ISSN 2220-3206 (online)

World Journal of *Psychiatry*

World J Psychiatr 2018 November 9; 8(5): 114-136

Published by Baishideng Publishing Group Inc

WJP World Journal of Psychiatry

Contents

Volume 8 Number 5 November 9, 2018

ABOUT COVER

Editorial Board Member of *World Journal of Psychiatry*, Vicki A Nejtek, PhD, Associate Professor, Director of Co-Occurring Disorders Research, University of North Texas Health Science Center, Texas College of Osteopathic Medicine, Taxs, TX 76107-266, United States

AIM AND SCOPE

World Journal of Psychiatry (*World J Psychiatr*, *WJP*, online ISSN 2220-3206, DOI: 10.5498) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJP covers topics concerning behavior and behavior mechanisms, psychological phenomena and processes, mental disorders, behavioral disciplines and activities, adjustment disorders, anxiety disorders, delirium, dementia, amnestic disorders, cognitive disorders, dissociative disorders, eating disorders, factitious disorders, impulse control disorders, mental disorders diagnosed in childhood, mood disorders, neurotic disorders, personality disorders, schizophrenia and disorders with psychotic features, sexual and gender disorders, sleep disorders, somatoform disorders, and substance-related disorders. Priority publication will be given to articles concerning diagnosis and treatment of psychiatric diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJP*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Psychiatry is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), China National Knowledge Infrastructure (CNKI), and Superstar Journals Database.

NAME OF JOURNAL
World Journal of Psychiatry

ISSN
ISSN 2220-3206 (online)

LAUNCH DATE
December 31, 2011

EDITORIAL BOARD MEMBERS
All editorial board members resources online at http://www.wjgnet.com/2220-3206/editorialboard.htm

EDITORIAL OFFICE
Jin-Lei Wang, Director
World Journal of Psychiatry
Baishideng Publishing Group Inc
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLISHER
Baishideng Publishing Group Inc
8226 Regency Drive,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLICATION DATE
November 9, 2018

INSTRUCTIONS TO AUTHORS
http://www.wjgnet.com/bpg/gerinfo/204

ONLINE SUBMISSION
http://www.f6publishing.com

World Journal of Psychiatry

Submit a Manuscript: http://www.f6publishing.com

World J Psychiatr 2018 November 9; 8(5): 125-136

DOI: 10.5498/wjp.v8.i5.125

ISSN 2220-3206 (online)

REVIEW

Women who suffer from schizophrenia: Critical issues

Mary V Seeman

Mary V Seeman, Department of Psychiatry, University of Toronto, Institute of Medical Science, Toronto, ON M5P 3L6, Canada

ORCID number: Mary V Seeman (0000-0001-6797-3382).

Author contributions: Seeman MV is the sole author and responsible for every aspect of this paper; she received no assistance and no funding.

Conflict-of-interest statement: None.

Manuscript source: Unsolicited manuscript

Correspondence to: Mary V Seeman, DSc, FRCP (C), MD, Emeritus Professor, Professor, Department of Psychiatry, University of Toronto, Institute of Medical Science, #605 260 Heath St. W., Toronto, ON M5P 3L6, Canada. mary.seeman@utoronto.ca
Telephone: +1-416-4863456

Received: July 18, 2018
Peer-review started: July 18, 2018
First decision: August 2, 2018
Revised: August 24, 2018
Accepted: October 11, 2018
Article in press: October 11, 2018
Published online: November 9, 2018

Abstract

Many brain diseases, including schizophrenia, affect men and women unequally - either more or less frequently, or at different times in the life cycle, or to varied degrees of severity. With updates from recent findings, this paper reviews the work of my research group over the last 40 years and underscores issues that remain critical to the optimal care of women with schizophrenia, issues that overlap with, but are not identical to, the cares and concerns of men with the same diagnosis. Clinicians need to be alert not only to the overarching needs of diagnostic groups, but also to the often unique needs of women and men.

Key words: Schizophrenia; Women; Gender differences; Unmet needs

Core tip: Schizophrenia and related disorders are expressed differently in men and women. Causative factors may differ, as can the expression, timing and severity of symptoms. Prevention, course of illness, and treatment response are all intimately linked to gender.

Seeman MV. Women who suffer from schizophrenia: Critical issues. *World J Psychiatr* 2018; 8(5): 125-136 Available from: URL: http://www.wjgnet.com/2220-3206/full/v8/i5/125.htm DOI: http://dx.doi.org/10.5498/wjp.v8.i5.125

INTRODUCTION

This review focuses on my experience dealing with clinical issues critical to women with schizophrenia. My work in this field began many years ago, and results are being continually updated as new information emerges. The paper is divided into the following main sections: Potential prevention strategies for women, the need for early and accurate diagnosis, the troubling complexities of the mental health system, effective treatment of schizophrenia and avoidance of adverse effects, the provision of access to vocational and avocational opportunities, attention to stigma, self-harm and suicide, the need for maintenance of physical, reproductive, and

emotional health. Many of these issues are not specific to schizophrenia, nor are they all specific to women. But, directly or indirectly, they all bear on the health and well being of women with schizophrenia.

In each of the sections listed above, I reference my own work plus recent key papers from the PubMed database. Most of these topic areas continue to be the focus of intense research, and many questions await resolution. The paper ends by broadly outlining future directions for the field.

POTENTIAL PREVENTION STRATEGIES

Schizophrenia is defined by its symptoms, which are thought to arise from the interaction of inherited or *de novo* genetic polymorphisms with exposure to environmental stressors at critical periods of a person's life. The details of specific gene mutations, the severity and identity of stressors, and critical chronology remain largely unknown. The strongest contributor to identifiable disease risk is a history of schizophrenia in close family members[1]. Knowledge of family history can now be combined with genetic risk scores from whole genome scans, which together, provide valuable information about a person's vulnerability to schizophrenia[2]. Nevertheless, when it comes to prevention, even in the era of Clustered Regularly Interspaced Short Palindromic Repeats (commonly known as CRISPR)[3], it is not possible to edit out the hundreds of genes that potentially contribute to schizophrenia in any one individual. Even if in the future all suspicious genes could be eliminated, profound ethical concerns make this form of prevention doubtful[4,5].

Some investigators believe that prevention strategies for men and women need to differ. The genetic predisposition to schizophrenia may, for instance, be sexually dimorphic[6-8], although evidence for this is sparse. On the other hand, because male and female DNA is so often exposed to somewhat dissimilar environmental inputs, it may well transpire that the turning off and on of genes in particular sets of cells - the domain of epigenetics - is relatively sex-specific. Therefore, developments in epigenetics may one day enable the prevention of sex-specific expression of schizophrenia-inducing genes[9,10]. However, for the time being, genetic counseling for women and men[11] and individual contraception counseling[12] are the best ways to try to prevent the transmission of schizophrenia at the gene level.

Women with schizophrenia planning to be mothers and wanting to prevent schizophrenia in their offspring can be counseled (although this is, of course, impractical) to choose relatively young - but not too young - mates with no family history of psychosis[13] and to strategically plan the conception in order to avoid giving birth during late winter or early spring[14]. There is no direct evidence that this will work to prevent schizophrenia in the next generation, but there is an association (which does not imply causation) between season of birth and schizophrenia in offspring. The potential connection has been attributed either to fetal and/or neonatal exposure to infectious/immune factors or to the lack of sunlight and low levels of vitamin D. Associated preventive measures include adequate nutrition during pregnancy, and Vitamin D and folic acid supplements[15]. Other suggestions for mothers with schizophrenia to boost the health of their infants are: limits on maternal weight gain during pregnancy, appropriate immunization, low doses of antipsychotic (AP) drugs during pregnancy and lactation, abstention from tobacco, alcohol and other substances[16-18], and rapid treatment of infection and inflammation[19-21]. Nutritional deficiency, stress, and toxic substances in pregnant women have long been recognized to increase the risk for schizophrenia in offspring[22-24]. Infection, inflammation and immune reactivity have more recently been considered serious contributors to schizophrenia susceptibility[21,25].

