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Published in:
Current opinion in psychiatry

DOI:
10.1097/YCO.0000000000000781

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2022

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

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Download date: 10-11-2022
Precision psychiatry and the clinical care for people with schizophrenia: sex, race and ethnicity in relation to social determinants of mental health

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Personalized psychiatry, dubbed ‘Precision Psychiatry’ is a field that has developed because of the many genetic findings that have recently emerged across all major psychiatric disorders and follows the lead from a similar focus in all medical disciplines. One medication, one dose and one treatment plan no longer is the way to treat all patients with similar diagnoses. There is a new journal in this field called *Personalized Medicine in Psychiatry*, published by Elsevier (https://www.journals.elsevier.com/personalized-medicine-in-psychiatry) and The first Congress of Precision Psychiatry was recently held this year (https://mghcme.org/syllabi/precision-psychiatry) as well. Despite these initiatives, precision psychiatry is still in its infancy. Yet, a few easily determined demographic factors can be taken into account to move towards more personalized treatment of patients with a psychosis.

Age has long been used for tailoring treatments [1], by reduced doses and treatment of concurrent medical comorbidities, but other factors are now recognized to be of importance for individualizing care, such as environmental social determinants of health, genetic variation and cognitive status. Sex of the individual has historically been only secondarily considered at best in psychiatric research. As a result, research that is specifically relevant to women in different age groups is scarce, specifically when considering type and dose of medications. How do we know that women have the same responses compared with men and metabolize the medications in a similar fashion? Certainly, their body fat distributions are different, as are other aspects of their physiology that are relevant to medication metabolism. Women with psychoses have a more variable age of onset, more predominant affective symptoms, milder negative symptoms and relative absence of comorbid substance abuse than men, for example [2]. The duration of untreated psychosis is longer in women than in men [3]. This does not mean that psychotic women are not receiving any care, they are in fact mostly in care, but for other disorders such as depression, anxiety disorder or personality disorder [2]. Yet, a longer duration of untreated illness (DUP) is a negative factor for outcome, so early detection programs specifically targeting women may do well to screen for psychosis among attendants of affective disorder programs.

This knowledge is generally not used to provide sex-specific psychosis care. A simple poll among Dutch psychiatrists showed that 79% provide similar treatment for men and women with psychoses, although it is not clear that they respond equally well to the same medications and at the same doses. After, or even before, diagnosis of a schizophrenia-spectrum disorder, many countries offer special early intervention care, tailored to the needs of patients with an (emerging) first psychosis. However, these early intervention services are perfectly tailored to the needs of male patients, not so much to those of female patients. Women often do not meet the age restrictions that many early intervention teams hold: a maximum age of 24 or 28, while female psychosis begins at a later age in some 50% of cases [4]. For women who do meet the age restrictions, the content of the program may not be suitable, as they often have family duties and drug abuse may not be a problem as it frequently is with men. Furthermore, many of the women need trauma-related therapy [5], which is not a general part of most early intervention services. Larger catchment areas may therefore consider early intervention programs for women with a first psychosis, which could include care for children, trauma-related therapy and attention to female sexual health [6].

Antipsychotics also need dosing by sex, with lower dose for most drugs for premenopausal...
race appears to be an all too easy and at sometimes erroneous marker for differences, overall, the genetics of population of origin is important. For example, gene variations for specific enzymes responsible for drug metabolism of carbamazepine and clozapine, and gene variation increasing risk for diseases, vary in prevalence in different populations throughout the world [13–15]. Although rare in one population, an allele could be common in another. Thus, geographic ancestral origin is important, although not race per se. Skin color is only a rough proxy for culture and geographic origin.

