

also gearing up for an escalation of domestic violence in coming months. Governments everywhere are struggling to manage both the economic and social fallout of containment measures, and what this means for citizens. In the past few months, the Australian government has announced an additional \$150m for domestic violence services and free child care for working parents with children under five years of age.

These measures are welcome and, in the case of free child care, represent a huge turnaround in Australian government policy. However, other public health measures that normally provide support to families have been drastically curtailed. For example, publicly funded maternal and child health services can no longer provide new mothers groups or home visiting services. Programs specifically designed to provide culturally appropriate care and support to socially disadvantaged populations, such as group pregnancy care for families of refugee background, have also been wound back². In low and middle income countries, evidence suggests there will be even more stark consequences of containment measures for children and families who are already vulnerable³.

It has long been recognized that perinatal mental ill health has a complex etiology with both biological and social determinants⁴. The contribution of social and environmental factors such as gender-based violence, racism and forced migration is reflected in the higher prevalence of perinatal mental health disorders among women experiencing intimate partner violence and other adverse life circumstances^{5,6}. In a longitudinal study of over 1,500 first-time mothers conducted by our group, one in three women experienced depressive symptoms during the first 12 months post-

partum, and of these, two fifths (40%) had experienced emotional and/or physical violence by a current or former intimate partner in the first year after childbirth⁶.

Gender-based violence, racism and other forms of human rights abuse have their roots in institutions and systems that fail to give all citizens equitable access to social and economic resources. Consideration of these contextual factors in framing service delivery responses is a critical element of high-quality mental health care, clearly articulated in the United Nations Sustainable Development Goals. As Howard and Khalifeh argue, public health interventions are also needed to tackle social determinants of risk for poor perinatal mental health at a systems and community level.

The COVID-19 pandemic necessitates worldwide action to strengthen both public health interventions promoting perinatal mental health and the capacity of mental health care services to support and enable the resilience of families dealing with cumulative social and economic stresses at times of crisis⁷. Howard and Khalifeh identify significant evidence gaps related to treatment efficacy, especially for women facing difficulties related to poverty, racism, stigma and interpersonal violence. They also draw attention to the paucity of evidence regarding large scale community-level interventions tackling system change with local contextual solutions. Strategies that work for particular communities and contexts may not work in others. In the Australian setting, this is most evident in relation to First Nations people, who experience markedly worse perinatal mental health outcomes than non-Indigenous Australians⁸.

Mental health clinicians, health services and communities all have important roles

to play in the development of rapid responses to limit the escalation and persistence of perinatal and other mental health disorders as a result of the COVID-19 pandemic. It is critical that the opportunity is not lost to ensure that these responses include the development and testing of co-designed strategies that build community-level resilience, foster strengths-based, trauma informed approaches, and tackle the sources of mental health inequalities globally. Better tailoring of individual level responses, taking account of social, economic and cultural contexts and engaging consumers and communities in the co-design of local primary health care and mental health services, is also needed to avoid further entrenchment of health inequalities⁹.

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Postpartum psychosis: an important clue to the etiology of mental illness

Howard and Khalifeh¹ masterfully review the epidemiology of perinatal mental health conditions and the evidence base for their management. Here I address a further issue and exciting opportunity: the

role that the study of severe perinatal mental illness can play in advancing our understanding of the etiology of mental health conditions.

The close relationship of severe epi-

sodes of mental illness to childbirth, episodes labelled postpartum psychosis, has been observed for hundreds, if not thousands, of years, and more recently this link has received support from clinical and ep-

idemiological studies². Despite this long history, we have failed to take advantage of this important clue to the pathophysiology of mental illness.

One reason may be the confusion that remains around classification, with both DSM and ICD not dealing adequately with severe postpartum mental illness. As with many mental health conditions, there may be fuzziness around the boundaries, but there is clarity at the core of the concept of postpartum psychosis, and this concept remains useful and in widespread use by clinicians and women themselves. For example, the main third sector organization supporting women and their families in the UK is called Action on Postpartum Psychosis (app-network.org). Despite this nosological confusion, however, there is no doubt that “we know it when we see it”.

