


# Hormonal contraceptives and women's mental health – A long-term perspective

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## **Belinda Pletzer of the University of Salzburg discusses the importance of researching the mental health effects of hormonal contraceptives and the need to identify women at risk for adverse mood reactions before they start hormonal contraception**

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The mental health effects of hormonal contraceptives have received much media attention over the last decade, resulting in increased skepticism towards hormonal treatments and a reduction in hormonal contraceptive use. Recognizing hormonal contraceptives as a potential trigger of mood symptoms was a crucial and empowering step for women's mental health research and care. However, we still need to find a balance in weighing the reproductive – and probably also mental – health benefits of hormonal contraceptives against the risks of adverse reactions. Information is key to achieving that goal. Thus, research into the mental health effects of hormonal contraceptives is of utmost importance.

In the last decade, we increasingly observed that even women who do not experience adverse side effects of hormonal contraceptives often discontinue for fear of long-term effects on their mental health. Thus, one of the most pressing user questions appears to be whether the effects of hormonal contraceptives on mental health accumulate with longer duration of use. The evidence acquired with regard to this question mostly concerns oral contraceptive (OC) pills.

### **What we know so far – long-term effects of contraceptive pill use**

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As researchers, we classify women as long-term OC users if they have been on their respective pill for at least six months. Anything below that is considered short-term use. This cut-off is, of course, not arbitrary. Following up on case reports of women experiencing adverse affective reactions to their OC, large-scale studies have repeatedly compared various mental health indicators, including depression scores, anxiety scores, and suicide risk between long-term OC users and non-users. <sup>(1)</sup> With high consistency, they conclude that long-term OC users have better mental health than non-users.

Originally, this was attributed to mood-stabilizing effects of OCs, which abolish endogenous hormonal fluctuations. However, we now assume that this finding tells us more about the patients rather than the OCs they are or are not using. Women who become long-term users of OC, i.e., women who make it through the first six months of treatment, are, with the great majority, women who tolerate their pill well and probably even experience beneficial effects. The large-scale registry studies, which spiked the

interest in the effects of hormonal contraceptives on mental health, also demonstrate that the depression rates in hormonal contraceptive users peak at six months and drop after that. <sup>(2)</sup> That's not because symptoms get better after six months of use but because women who experience adverse mood reactions are likely to discontinue treatment within the first six months.

Thus, while randomized placebo-controlled trials convincingly demonstrate that there is a risk of developing mental health symptoms when starting OC use, this risk is not equally distributed across women. About 4-10 % of women develop serious affective reactions when starting OC treatment. <sup>(3)</sup> However, this happens already in the first few months of use. Thus, the good news is that mental health reactions to hormonal contraceptive treatment can be detected early. Women who don't have any problems in the first six months of use very likely don't have to worry about the accumulative effects of long-term use on their mental health. While there are no placebo-controlled trials that follow women who start contraceptive treatment over multiple years, we were recently able to demonstrate that in long-term OC users, the duration of use is not related to their mental health. <sup>(4)</sup>

## **Where we go from there – individualizing hormonal contraception**

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However, many women are particularly interested in more long-lasting contraceptive options like hormonal IUDs (intra-uterine devices) or hormonal contraceptive implants, for which discontinuation is more cumbersome than for contraceptive pill users. Compared to OC pills, we know relatively little about the long-term mental health effects of hormonal IUDs or contraceptive implants. Recent evidence comes from registry-based studies and is thus purely correlational. While confirmation via placebo-controlled trials is still required, it appears that among hormonal IUD users, the prevalence of depression appears to increase in a dose- and time-dependent manner. <sup>(5)</sup> This is likely attributable to the fact that among hormonal IUD users, not everyone who experiences adverse mood effects in the short term can easily discontinue.

Thus, for women's mental health care, the most pressing question is not whether the mental health effects of hormonal contraceptives accumulate in the long term. Rather, we need to know how to effectively and efficiently identify women who are at risk for adverse mood reactions BEFORE they start hormonal contraception, particularly long-lasting hormonal contraceptives. Thus, we want to move towards a precision medicine approach to hormonal contraceptives. <sup>(6)</sup>

We currently know that the risk for developing adverse mood symptoms is higher in adolescents, as well as in women who have previously experienced adverse mood reactions to hormonal contraceptives. <sup>(6)</sup> More generally, women with previous mental health problems or higher baseline depression are at higher risk for adverse reactions to hormonal contraceptives. <sup>(6-8)</sup> This information is immediately transferable to clinical practice. By considering mental health history in reproductive health care, we can identify those women who need closer monitoring through the first months of hormonal contraceptive use. In the long-term, however, this measure is unsatisfactory as it will

become more effective with increasing age and after women have already undergone a certain amount of suffering. Thus, better predictors of adverse mood reactions to hormonal contraceptives are needed, especially for younger women.

This issue is not specific to hormonal contraception. Any hormonal transition period comes with an increased risk of developing mental health symptoms. The prevalence gap in mood disorders between men and women arises with puberty; 3-8% of women suffer from premenstrual dysphoric disorder, and 10-15% of women suffer from postpartum depression. From puberty to menopause, a certain percentage of women seem to respond to hormonal changes with adverse mood symptoms. <sup>(9)</sup>

Recent studies show that these are probably not isolated events. Women who experience stronger premenstrual symptoms are at higher risk of developing postpartum depression. <sup>(10)</sup> Likewise, women who develop adverse mood symptoms during hormonal contraceptive treatment are also at higher risk of developing postpartum depression. <sup>(11)</sup> Thus, if women develop mood symptoms when they start hormonal contraceptive treatment, it's likely because they have a heightened sensitivity to hormonal changes in general. Accordingly, to establish a comprehensive profile of individualized responses to hormonal contraceptives, we need to better characterize hormone sensitivity across the female lifespan by combining psychometric, endocrinological, genetic, and neuroimaging approaches.

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