Obstetric complications pose a potential risk to the infant brain. They are more common in the birth history of those who go on to develop schizophrenia than in their psychiatrically well peers, but it is not known whether obstetric complications arise from prior fetal problems or whether they result from substandard obstetric care[26,27]. Regardless, women with schizophrenia require exemplary care during pregnancy, labor, and delivery. The quality of maternal care of young children is also critical, as early physical and psychological trauma have been associated (again, this is an association that may not be contributory) with the later development of schizophrenia[26,28,29]. Such trauma is theoretically preventable through parent support and parent training groups, family health education, and child welfare monitoring, but interventions such as these require intensive collaborative work at the level of whole communities.

Further theoretical possibilities for prevention (based entirely on studies of association) are keeping children in their country of birth, since migration is a risk factor for schizophrenia[30,31], residing in rural rather than urban parts of the country[32,33], keeping children and adolescents away from alcohol and drugs[34] and teaching them emotion-regulating strategies (reappraising, accepting, and refocusing[35]) to prevent adversities such as discrimination and social defeat from culminating in paranoid delusions[36].

Given that fewer women than men are reported to develop schizophrenia (2/1 male/female ratio in the under-20 age bracket, although the discrepancy tends to even out with increasing age)[37], that the "female" hormone estrogen is known to be neuroprotective[38,39], and that women are especially vulnerable to psychosis during the postpartum period when estrogen levels precipitously drop[40], my research group predicted in the 1990s that, among women with schizophrenia, girls with early menarche (early pubertal rise in estrogen levels) would show a later onset of schizophrenia than girls who enter puberty at older ages[41]. This is precisely what we found in our clinic population, and this finding has been replicated by some groups, but not by all[42-44].

If accurate, this observation could lead to weight gain strategies[45] that bring menarche forward. This would, of course, not prevent schizophrenia, but might delay its onset in vulnerable women.

Knowing that low estrogen periods are times of special risk for psychotic episodes is especially useful for secondary prevention (prevention of recurrent episodes of psychosis) in women diagnosed with schizophrenia. Relapse can be prevented by increasing the dose of AP medication at low estrogen times in the menstrual month[46,47], during the postpartum period[48], after menopause[49,50], whenever therapeutic estrogen is stopped[51,52], or during therapy with anti-estrogen drugs[53,54]. These theoretical examples suggest that effective prevention of schizophrenia may, in the future, be possible in a sex-specific manner[55,56], though this is not the case presently.

EARLY ACCURATE DIAGNOSIS

It is well-established that delay in seeking treatment once psychotic symptoms have emerged is associated with impaired treatment response and a relatively poor prognosis[57]. Our group found that, on retrospective interview, the first sign of behavioral disturbance eventually leading to a diagnosis of schizophrenia occurred at approximately the same age in women and men, but that the pre-psychotic prodrome was almost twice as long for women[58]. The duration of untreated psychosis did not differ between the two sexes, but the interval between first behavioral sign and first treatment did - the lag was six years for men and nine years for women[58]. The corollary to this finding is that factors other than early diagnosis must determine prognosis because women's outcome relative to men's, despite a longer untreated interval, is generally superior, at least over the reproductive years[59,60]. Potential factors that favor women, besides estrogen levels, are premorbid functioning generally superior to that of premorbid men, more friendships, closer family relations, greater academic success, and a relative absence of substance abuse[61-63].

As important as the speed of diagnosis is its accuracy. Diagnosis leads, at least in theory, to disease-specific treatment, although this is not always true in psychiatry where illness categories often overlap and the same treatments are used for different diagnostic entities. Nevertheless, it is my clinical experience that women's diagnoses frequently changes from depression to posttraumatic stress syndrome to eating disorder to schizophrenia to bipolar disorder (not necessarily in that order). This may be because it is more difficult to apply textbook schizophrenia criteria to women than to men. Women do not always exhibit the characteristic symptoms; they show few "negative" symptoms, few cognitive symptoms, and they rarely show flattened affect[64-66]. Prior to being diagnosed with a schizophrenia-related disorder, women with psychosis are often considered to be suffering from a mood disorder whereas, in men, a first tentative diagnosis is frequently alcohol or drug-induced psychosis[67]. Differential diagnoses sometimes missed in women include thyroid disease, autoimmune disorder, corticosteroid treatment, and anorexia-related starvation. All these conditions are much more prevalent in women than in men[68,69] and need to be ruled out before a diagnosis of schizophrenia is made.

COMPLEXITY OF THE MENTAL HEALTH SYSTEM

The mental health system in most countries is very complex and leaves individuals who experience mental distress not knowing whether to turn to physicians or social workers or psychologists or spiritual counselors. Family doctors may or may not recognize symptoms of early psychosis and, even when they do, may not know where to refer their patients. Waiting lists for the various mental health professionals are often long. Visits may or may not be covered by available insurance. Navigation services that help patients identify financial, linguistic, cultural, logistical and educational barriers to mental health care and provide guidance to access are badly needed by both women and men[70]. The routes to care differ in the two sexes, obstetricians and midwives sometimes serving as intermediaries for women, and guidance counselors and police more often paving care routes for men.

EFFECTIVE TREATMENT

Treatment is known to be most effective when it is individualized to meet the specific needs of the person being treated. Gender, age, family situation, place of residence, state of health, and personal preferences all play a part in determining optimal intervention. One example is the decision-making process around drug dosing. In women of reproductive age, effective drug doses can usually be lower than doses recommended for men[71-75]. Women's ability to respond at lower doses has been attributed to the effects of female hormones on the absorption and metabolism of AP drugs and also to women's relatively increased blood flow to the brain, carrying with it more drug to cell receptor targets[76]. The presence of estrogen at the dopamine receptor site helps to slow the transmission of dopamine[77], an excess of which is thought responsible for psychotic symptoms.

In addition, because AP drugs are lipophilic and women's reserves of adipose tissue are on average larger than men's, women store these drugs in their bodies for comparatively longer periods. This means that psychotic relapse after drug discontinuation is not as rapid in women[78-80]. It also means that, in theory, the intervals between women's intramuscular depot AP injections can be longer than those in men, but the sex-specific spacing of AP depot drugs has not yet been researched.

Another reason why AP drug doses can generally be

Table 1 Side effects of antipsychotics that negatively affect appearance[124]

Weight gain
Bad teeth
Hirsutism
Acne
Hair loss
Salivation
Slurred speech
Blepharospasm
Parkinsonian gait
Dyskinesias
Urinary incontinence

lower in women than in men is because many women take more concomitant drugs than men do, notably antidepressants, mood stabilizers, analgesics, and contraceptives or hormone replacements, all of which can interact with and influence the blood level of AP medication[78,81].

An important aspect of pharmacotherapy for women is that levels of female hormones change over the course of a monthly cycle and also over reproductive phases such as pregnancy, lactation, and menopause. This affects the dosage requirement of AP medication, *i.e.*, there will be a need for higher doses during low estrogen phases[47-50,82,83]. Adjunctive estrogen or selective estrogen receptor modulators can make treatment more effective and can reduce AP doses and, thus, help to prevent side effects. This applies to both sexes, but is especially applicable to women[84-90].

Besides pharmacotherapy, other aspects of schizophrenia treatment need to be differentiated according to the patient's gender, *e.g.*, substance abuse treatment, cancer screening (breast, prostate, cervix)[91-96], interventions for sexual dysfunction[97-99], contraceptive prescribing[12], treatment of comorbidities (osteoporosis and cardiovascular care for instance[100,101]), safeguards against domestic abuse and victimization[102-108], screening for proclivity to violence[109], provision of parenting support and child custody issues[110-112].

DRUG SIDE EFFECTS

Effective treatment means the removal of symptoms and improvement of function; ideally, it also means freedom from adverse side effects. Side effects cause distress, stop patients from regularly taking the medicines they need, and often cause serious harm to health, perhaps even contributing to the high mortality rate among individuals with schizophrenia[113]. Unfortunately, AP medications have many side effects[114] and on average, women suffer more negative effects than men[115,116]. Women may be more vulnerable than men to adverse drug reactions because the doses recommended when a drug goes on the market are calculated on the basis of a 70 kg man.