What, then, is postpartum psychosis and why is this condition potentially so important in our understanding of the etiology of mental disorders? Postpartum psychosis is a severe episode of mental illness that impacts around 1 in 1,000 women following childbirth². Onset is in the immediate postpartum, most often the first or second postpartum week. The symptoms are most commonly of an affective psychosis, with perplexity common, and often a rapidly and constantly changing (“kaleidoscopic”) presentation.

Postpartum psychosis is a true psychiatric emergency, with admission to hospital usually required, but, despite the initial severity and rapidity of presentation, prognosis is good, with most episodes responding well to treatment, predominantly medication in the acute stage. Following the initial psychotic phase, however, women may experience longer episodes of depression, and many of them report that full recovery takes many months. Psychological interventions, including peer support, in the longer term can be very helpful in the recovery process.

Although around 50% of women with postpartum psychosis have not experienced a previous episode of mental illness, there is a clear link to bipolar disorder, especially bipolar I disorder. Women with a previous diagnosis of bipolar disorder are at high risk (around one in five deliver-

ies)³. In addition, women who experience postpartum psychosis as a first episode, even if not clearly bipolar at initial presentation, are at high risk of subsequent bipolar illness⁴.

The evidence is clear, therefore, that childbirth is a potent trigger of episodes of severe mental illness, and that this risk is not spread evenly across all mental illness, but shows a specific link to bipolar disorder. What are the mechanisms behind this association? Although psychological and social factors clearly play an important role in perinatal mental health conditions in general, and postnatal depression in particular, when it comes to postpartum psychosis biological factors are likely to be primary, with hormonal, immunological, circadian rhythm, and genetic factors all suggested to play a role².

There is a dramatic rise in levels of reproductive hormones (oestrogen and progesterone) in pregnancy and a precipitous fall in the immediate postpartum, corresponding to the exact time that sees the peak onset for postpartum psychosis. Periods of hormonal fluctuation, in the menstrual cycle for example, are known to be associated with mood symptoms, and this had led to hormonal factors being considered in the etiology of postpartum psychosis. The evidence base for this assertion remains, however, mostly circumstantial. There have been no consistently demonstrated abnormalities in hormonal levels in women experiencing perinatal mental illness, but it remains possible that women with postpartum episodes are differentially sensitive to the normal hormonal fluctuations associated with pregnancy and childbirth⁵.

In recent years, the role that immunological mechanisms and inflammation play in psychiatric disorders has received considerable attention. This, combined with the fact that pregnancy is a major immunological challenge, has led some to hypothesize that immune and neuro-inflammatory mechanisms play a role in the etiology of postpartum psychosis. Further support comes from the evidence of increased risk in first pregnancies, a finding shared with other pregnancy-related disorders, such as pre-eclampsia, which are thought to be driven by immunologi-

cal mechanisms. Studies have found some evidence pointing to the role of immune biomarkers. For example, women with postpartum psychosis in one study did not display the expected T cell elevation following childbirth, but rather presented a monocytosis⁶. In addition, small numbers of women with postpartum psychosis (around 2%) were reported to have anti-neuronal autoantibodies in one study⁷.

A further clue to etiology comes from the known link between circadian rhythm disturbance and the triggering of mood disorder, particularly mania, combined with the almost universal disturbance of sleep patterns that having a baby involves. Although it has not been studied extensively, there is some evidence in support of this hypothesis. For example, one study found that women with bipolar disorder who reported that sleep loss triggered episodes of mania were more than twice as likely to have experienced postpartum psychosis⁸.

A further hypothesis receiving attention is the potential involvement of genetic factors. Family and linkage studies suggest a genetic etiology, and a number of linkage and candidate gene studies have been reported, but are yet to yield replicated results². Sample sizes have been limited up to now, but large-scale collaborative efforts are underway to significantly increase the numbers available.

In summary, childbirth is a potent trigger for severe mood disorder, and this link gives us unrivalled opportunities for research into etiology. In no other scenario can we identify individuals, currently well, who are at such a high risk of experiencing a severe episode of mental illness in a defined two-week period. In addition to understanding more about etiology, we also have a significant opportunity for prevention, through the development of predictive models identifying which women are at very high risk⁹.

We need, therefore, to take advantage of the vital clue that postpartum psychosis represents. First, we need this condition to be better dealt with by the ICD and DSM classification systems, which currently are of little help in ensuring that these episodes are recorded. Second, we need to build large cohorts of women who have

experienced this condition for international collaborations to look, for example, at its genetic underpinnings. Finally, we need prospective studies of selected populations, for example women with previous episodes of bipolar disorder, applying a range of paradigms, from imaging to other biomarkers, allowing us to better identify subjects at high risk.

