. Evidence is limited by observational design, lack of control for confounding, antidepressant prescriptions used as an indirect proxy for depressive symptoms,<sup>11</sup> unspecified OC formulation,<sup>12</sup> and cross-sectional studies that preclude temporal assessment, lacking validated self-report measures.<sup>15</sup>

In a prospective cohort study,<sup>11</sup> HC use was associated with increased antidepressant prescriptions among women with prior mental health diagnoses<sup>c</sup> (OR 1.19; 95% CI 1.08–1.31;  $p < 0.05$ ,  $n = 113,711$ ). A subsample of teenage girls aged 12–17 with previous mental health conditions and low income who used HC were 7.8% (95% CI: 4.7–10.9,  $n = 6,838$ ) more likely to use antidepressants than non-HC users, which suggests they may have experienced more depression compared to those who did not use hormonal contraception.

A cross-sectional survey<sup>15</sup> found that women with a psychiatric history<sup>d</sup> were twice as likely to report HC-related mood side effects than those without psychiatric history (61.2% vs 29.5%;  $p < 0.001$ ,  $n = 188$ ). Among women with psychiatric history, 38.8% reported worsening of symptoms, 20.0% no change, and 11.0% improvement ( $n = 80$ ). Mood changes were the most frequently reported side effect (61.2%).

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<sup>b</sup> It included depression (30.10%), anxiety (22.20%), epilepsy (9.50%), bipolar affective disorder (7.90%), ADHD (7.90%), attempted suicide (7.90%) and eating disorders (6.3%).

<sup>c</sup> Pre-existing mental health conditions were defined broadly as *any psychiatric disorder* or *any dispensed psychotropic medication* within the previous three years.

<sup>d</sup> The most common psychiatric diagnoses were anxiety, depression, OCD, and bipolar disorder (with smaller proportions reporting ADHD, eating disorders or PTSD).

Nonetheless, a longitudinal study on unspecified OC use ( $n = 725$ )<sup>12</sup> found that among women aged 25, the association between OC use and increased depression was weaker among those with previous MDD at age 19 compared to women without a history of MDD. This finding suggests that OC use during adolescence does not significantly elevate the risk of depression for those previously diagnosed.

### Conclusion

Overall, the evidence does not show a consistent or clinically significant worsening or improvement of mental health outcomes with hormonal contraceptive use in those with pre-existing mental health conditions. Where differences exist, these are generally small ( $OR \approx 1.19.1-1.90$ ) and primarily limited by study design, short follow-up, and heterogeneity in anxiety and mood (affective) assessments.

Certainty of evidence ranges from low to moderate, constrained by heterogeneity of contraceptive formulations, self-report bias, absence of baseline mental health stratification and diverse outcome definitions.

There is a clear need for further research in this area, which would support individuals with mental health conditions to make informed choices about hormonal contraception.

Please see existing CoSRH guidance for advice and evidence regarding mood changes in individuals using hormonal contraception, who do not have a pre-existing mental health condition.

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