There are well-known gender differences in drug reactions. In a recent study of over a thousand patients with psychosis, twice as many women as men described their side effect burden as severe. In this study[117], the effects that women complained of (more than men) included: Concentration difficulties, sedation, blurred vision, nausea, constipation, dizziness on rising, heart palpitations, pruritus, photosensitivity, increased pigmentation, weight change, galactorrhoea and headache.

Women have unique risk factors for some adverse effects of APs, such as Torsade de Pointes[118], which is a form of ventricular tachycardia that occurs in patients whose QT interval is relatively long. The QT interval is a measure of the time between the start of the Q wave and the end of the T wave on the electrocardiogram; it is the time it takes for the heart to come back to normal after depolarization, which, on average, is longer in postpubertal women than it is in men. For this reason, two-thirds of Torsade de Pointes occur in women[118]. That being said, more men with schizophrenia than women die of heart disease. Much remains unknown about gender differences in cardiovascular function and cardiac response to therapeutic drugs.

The hypercoagulability state induced by APs raises the risk for venous thromboembolism, pulmonary embolism, and cerebrovascular accident. The use of oral contraceptives, as well as hormone replacement therapies, pregnancy, the immediate postpartum state, and obstetrical complications are all risk factors for these complications[119]. There are many such factors, however, including ethnicity[120]. Despite the many contributing factors, pregnant women on APs have been shown to be at significantly higher risk for venous thromboembolism than pregnant women in the general population[121,122].

With respect to the potential for AP to heighten the risk of breast cancer *via* weight gain and prolactinemia, the jury is still out[94] on this important concern. What is known, however, is that the cancer death rate of women with schizophrenia is high relative to women in the general population[95], although this cannot be attributed to AP drugs. Many side effects of APs, *e.g.*, weight gain, skin blemishes, and hair loss[123], negatively affect appearance (Table 1)[124]. Women are more sensitive to such effects than men are.

APs also have negative reproductive effects. They can disrupt menstrual cycles[125], interfere with a woman's ability to conceive[126], increase the risk for gestational diabetes[127], increase the risk of premature labor[127] and, by entering breast milk, can make breastfeeding a risk for infants of mothers with schizophrenia[128]. The secondary effect of hyperprolactinemia can lead to hirsutism, amenorrhea, galactorrhea, pseudocyesis[129], and osteoporosis[125].

In addition, older women may be more susceptible than older men to tardive dyskinesia (TD)[114]. It is known that TD prevalence is influenced not only by age and sex, but also by many confounding factors, such as individual genetics[130], the specific AP used, its dose, treatment duration, alcohol, tobacco, and marijuana usage, ethnicity, the precise definition of TD, the rating

scale used to assess TD, the predominant symptoms (positive or negative) and the presence or absence of prior brain damage. Because estrogen modulates dopamine-mediated behaviors and protects against oxidative stress-induced cell damage caused by long-term exposure to AP medication, one hypothesis is that when all the confounding factors are controlled, TD prevalence is equal in women and men prior to menopause and becomes subsequently higher in women[131].

Because of sex differences in immunity, women are also more susceptible to the agranulocytosis inducible by clozapine[132]. In general, older individuals, men as well as women, are at relatively increased risk of adverse effects of all drugs[133].

VOCATIONAL AND AVOCATIONAL OPPORTUNITIES

Women with schizophrenia want meaning in their lives, as do men. Meaning comes in several forms: hope in the future, the belief that one is needed, interest in what one is doing, earning money, engaging in artistic endeavors, pursuing a goal. In our study of clinic members with longstanding schizophrenia, more women than men were working outside the home[134], probably because "women's" jobs were more plentiful at the time in our region. Job availability always depends on time, place, and economic conditions. When homeless, or living in room and board homes or with parents, the housewife role is not readily available to women with schizophrenia. Many prefer self-employment opportunities[135] and appreciate assistance in the form of supported employment, individual placement, and job buddies. They welcome opportunities to learn, to volunteer and to be of help to others. Like men, women need creative channels to enable self-expression as they seek ways to be meaningfully occupied[136].

FREEDOM FROM STIGMA

Stigma (being devalued and discriminated against, with consequent loss of self-respect) is a significant problem in schizophrenia[137]. The diagnostic label of schizophrenia is itself frightening to many people, conjuring up fears of dangerousness, unprovoked and uncontrollable violence, irrationality, and incurability. The population at large does not always appreciate the fact that those who suffer from schizophrenia, and this is especially true for women, are more often victims than perpetrators of violence[138]. Different studies have used different definitions of both violence and of victimization, making these terms difficult to quantify across studies. Within a one-year period, it has been estimated that between 11% and 52% of persons with serious mental illness (SMI) exhibit violence at a 2-8 higher rate than that found in the general population[139]. The same study found rates of victimization in persons with SMI to be between 20% and 42%, 23 times that of the general population. Perpetration of violence and victimization are risk factors for each other and often overlap in the same person. Interestingly, Desmarais *et al*[139] reported higher rates of perpetration of violence among women with SMI than among men. They speculate that this is due to the fact that violence in this population most often occurs in the context of close relatives, and women with SMI are more likely than men to be living with family; consequently, they have more opportunity to vent their rage at domestic targets such as husbands and parents.

Women with schizophrenia are too often victims of sexual exploitation, domestic abuse, and random violence[106-108]. Risk factors are age, place of residence, and degree of psychopathology, in addition to personality and behavioral factors[140]. The factors that contribute to the perpetration of violence have been described by the same research team as substance abuse, young age, homelessness, unemployment, low educational attainment, low socioeconomic status, membership in an ethnic minority, past hospitalization for psychosis, past conviction for violent crime, personality factors, and residence in disorganized neighborhoods[140]. These are risk factors for both women and men, but they occur more frequently in men.

In general, schizophrenia is a heavily stigmatized illness, men perhaps suffering more than women because of the perception that they are prone to act out violently and indiscriminately. Women, however, suffer from a specific form of stigma - the frequent conviction of health workers that individuals with schizophrenia should not bear children, and, in the event of pregnancy, should seek abortion. Women with this illness are widely considered incapable of being good mothers, making prenatal care more problematic, as women fear disclosing that they are pregnant, afraid that their infants will be apprehended at birth[141,142]. Healthcare professionals may not be aware of their own discriminatory attitudes, often communicated inadvertently by words and gestures[143]. Finding effective ways of combating biased attitudes both in oneself and in others is a critical issue for all care providers treating patients with stigmatized illnesses.

RELIEF FROM THOUGHTS OF SELF-HARM AND SUICIDE

In the context of schizophrenia, triggers for male suicidal activity (ideation, attempts, and completed suicide) have been described as being: (1) psychotic symptoms and (2) the prospect of chronic disability, while triggers for suicidal activity in women have been mainly attributed to depression. Male suicides in this population decline with age, whereas this is not the case for women. In a longitudinal study, a 10.5% rate of suicide in the first two years after hospital discharge in men dropped to 0% twenty years later, while women's rate of suicide (6%) was spread more evenly over the twenty years[144].

Table 2 Existential concerns[179,180]

Meaning
Fear
Justice
Mortality
Identity
Relatedness
Freedom of choice

Suicide in women with schizophrenia is not as rare (relative to men) as it is in the general population[145]. The clinical implications are that both depression and substance abuse need to be vigorously treated in patients with schizophrenia because both contribute to impulsive acts of self-harm. In treatment settings, suicidal ideas are often "contagious"[146], with one completed suicide sometimes sparking a series of further self-harm attempts[147]. The index of suspicion needs to be high and suicidal ideation needs to be taken seriously[148].

PHYSICAL HEALTH

The life expectancy of individuals with schizophrenia is significantly shorter than that of the general population, with 90% of deaths attributable to physical illness. The assumption is that early mortality in schizophrenia is secondary, if not to suicide, then to lifestyle factors such as heavy smoking, alcohol abuse, and lack of physical activity[149-151]. More recently, a new understanding of the brain-gut connection[152] has implicated nutritional factors. In addition, there is the probability of shared susceptibility genes between schizophrenia and physical diseases that can decrease health-related quality of life and hasten death, auto-immune disease (*e.g.*, Crohn's disease, multiple sclerosis, systemic lupus erythematosus, type 1 diabetes, and ulcerative colitis) being one such category of illness[153].