There appears to be an inherent bias that pervades our field that creates disparities within our system of mental healthcare between people of different races that was documented back as early as the 1990s [16]. It is not a bias that clinicians in general are aware of and, if asked, they would say that they act impartially and have no biases. Yet, these are part of the way in which the world is perceived by people of different backgrounds. For example, patients of an African–American heritage are significantly more likely to be diagnosed with schizophrenia than Whites [17,18]. The reason for this is highly unlikely to be biological, but rather related to personal bias when examining patients. Evaluations of patients to determine diagnosis and treatment to avoid bias can be performed in a manner that uses structured interview programs, such as a SKID interview [19] and using quantitative and structured rating scales of symptoms. Outcomes of schizophrenia are significantly more apt to be poor in those patients of Black descent than White [20]. The latter again is highly likely not to be biological, but more related to a reduced access to care and reduced engagement in care that also may be a consequence of socioeconomic differences [4,21–23]. To mitigate the differences in outcome, specific measures need to be taken to intervene and reach patients individualizing their care to accommodate their reluctance or the barriers that prevent them from engaging in treatment. Research needs to focus now on those importantly needed interventions.

In summary, there has been much focus recently on the measurement of ‘social determinants of health’ as factors not only determining treatment responses, but also as variables important to consider when implementing interventions [24,25]. It seems clear that ‘race’ and ‘ethnicity’ may only be proxies for social determinants of health, and thus, when reports are generated showing differences between racial and ethnic groups and White groups, the underlining cause is likely not their genetic differences, but their social ones. The reasons for the latter differences are very basic and largely implicit biases ingrained in each society. The first

women [7]. Antipsychotic drugs (such as amisulpride) that show excellent efficacy-tolerability for men may not be efficacious for women [8]. Prolactin-raising antipsychotics lower oestrogens and deprive women of their natural protection from severe negative symptoms [7]. Specific medication recommendations for women are clearly needed.

There are three other vulnerable groups for whom we could provide more personalized care. One is pregnant women, which is a specific group at risk for postpartum disease, including psychosis. Some countries, such as the UK [9] and Hong Kong screen for this potentially dangerous and rapidly evolving form of psychosis after giving birth [10], but most countries do not. As mothers of newborns are often in contact with medical caregivers, a psychiatric screening for emerging postpartum psychosis could prevent much suffering, and provides another step towards personalized psychosis care.

Transgender persons (both male to female and female to male) are at an increased risk for schizophrenia-spectrum disorders [11] and also need specific treatment trials that address medication doses and metabolism for these individuals, many who have undergone sex affirming hormone, as well as surgical treatments. Nonbinary people report that sex nonconformity and social designation can be incredible painful and childhood trauma is much higher in this group [11]. Diagnosis in transgender people can be complex resulting in a longer DUP. In this group, not only stigma and discrimination, but also gender-affirming care such as the use of hormones can affect mental health in a negative way. Little is known about how to improve diagnostic and treatment trajectories for this group, but as it is a growing minority, more research is needed urgently.

Postmenopausal women constitute another rather large, vulnerable and overlooked group. Oestrogens protect women from severe negative symptoms and also from cardiovascular comorbidities, but only until menopause. Oestrogens also modulate the CYP1A2 enzyme, which metabolizes most anti-psychotics and (except for quetiapine and luraside) dose adjustment is needed for these medications after menopause [7]. Further, hormonal replacement treatment, or raloxifene aug-mentation in some studies result in improvement in negative symptoms and cognition in postmenopausal women [12], yet hormonal replacement therapy is rarely part of clinical care. A specific consultation hour for menopausal women may be an excellent addition for psychiatric outpatient clinics.

Sex and gender are the easiest factors to consider in precision psychiatry. However, diversity is more than gender. Patients also tend to be defined by their race, ethnicity and cultural background. Although
step is to recognize these biases, and then this recognition needs to be followed by sustained methods for overcoming them. The goal for us in mental health research is to assure that all persons with mental illness have the opportunity to receive the same evidence-based treatments for their symptoms and have the same potential for recovery so that they may experience the best possible quality of life. In many cases, these treatments will not be the same for each person.

Acknowledgements
None.

Financial support and sponsorship
None.

Conflicts of interest
There are no conflicts of interest.

REFERENCES