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Pregnancy specific anxiety: an under-recognized problem

Howard and Khalifeh¹ discuss the high prevalence of common mental disorders in the perinatal period and emphasize the need for early detection. Overall, research in this area has mostly focused on perinatal depression, and the role of anxiety has been relatively neglected until recently. It is also true, however, that anxiety and depression often co-exist.

A recent systematic review reports the prevalence of any clinically diagnosed anxiety disorder across the three trimesters of pregnancy to be 15.2%. In the first four weeks following childbirth, 17.8% of women experience significant anxiety symptoms. These rates are higher in low- and middle-income countries (LMICs) compared to high-income ones².

A form of anxiety which has not received the attention it deserves is pregnancy specific anxiety (PSA), i.e. the condition marked by worries, concerns and fears about pregnancy, childbirth, the health of the infant, and future parenting. This is considered to be distinct from generalized anxiety, as it occurs specifically during pregnancy and the anxiety revolves only around pregnancy-specific issues. PSA shows a different longitudinal course from generalized anxiety, is predictive of birth weight and gestational age at birth, and is more common in nulliparous women.

An overlapping construct is that of pregnancy related anxiety (PRA), which was proposed following a concept analysis of 38 studies³. PRA is described as the nervousness and fear about the baby's health, the mother's health and appearance, the experience with the health care system, and social and financial issues in the context of pregnancy, childbirth and parenting.

While the prevalence of PSA is reported to be around 29% in high-income countries⁴, studies from LMICs such as India, Iran, Tanzania and China have reported rates up to 55.7%. Most studies report higher rates of PSA in the third trimester of pregnancy^{5,6}.

The interest in PSA has led to the development of two specific tools: the Perinatal Anxiety Screening Scale (PASS) and the Pregnancy-Related Anxiety Questionnaire - Revised (PRAQ-R). The PASS is a 31-item questionnaire used to screen a broad range of anxiety symptoms in perinatal women, with pregnancy-specific anxiety questions as a separate part⁷. The PRAQ-R is a 10-item questionnaire specifically focusing on symptoms of PSA, such as fear of giving birth, worries about bearing a physically or mentally challenged child, and concern about one's own appearance⁸.

The risk factors for PSA are different in LMICs compared to high-income countries. Studies conducted in India and Africa have emphasized that – despite good family support and marital life – perceived stress, active depression and the number of people living in the home predicted PSA⁵. In high-income countries, young age, being unmarried, lower education, lower household income, being nulliparous, and having an undesired pregnancy were associated with a higher risk for PSA⁴.

PSA has also been found to be related to pregnancy outcomes. Among Iranian women, PSA in the third trimester was associated with preterm birth. A study from the US found high levels of PSA to be significantly associated with an increased risk for spontaneous preterm birth, even after adjusting for several confounding factors.

A cohort study in China found that PSA in the second and third trimesters was associated with small-for-gestational-age infants.

PSA may also play a role in birth preferences, as shown by a multi-ethnic prospective cohort study from Amsterdam, which found that women with PSA were more likely to receive pain relief/sedation and had an increased risk for primary caesarean section.

Another important finding is the relationship of PSA to infant temperament. In a systematic review, Erickson et al⁹ found an association between PSA and infant temperament in seven of the nine studies reviewed, three of which included large, representative, population-based samples. In a study of 282 mothers, PSA during second and third trimesters was significantly associated with infant's negative emotional reactivity, mainly fearfulness. PSA emerged as the only significant predictor even after controlling for background factors and for postnatal depressive and general anxiety symptoms¹⁰.

PSA has also been shown to have persisting effects in the postnatal period. Women who had PSA at 32 weeks of gestation exhibited clinically significant anxiety at six months postpartum even after controlling for prenatal generalized anxiety.

The risk for PSA is likely to be particularly high in countries with high maternal and infant mortality rates. In African countries, maternal mortality rates range from 163 to 533 per 100,000. In some African countries, 51 per 1,000 infants may not survive their first year. In addition, pregnant women in these areas may face challenges such as food insecurity and lack of adequate maternity services, which may