Social precipitants of early death are critical in this population: Poverty[154], homelessness[155], social isolation[156], poor hygiene[157], malnourishment[158], exposure to toxic substances[159] and adverse treatment effects[114]. High mortality from diabetes, cardiovascular disease and malignancies can, in part, be due to a relative lack of screening, delays in diagnosis, and suboptimal treatment[94,95,160-162]. Javatilleke *et al*[163] conclude their list of causes of lost life expectancy in severe mental illness by pointing out that the range of causes is very broad, with many putative causes varying according to gender.

REPRODUCTIVE HEALTH

Reproductive health includes sexual health (libido, sexual function, the ability to establish and maintain sexual relationships)[99,164,165], menstrual health[47,125,166], the preservation of fertility[167,168], contraception[12], prenatal care[122], pregnancy[18,169], postpartum care[170] and lactation support[171], parenting support and training groups, home visiting, peer support, respite care[111,112,172,173], and menopausal care[49,50,83,174].

Clinicians may not realize that during pregnancy, physiological changes such as delay in gastric emptying and increase in gastric pH prolong the time it takes for AP drugs to reach peak levels. Increased cardiac output steps up blood flow to the liver and may boost the speed of drug elimination. There is an overall increase in body water, which only affects hydrophilic drugs such as lithium, and there is also an increase in the lipid compartment, which provides extra storage space for lipophilic drugs (including APs). The blood flow to the kidneys is increased, as is the glomerular filtration rate, which means a greater degree of renal clearance. The plasma albumin concentration is reduced so that more free drug is available to the brain. Enzyme activity is affected by the increase in pregnancy hormones; some enzymes are affected more than others. For most APs, the net serum concentration in the third trimester is significantly decreased from what it was at the beginning of pregnancy. The exceptions are olanzapine and clozapine, both of which are inactivated by Cytochrome P450 enzyme 1A2, whose activity decreases during the 2nd and 3rd trimester of pregnancy because of rising estrogen levels. This enzyme is also highly inducible by smoking and, since women tend to reduce their cigarette smoking during pregnancy, the activity of this enzyme is further reduced. Therefore, the serum levels of olanzapine and clozapine rise during pregnancy[175-177].

FURTHER AREAS OF CONCERN

There are other areas of concern to women with schizophrenia. Some of these are the availability of crisis support[178], the achievement of nightmare-free restorative sleep[179-182], the safety of treatment settings[104,183], the safety and affordability of housing[184], access to skills training in new technologies[185] and assistance with existential concerns[186,187]. Whereas existential issues such as free will, personal identity, fears for the future, contemplation of mortality, justice concerns, finding meaning in life, and relating to others are all similar in men and women, as women age, they express more security fears, while aging men are more likely to report not being valued and fearing that they are a burden to others. Physical appearance may be more central to identity for women than for men[188] (Table 2).

FUTURE DIRECTIONS

Many of the issues that are critical to the care provision of women diagnosed with schizophrenia stem from a failure to recognize male/female differences in this illness. Sex differences are based in dimorphic brain structure and function, particularly evident in the dopaminergic system that is so crucial to the development of schizophrenia[189]. They are driven by sex hormones, but also depend, to an extent not yet fully understood, on non-gonadal functions of the X and

Y chromosomes because genes on sex chromosomes influence brain development disproportionally to their relatively small number. The number of sex chromosomes, X chromosome inactivation patterns, X-linked imprinting effects, and the indirect effects of sex chromosomes on the expression of autosomal genes all contribute to sex differences in neuropsychiatric disease[190].

Future research into sex differences in brain disorders such as schizophrenia will benefit from a fuller understanding of the causes of sex differences and their effects not only on brain and behavior but also on metabolic, cardiovascular, inflammatory and immune parameters. The field also needs to better understand the timing of the emergence of sex differences. Longitudinal studies that track developmental processes over time are needed. The effect of puberty with its influx of sex-specific hormones on brain maturation needs to be better understood. Biological sex differences need to be disentangled from environmental influences, an important issue for all psychiatric diseases. Sex differences in the brain, whether innate or secondary to exposure and learning, confer differential risk or resilience that fosters or inhibits the expression of specific symptoms, psychiatric diagnoses, and their outcomes.

REFERENCES

1 **Murray RM**, Lewis SW, Reveley AM. Towards an aetiological classification of schizophrenia. *Lancet* 1985; **1**: 1023-1026 [PMID: 2859472 DOI: 10.1016/S0140-6736(85)91623-X]
2 **Lu Y**, Pouget JG, Andreassen OA, Djurovic S, Esko T, Hultman CM, Metspalu A, Milani L, Werge T, Sullivan PF. Genetic risk scores and family history as predictors of schizophrenia in Nordic registers. *Psychol Med* 2018; **48**: 1201-1208 [PMID: 28942743 DOI: 10.1017/S0033291717002665]
3 **Sander JD**, Joung JK. CRISPR-Cas systems for editing, regulating and targeting genomes. *Nat Biotechnol* 2014; **32**: 347-355 [PMID: 24584096 DOI: 10.1038/nbt.2842]
4 **Brokowski C**, Pollack M, Pollack R. Cutting eugenics out of CRISPR-Cas9. *Ethics Biol Eng Med* 2015; **6**: 263-279 [DOI: 10.1615/EthicsBiologyEngMed.2016016260]
5 **Sugarman J**. Ethics and germline gene editing. *EMBO Rep* 2015; **16**: 879-880 [PMID: 26138102 DOI: 10.15252/embr.201540879]
6 **Bergen SE**, O'Dushlaine CT, Lee PH, Fanous AH, Ruderfer DM, Ripke S; International Schizophrenia Consortium, Swedish Schizophrenia Consortium, Sullivan PF, Smoller JW, Purcell SM, Corvin A. Genetic modifiers and subtypes in schizophrenia: investigations of age at onset, severity, sex and family history. *Schizophr Res* 2014; **154**: 48-53 [PMID: 24581549 DOI: 10.1016/j.schres.2014.01.030]
7 **Goldstein JM**, Cherkerzian S, Tsuang MT, Petryshen TL. Sex differences in the genetic risk for schizophrenia: history of the evidence for sex-specific and sex-dependent effects. *Am J Med Genet B Neuropsychiatr Genet* 2013; **162B**: 698-710 [PMID: 24132902 DOI: 10.1002/ajmg.b.32159]
8 **Magi R**, Lindgren CM, Morris AP. Meta-analysis of sex-specific genome-wide association studies. *Genet Epidemiol* 2010; **34**: 846-853 [PMID: 21104887 DOI: 10.1002/gepi.20540]
9 **Kundakovic M**. Sex-specific epigenetics: Implications for environmental studies of brain and behavior. *Curr Environ Health Rep* 2017; **4**: 385-391 [PMID: 28986864 DOI: 10.1007/s40572-017-0172-x]
10 **Ratnu VS**, Emami MR, Bredy TW. Genetic and epigenetic factors underlying sex differences in the regulation of gene expression in the brain. *J Neurosci Res* 2017; **95**: 301-310 [PMID: 27870402 DOI: 10.1002/jnr.23886]
11 **Costain G**, Bassett AS. Clinical applications of schizophrenia genetics: genetic diagnosis, risk, and counseling in the molecular era. *Appl Clin Genet* 2012; **5**: 1-18 [PMID: 23144566 DOI: 10.2147/TACG.S21953]
12 **Seeman MV**, Ross R. Prescribing contraceptives for women with schizophrenia. *J Psychiatr Pract* 2011; **17**: 258-269 [PMID: 21775827 DOI: 10.1097/01.pra.0000400263.52913.dc]
13 **Frans E**, MacCabe JH, Reichenberg A. Advancing paternal age and psychiatric disorders. *World Psychiatry* 2015; **14**: 91-93 [PMID: 25655163 DOI: 10.1002/wps.20190]
14 **Escott-Price V**, Smith DJ, Kendall K, Ward J, Kirov G, Owen MJ, Walters J, O'Donovan MC. Polygenic risk for schizophrenia and season of birth within the UK Biobank cohort. *Psychol Med* 2018: 1-6 [PMID: 29501066 DOI: 10.1017/S0033291718000454]
15 **Hollis BW**, Johnson D, Hulsey TC, Ebeling M, Wagner CL. Vitamin D supplementation during pregnancy: double-blind, randomized clinical trial of safety and effectiveness. *J Bone Miner Res* 2011; **26**: 2341-2357 [PMID: 21706518 DOI: 10.1002/jbmr.463]
16 **Seeman MV**, Cohen R. A service for women with schizophrenia. *Psychiatr Serv* 1998; **49**: 674-677 [PMID: 9603575 DOI: 10.1176/ps.49.5.674]
17 **Seeman MV**. Prevention inherent in services for women with schizophrenia. *Can J Psychiatry* 2008; **53**: 332-341 [PMID: 18551854 DOI: 10.1177/070674370805300508]
18 **Seeman MV**. Clinical interventions for women with schizophrenia: pregnancy. *Acta Psychiatr Scand* 2013; **127**: 12-22 [PMID: 22715925 DOI: 10.1111/j.1600-0447.2012.01897.x]
19 **Brown AS**, Patterson PH. Maternal infection and schizophrenia: implications for prevention. *Schizophr Bull* 2011; **37**: 284-290 [PMID: 21134972 DOI: 10.1093/schbul/sbq146]
20 **Meyer U**. Developmental neuroinflammation and schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry* 2013; **42**: 20-34 [PMID: 22122877 DOI: 10.1016/j.pnpbp.2011.11.003]
21 **Solek CM**, Farooqi N, Verly M, Lim TK, Ruthazer ES. Maternal immune activation in neurodevelopmental disorders. *Dev Dyn* 2018; **247**: 588-619 [PMID: 29226543 DOI: 10.1002/dvdy.24612]
22 **Brown AS**, Susser ES. Prenatal nutritional deficiency and risk of adult schizophrenia. *Schizophr Bull* 2008; **34**: 1054-1063 [PMID: 18682377 DOI: 10.1093/schbul/sbn096]
23 **Jablensky AV**, Morgan V, Zubrick SR, Bower C, Yellachich LA. Pregnancy, delivery, and neonatal complications in a population cohort of women with schizophrenia and major affective disorders. *Am J Psychiatry* 2005; **162**: 79-91 [PMID: 15625205 DOI: 10.1176/appi.ajp.162.1.79]
24 **van Os J**, Selten JP. Prenatal exposure to maternal stress and subsequent schizophrenia. The May 1940 invasion of The Netherlands. *Br J Psychiatry* 1998; **172**: 324-326 [PMID: 9715334 DOI: 10.1192/bjp.172.4.324]
25 **Müller N**. Inflammation in schizophrenia: Pathogenic aspects and therapeutic considerations. *Schizophr Bull* 2018; **44**: 973-982 [PMID: 29648618 DOI: 10.1093/schbul/sby024]
26 **Belbasis L**, Köhler CA, Stefanis N, Stubbs B, van Os J, Vieta E, Seeman MV, Arango C, Carvalho AF, Evangelou E. Risk factors and peripheral biomarkers for schizophrenia spectrum disorders: an umbrella review of meta-analyses. *Acta Psychiatr Scand* 2018; **137**: 88-97 [PMID: 29288491 DOI: 10.1111/acps.12847]
27 **Buoli M**, Bertino V, Caldiroli A, Dobrea C, Serati M, Ciappolino V, Altamura AC. Are obstetrical complications really involved in the etiology and course of schizophrenia and mood disorders? *Psychiatry Res* 2016; **241**: 297-301 [PMID: 27232550 DOI: 10.1016/j.psychres.2016.05.014]
28 **Abajobir AA**, Kisely S, Scott JG, Williams G, Clavarino A, Strathearn L, Najman JM. Childhood maltreatment and young adulthood hallucinations, delusional experiences, and psychosis: A longitudinal study. *Schizophr Bull* 2017; **43**: 1045-1055 [PMID: 28338760 DOI: 10.1093/schbul/sbw175]

29 **Morgan C**, Fisher H. Environment and schizophrenia: environmental factors in schizophrenia: childhood trauma--a critical review. *Schizophr Bull* 2007; **33**: 3-10 [PMID: 17105965 DOI: 10.1093/schbul/sbl053]

30 **Alegría M**, Álvarez K, DiMarzio K. Immigration and mental health. *Curr Epidemiol Rep* 2017; **4**: 145-155 [PMID: 29805955 DOI: 10.1007/s40471-017-0111-2]

31 **Hogerzeil SJ**, van Hemert AM, Veling W, Hoek HW. Incidence of schizophrenia among migrants in the Netherlands: a direct comparison of first contact and longitudinal register approaches. *Soc Psychiatry Psychiatr Epidemiol* 2017; **52**: 147-154 [PMID: 27847980 DOI: 10.1007/s00127-016-1310-8]

32 **DeVylder JE**, Kelleher I, Lalane M, Oh H, Link BG, Koyanagi A. Association of urbanicity with psychosis in low-andmiddle-inclome countries. *JAMA Psychiatry* 2018; **75**: 678-686 [PMID: 29799917 DOI: 10.1001/jamapsychiatry.2018.0577]

33 **Plana-Ripoll O**, Pedersen CB, McGrath JJ. Urbanicity and risk of schizophrenia - new studies and old hypotheses *JAMA Psychiatry* 2018; **75**: 687-688 [PMID: 29799914 DOI: 10.1001/jamapsychiatry.2018.0551]

34 **Nielsen SM**, Toftdahl NG, Nordentoft M, Hjorthøj C. Association between alcohol, cannabis, and other illicit substance abuse and risk of developing schizophrenia: a nationwide population based register study. *Psychol Med* 2017; **47**: 1668-1677 [PMID: 28166863 DOI: 10.1017/S0033291717000162]

35 **Lincoln TM**, Sundag J, Schlier B, Karow A. The relevance of emotion regulation in explaining why social exclusion triggers paranoia in individuals at clinical high risk of psychosis. *Schizophr Bull* 2018; **44**: 757-767 [PMID: 29878274 DOI: 10.1093/schbul/sbx135]

36 **Selten JP**, Booij J, Buwalda B, Meyer-Lindenberg A. Biological mechanisms whereby social exclusion may contribute to the etiology of psychosis: A narrative review. Schizophr Bull 2017; **43**: 287-292 [PMID: 28053019 DOI: 10.1093/schbul/sbw180]

37 **McGrath J**, Saha S, Chant D, Welham J. Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidemiol Rev* 2008; **30**: 67-76 [PMID: 18480098 DOI: 10.1093/epirev/mxn001]

38 **Agius M**, Hockings H, Wilson C, Lane D. Is oestrogen neuroprotective? *Psychiatr Danub* 2009; **21** Suppl 1: 120-127 [PMID: 19789496]

39 **Brann DW**, Dhandapani K, Wakade C, Mahesh VB, Khan MM. Neurotrophic and neuroprotective actions of estrogen: basic mechanisms and clinical implications. *Steroids* 2007; **72**: 381-405 [PMID: 17379265 DOI: 10.1016/j.steroids.2007.02.003]

40 **Jones I**, Chandra PS, Dazzan P, Howard LM. Bipolar disorder, affective psychosis, and schizophrenia in pregnancy and the post-partum period. *Lancet* 2014; **384**: 1789-1799 [PMID: 25455249 DOI: 10.1016/S0140-6736(14)61278-2]

41 **Cohen RZ**, Seeman MV, Gotowiec A, Kopala L. Earlier puberty as a predictor of later onset of schizophrenia in women. *Am J Psychiatry* 1999; **156**: 1059-1064 [PMID: 10401452 DOI: 10.1176/ajp.156.7.1059]

42 **Kiliçaslan EE**, Erol A, Zengin B, Çetinay Aydin P, Mete L. Association between age at onset of schizophrenia and age at menarche. *Noro Psikiyatr Ars* 2014; **51**: 211-215 [PMID: 28360628 DOI: 10.4274/npa.y6675]

43 **Ullsperger JM**, Nikolas MA. A meta-analytic review of the association between pubertal timing and psychopathology in adolescence: Are there sex differences in risk? *Psychol Bull* 2017; **143**: 903-938 [PMID: 28530427 DOI: 10.1037/bul0000106]

44 **Ruiz A**, Blanco R, Santander J, Miranda E. Relationship between sex differences in onset of schizophrenia and puberty. *J Psychiatr Res* 2000; **34**: 349-353 [PMID: 11104849 DOI: 10.1016/S0022-3956(00)00030-3]

45 **Nwankwo M**, Danborno B, Hamman WO. Relationship between body mass index and timing of maturation. *J Exp Clin Anat* 2015; **14**: 95-100 [DOI: 10.4103/1596-2393.177016]

46 **Hallonquist JD**, Seeman MV, Lang M, Rector NA. Variation in symptom severity over the menstrual cycle of schizophrenics. *Biol Psychiatry* 1993; **33**: 207-209 [PMID: 8448269 DOI: 10.1016/0006-3223(93)90141-Y]

47 **Seeman MV**. Menstrual exacerbation of schizophrenia symptoms. *Acta Psychiatr Scand* 2012; **125**: 363-371 [PMID: 22235755 DOI: 10.1111/j.1600-0447.2011.01822.x]

48 **Seeman MV**, Gupta R. Selective review of age-related needs of women with schizophrenia. *Clin Schizophr Relat Psychoses* 2015; **9**: 21-29 [PMID: 23471090 DOI: 10.3371/CSRP.SEGU.030113]

49 **Brzezinski A**, Brzezinski-Sinai NA, Seeman MV. Treating schizophrenia during menopause. *Menopause* 2017; **24**: 582-588 [PMID: 27824682 DOI: 10.1097/GME.0000000000000772]

50 **Seeman MV**. Treating schizophrenia at the time of menopause. *Maturitas* 2012; **72**: 117-120 [PMID: 22503514 DOI: 10.1016/j.maturitas.2012.03.008]

51 **Chandra PS**. Post-ovariectomy and oestrogen therapy related recurrence of oestrogen withdrawal associated psychosis. *Acta Psychiatr Scand* 2002; **106**: 76; author reply 76-76; author reply 77 [PMID: 12100352 DOI: 10.1034/j.1600-0447.2002.t01-2-02001.x]

52 **Moffitt O**, Findley JC. A case of first-onset psychosis and repeated relapses secondary to discontinuation of non-prescription estrogen replacement therapy in a transgendered female. *Gynecol Endocrinol* 2016; **32**: 796-798 [PMID: 27426632 DOI: 10.1080/09513590.2016.1202230]

53 **Seeman MV**. Transient psychosis in women on clomiphene, bromocriptine, domperidone and related endocrine drugs. *Gynecol Endocrinol* 2015; **31**: 751-754 [PMID: 26291819 DOI: 10.3109/09513590.2015.1060957]

54 **Holka-Pokorska J**, Piróg-Balcerzak A, Stefanowicz A. ["Mid-stimulation psychosis" in the course of in vitro fertilization procedure with the use of clomiphene citrate and bromocriptine - case study]. *Psychiatr Pol* 2014; **48**: 901-916 [PMID: 25639012 DOI: 10.12740/PP/24434]

55 **Grigoriadis S**, Seeman MV. The role of estrogen in schizophrenia: implications for schizophrenia practice guidelines for women. *Can J Psychiatry* 2002; **47**: 437-442 [PMID: 12085678 DOI: 10.1177/070674370204700504]

56 **Mendrek A**, Stip E. Sexual dimorphism in schizophrenia: is there a need for gender-based protocols? *Expert Rev Neurother* 2011; **11**: 951-959 [PMID: 21721913 DOI: 10.1586/ern.11.78]

57 **Millan MJ**, Andrieux A, Bartzokis G, Cadenhead K, Dazzan P, Fusar-Poli P, Gallinat J, Giedd J, Grayson DR, Heinrichs M, Kahn R, Krebs MO, Leboyer M, Lewis D, Marin O, Marin P, Meyer-Lindenberg A, McGorry P, McGuire P, Owen MJ, Patterson P, Sawa A, Spedding M, Uhlhaas P, Vaccarino F, Wahlestedt C, Weinberger D. Altering the course of schizophrenia: progress and perspectives. *Nat Rev Drug Discov* 2016; **15**: 485-515 [PMID: 26939910 DOI: 10.1038/nrd.2016.28]

58 **Cohen RZ**, Gotowiec A, Seeman MV. Duration of pretreatment phases in schizophrenia: women and men. *Can J Psychiatry* 2000; **45**: 544-547 [PMID: 10986572 DOI: 10.1177/070674370004500605]

59 **Ran MS**, Mao WJ, Chan CL, Chen EY, Conwell Y. Gender differences in outcomes in people with schizophrenia in rural China: 14-year follow-up study. *Br J Psychiatry* 2015; **206**: 283-288 [PMID: 25573398 DOI: 10.1192/bjp.bp.113.139733]

60 **Seeman MV**. Current outcome in schizophrenia: women vs men. *Acta Psychiatr Scand* 1986; **73**: 609-617 [PMID: 2875610 DOI: 10.1111/j.1600-0447.1986.tb02732.x]

61 **Childers SE**, Harding CM. Gender, premorbid social functioning, and long-term outcome in DSM-III schizophrenia. *Schizophr Bull* 1990; **16**: 309-318 [PMID: 2374886 DOI: 10.1093/schbul/16.2.309]

62 **Hanlon MC**, Campbell LE, Single N, Coleman C, Morgan VA, Cotton SM, Stain HJ, Castle DJ. Men and women with psychosis and the impact of illness-duration on sex-differences: The second Australian national survey of psychosis. *Psychiatry Res* 2017; **256**: 130-143 [PMID: 28633054 DOI: 10.1016/j.psychres.2017.06.024]

63 **Remington G**, Seeman MV. Schizophrenia and the influence of male gender. *Clin Pharmacol Ther* 2015; **98**: 578-581 [PMID: 26260896 DOI: 10.1002/cpt.201]

64 **Heitz U**, Studerus E, Menghini-Müller S, Papmeyer M, Egloff L, Ittig S, Navarra A, Andreou C, Riecher-Rössler A. Gender differences in first self-perceived signs and symptoms in patients with an at-risk mental state and first-episode psychosis. *Early Interv*

Psychiatry 2017 [PMID: 29235240 DOI: 10.1111/eip.12528]
65 **Seeman MV**. Gendering psychosis: the illness of Zelda Fitzgerald. *Med Humanit* 2016; **42**: 65-69 [PMID: 26392268 DOI: 10.1136/medhum-2015-010734]
66 **Thorup A**, Petersen L, Jeppesen P, Ohlenschlaeger J, Christensen T, Krarup G, Jorgensen P, Nordentoft M. Gender differences in young adults with first-episode schizophrenia spectrum disorders at baseline in the Danish OPUS study. *J Nerv Ment Dis* 2007; **195**: 396-405 [PMID: 17502805 DOI: 10.1097/01.nmd.0000253784.59708.dd]
67 **Fiorentini A**, Volonteri LS, Dragogna F, Rovera C, Maffini M, Mauri MC, Altamura CA. Substance-induced psychoses: a critical review of the literature. *Curr Drug Abuse Rev* 2011; **4**: 228-240 [PMID: 21999698 DOI: 10.2174/1874473711104040228]
68 **Seeman MV**. All psychosis is not schizophrenia, especially not in women. *Clin Schizophr Related Psychoses* 2007; **1**: 77-82 [DOI: 10.3371/CSRP.1.3.8]
69 **Seeman MV**. Psychosis in women: Consider midlife medical and psychological triggers. *Curr Psychiatry* 2010; **9**: 64-68, 75-76
70 **Anderson JE**, Larke SC. Navigating the mental health and addictions maze: a community-based pilot project of a new role in primary mental health care. *Ment Health Fam Med* 2009; **6**: 15-19 [PMID: 22477883]
71 **Crawford MB**, DeLisi LE. Issues related to sex differences in antipsychotic treatment. *Curr Opin Psychiatry* 2016; **29**: 211-217 [PMID: 26906336 DOI: 10.1097/YCO.0000000000000243]
72 **Lange B**, Mueller JK, Leweke FM, Bumb JM. How gender affects the pharmacotherapeutic approach to treating psychosis - a systematic review. *Expert Opin Pharmacother* 2017; **18**: 351-362 [PMID: 28129701 DOI: 10.1080/14656566.2017.1288722]
73 **Rabinowitz J**, Werbeloff N, Caers I, Mandel FS, Stauffer V, Ménard F, Kinon BJ, Kapur S. Determinants of antipsychotic response in schizophrenia: implications for practice and future clinical trials. *J Clin Psychiatry* 2014; **75**: e308-e316 [PMID: 24813414 DOI: 10.4088/JCP.13m08853]
74 **Seeman MV**. Gender differences in the prescribing of antipsychotic drugs. *Am J Psychiatry* 2004; **161**: 1324-1333 [PMID: 15285956 DOI: 10.1176/appi.ajp.161.8.1324]
75 **Seeman MV**. Gender differences in schizophrenia. *Can J Psychiatry* 1982; **27**: 107-112 [PMID: 6121620 DOI: 10.1177/070674378202700204]
76 **Gur RE**, Gur RC. Gender differences in regional cerebral blood flow. *Schizophr Bull* 1990; **16**: 247-254 [PMID: 2374883 DOI: 10.1093/schbul/16.2.247]
77 **Gordon JH**, Gorski RA, Borison RL, Diamond BI. Postsynaptic efficacy of dopamine: possible suppression by estrogen. *Pharmacol Biochem Behav* 1980; **12**: 515-518 [PMID: 7190291 DOI: 10.1016/0091-3057(80)90182-3]
78 **Franconi F**, Campesi I. Pharmacogenomics, pharmacokinetics and pharmacodynamics: interaction with biological differences between men and women. *Br J Pharmacol* 2014; **171**: 580-594 [PMID: 23981051 DOI: 10.1111/bph.12362]
79 **Seeman MV**. Women and psychosis. *Womens Health* (Lond) 2012; **8**: 215-224 [PMID: 22375723 DOI: 10.2217/WHE.11.97]
80 **Smith S**. Gender differences in antipsychotic prescribing. *Int Rev Psychiatry* 2010; **22**: 472-484 [PMID: 21047160 DOI: 10.3109/09540261.2010.515965]
81 **Marazziti D**, Baroni S, Picchetti M, Piccinni A, Carlini M, Vatteroni E, Falaschi V, Lombardi A, Dell'Osso L. Pharmacokinetics and pharmacodynamics of psychotropic drugs: effect of sex. *CNS Spectr* 2013; **18**: 118-127 [PMID: 23374978 DOI: 10.1017/S1092852912001010]
82 **González-Rodríguez A**, Catalán R, Penadés R, Ruiz Cortés V, Torra M, Seeman MV, Bernardo M. Antipsychotic response worsens with postmenopausal duration in women with schizophrenia. *J Clin Psychopharmacol* 2016; **36**: 580-587 [PMID: 27626286 DOI: 10.1097/JCP.0000000000000571]
83 **González-Rodríguez A**, Seeman MV. Pharmacotherapy for schizophrenia in postmenopausal women. *Expert Opin Pharmacother* 2018; **19**: 809-821 [PMID: 29676942 DOI: 10.1080/14656566.2018.1465563]
84 **Kulkarni J**, Gavrilidis E, Worsley R, Hayes E. Role of estrogen treatment in the management of schizophrenia. *CNS Drugs* 2012; **26**: 549-557 [PMID: 22626057 DOI: 10.2165/11630660-000000000-00000]
85 **Kulkarni J**, Gavrilidis E, Worsley R, Van Rheenen T, Hayes E. The role of estrogen in the treatment of men with schizophrenia. *Int J Endocrinol Metab* 2013; **11**: 129-136 [PMID: 24348584 DOI: 10.5812/ijem.6615]
86 **Labad J**, Martorell L, Huerta-Ramos E, Cobo J, Vilella E, Rubio-Abadal E, Garcia-Pares G, Creus M, Núñez C, Ortega L, Miquel E; RALOPSYCAT Group, Usall J. Pharmacogenetic study of the effects of raloxifene on negative symptoms of postmenopausal women with schizophrenia: A double-blind, randomized, placebo-controlled trial. *Eur Neuropsychopharmacol* 2016; **26**: 1683-1689 [PMID: 27546373 DOI: 10.1016/j.euroneuro.2016.08.006]
87 **Usall J**, Huerta-Ramos E, Labad J, Cobo J, Núñez C, Creus M, Parés GG, Cuadras D, Franco J, Miquel E, Reyes JC, Roca M; RALOPSYCAT Group. Raloxifene as an adjunctive treatment for postmenopausal women with schizophrenia: A 24-week double-blind, randomized, parallel, placebo-controlled trial. *Schizophr Bull* 2016; **42**: 309-317 [PMID: 26591005 DOI: 10.1093/schbul/sbv149]
88 **Weickert TW**, Weickert CS. Raloxifene improves cognition in schizophrenia: Spurious result or valid effect? *Front Psychiatry* 2017; **8**: 202 [PMID: 29075208 DOI: 10.3389/fpsyt.2017.00202]
89 **Weiser M**, Levi L, Burshtein S, Hagin M, Matei VP, Podea D, Micluția I, Tiugan A, Păcală B, Grecu IG, Noy A, Zamora D, Davis JM. Raloxifene plus antipsychotics versus placebo plus antipsychotics in severely ill decompensated postmenopausal women with schizophrenia or schizoaffective disorder: A randomized controlled trial. *J Clin Psychiatry* 2017; **78**: e758-e765 [PMID: 28541645 DOI: 10.4088/JCP.15m10498]
90 **Wong J**, Seeman MV, Shapiro H. Case report: Raloxifene in postmenopausal women with psychosis: preliminary findings. *Am J Geriatr Psychiatry* 2003; **11**: 697-698 [PMID: 14609815 DOI: 10.1176/appi.ajgp.11.6.697]
91 **Caton CL**, Xie H, Drake RE, McHugo G. Gender differences in psychotic disorders with concurrent substance use. *J Dual Diagn* 2014; **10**: 177-186 [PMID: 25391275 DOI: 10.1080/15504263.2014.961882]
92 **Martens PJ**, Chochinov HM, Prior HJ, Fransoo R, Burland E; Need To Know Team. Are cervical cancer screening rates different for women with schizophrenia? A Manitoba population-based study. *Schizophr Res* 2009; **113**: 101-106 [PMID: 19419843 DOI: 10.1016/j.schres.2009.04.015]
93 **Seeman MV**. Preventing breast cancer in women with schizophrenia. *Acta Psychiatr Scand* 2011; **123**: 107-117 [PMID: 20958270 DOI: 10.1111/j.1600-0447.2010.01626.x]
94 **Seeman MV**. Breast cancer prevention and treatment in women with severe mental illness. *Int J Womens Health Wellness* 2017; **3**: 064 [DOI: 10.23937/2474-1353/1510064]
95 **Seeman MV**. Schizophrenia and cancer: low incidence, high mortality. *Res J Oncol* 2017; **1**: 6
96 **Torrey EF**. Prostate cancer and schizophrenia. *Urology* 2006; **68**: 1280-1283 [PMID: 17141844 DOI: 10.1016/j.urology.2006.08.1061]
97 **Basson R**, Gilks T. Women's sexual dysfunction associated with psychiatric disorders and their treatment. *Womens Health* (Lond) 2018; **14**: 1745506518762664 [PMID: 29649948 DOI: 10.1177/1745506518762664]
98 **Seeman MV**. Spotlight on sibling involvement in schizophrenia treatment. *Psychiatry* 2013; **76**: 311-322 [PMID: 24299090 DOI: 10.1521/psyc.2013.76.4.311]
99 **Seeman MV**, Benes C. Sexual problems in a women's clinic for schizophrenia. *Sexologies* 2000; **34**: 12-15
100 **Cauley JA**. Screening for Osteoporosis. *JAMA* 2018; **319**: 2483-2485 [PMID: 29946707 DOI: 10.1001/jama.2018.5722]
101 **Hung OY**, Titterington JS, Wenger NK. Evolving cardiovascular care for women: a decade of progress. *Future Cardiol* 2015; **11**: 275-279 [PMID: 26021632 DOI: 10.2217/fca.15.24]
102 **de Vries B**, van Busschbach JT, van der Stouwe ECD, Aleman A, van Dijk JJM, Lysaker PH, Arends J, Nijman SA, Pijnenborg GHM. Prevalence rate and risk factors of victimization in adult patients

with a psychotic disorder: A systematic review and meta-analysis. *Schizophr Bull* 2018 [PMID: 29547958 DOI: 10.1093/schbul/sby020]
103 **Kulkarni J**, Galletly C. Improving safety for women in psychiatry wards. *Aust N Z J Psychiatry* 2017; **51**: 192-194 [PMID: 27609938 DOI: 10.1177/0004867416667234]
104 **Seeman MV**. Single-sex psychiatric services to protect women. *Medscape Womens Health* 2002; **7**: 4 [PMID: 12466736]
105 **Seeman MV**. Bad, burdened or ill? Characterizing the spouses of women with schizophrenia. *Int J Soc Psychiatry* 2013; **59**: 805-810 [PMID: 22976376 DOI: 10.1177/0020764012456818]
106 **Seeman MV**. Sexual exploitation of women with schizophrenia. *Am Res J Addict Rehab* 2018; **2**: 1-8
107 **Seeman MV**. Sexual exploitation of a woman with schizophrenia. *J Clin Cases* 2018; **1**: 1-6 [DOI: 10.1057/jcc0000001]
108 **Van Deinse TB**, Macy RJ, Cuddeback GS, Allman AJ. Intimate partner violence and sexual assault among women with serious mental illness: A review of prevalence and risk factors. *J Soc Work* 2018; **(20)**: 146801731876642 [DOI: 10.1177/1468017318766425]
109 **Rund BR**. The association between schizophrenia and violence. *Schizophr Res* 2018; **pii**: S0920-9964(18)30123-3 [PMID: 29506766 DOI: 10.1016/j.schres.2018.02.043]
110 **Lau AS**. Making the case for selective and directed cultural adaptations of evidence-based treatments: examples from parent training. *Clin Psychol Sci Pract* 2006; **13**: 295-310 [DOI: 10.1111/j.1468-2850.2006.00042.x]
111 **Seeman MV**. Parenting issues in mothers with schizophrenia. *Curr Womens Health Rev* 2010; **6**: 51-57 [DOI: 10.2174/157340410790979734]
112 **Seeman MV**. Intervention to prevent child custody loss in mothers with schizophrenia. *Schizophr Res Treatment* 2012; **2012**: 796763 [PMID: 22966446 DOI: 10.1155/2012/796763]
113 **Ralph SJ**, Espinet A. Increased all-cause mortality by antipsychotic drugs: updated review and meta-analysis in dementia and general mental health care. *J Alzheimers Dis Rep* 2017; **1**: 1–25 [DOI: 10.3233/ADR-170042]
114 **Solmi M**, Murru A, Pacchiarotti I, Undurraga J, Veronese N, Fornaro M, Stubbs B, Monaco F, Vieta E, Seeman MV, Correll CU, Carvalho AF. Safety, tolerability, and risks associated with first- and second-generation antipsychotics: a state-of-the-art clinical review. *Ther Clin Risk Manag* 2017; **13**: 757-777 [PMID: 28721057 DOI: 10.2147/TCRM.S117321]
115 **Seeman MV**. Secondary effects of antipsychotics: women at greater risk than men. *Schizophr Bull* 2009; **35**: 937-948 [PMID: 18400811 DOI: 10.1093/schbul/sbn023]
116 **Seeman MV**. Schizophrenia: women bear a disproportionate toll of antipsychotic side effects. *J Am Psychiatr Nurses Assoc* 2010; **16**: 21-29 [PMID: 21659259 DOI: 10.1177/1078390309350918]
117 **Iversen TSJ**, Steen NE, Dieset I, Hope S, Mørch R, Gardsjord ES, Jørgensen KN, Melle I, Andreassen OA, Molden E, Jönsson EG. Side effect burden of antipsychotic drugs in real life - Impact of gender and polypharmacy. *Prog Neuropsychopharmacol Biol Psychiatry* 2018; **82**: 263-271 [PMID: 29122637 DOI: 10.1016/j.pnpbp.2017.11.004]
118 **Johannesen L**, Garnett C, Luo M, Targum S, Sørensen JS, Mehrotra N. Quantitative understanding of QTc prolongation and gender as risk factors for torsade de pointes. *Clin Pharmacol Ther* 2018; **103**: 304-309 [PMID: 29219167 DOI: 10.1002/cpt.783]
119 **Chow V**, Reddel C, Pennings G, Scott E, Pasqualon T, Ng AC, Yeoh T, Curnow J, Kritharides L. Global hypercoagulability in patients with schizophrenia receiving long-term antipsychotic therapy. *Schizophr Res* 2015; **162**: 175-182 [PMID: 25634682 DOI: 10.1016/j.schres.2014.12.042]
120 **Lazo-Langner A**, Liu K, Shariff S, Garg AX, Ray JG. Immigration, region of origin, and the epidemiology of venous thromboembolism: A population-based study. *Res Pract Thromb Haemost* 2018; **2**: 469-480 [PMID: 30046751 DOI: 10.1002/rth2.12113]
121 **Jönsson AK**, Schill J, Olsson H, Spigset O, Hägg S. Venous thromboembolism during treatment with antipsychotics: A review of current evidence. *CNS Drugs* 2018; **32**: 47-64 [PMID: 29423659 DOI: 10.1007/s40263-018-0495-7]
122 **Vigod SN**, Kurdyak PA, Dennis CL, Gruneir A, Newman A, Seeman MV, Rochon PA, Anderson GM, Grigoriadis S, Ray JG. Maternal and newborn outcomes among women with schizophrenia: a retrospective population-based cohort study. *BJOG* 2014; **121**: 566-574 [PMID: 24443970 DOI: 10.1111/1471-0528.12567]
123 **Seeman MV**. Skin and hair conditions in women with schizophrenia or related disorders. *Womens Health Res* 2018; **2**: 14-28 [DOI: 10.1057/whr0000008]
124 **Seeman MV**. Antipsychotics and physical attractiveness. *Clin Schizophr Relat Psychoses* 2011; **5**: 142-146 [PMID: 21983498 DOI: 10.3371/CSRP.5.3.4]
125 **Zhang-Wong JH**, Seeman MV. Antipsychotic drugs, menstrual regularity and osteoporosis risk. *Arch Womens Ment Health* 2002; **5**: 93-98 [PMID: 12510211 DOI: 10.1007/s00737-002-0002-4]
126 **Currier GW**, Simpson GM. Antipsychotic medications and fertility. *Psychiatr Serv* 1998; **49**: 175-176 [PMID: 9575000 DOI: 10.1176/ps.49.2.175]
127 **Galbally M**, Snellen M, Power J. Antipsychotic drugs in pregnancy: a review of their maternal and fetal effects. *Ther Adv Drug Saf* 2014; **5**: 100-109 [PMID: 25083265 DOI: 10.1177/2042098614522682]
128 **Gentile S**. Infant safety with antipsychotic therapy in breast-feeding: a systematic review. *J Clin Psychiatry* 2008; **69**: 666-673 [PMID: 18370569 DOI: 10.4088/JCP.v69n0421]
129 **Seeman MV**. Pseudocyesis, delusional pregnancy, and psychosis: The birth of a delusion. *World J Clin Cases* 2014; **2**: 338-344 [PMID: 25133144 DOI: 10.12998/wjcc.v2.i8.338]
130 **Zai CC**, Maes MS, Tiwari AK, Zai GC, Remington G, Kennedy JL. Genetics of tardive dyskinesia: Promising leads and ways forward. *J Neurol Sci* 2018; **389**: 28-34 [PMID: 29502799 DOI: 10.1016/j.jns.2018.02.011]
131 **Turrone P**, Seeman MV, Silvestri S. Estrogen receptor activation and tardive dyskinesia. *Can J Psychiatry* 2000; **45**: 288-290 [PMID: 10779888 DOI: 10.1177/070674370004500310]
132 **Hollingworth SA**, Winckel K, Saiepour N, Wheeler AJ, Myles N, Siskind D. Clozapine-related neutropenia, myocarditis and cardiomyopathy adverse event reports in Australia 1993-2014. *Psychopharmacology* (Berl) 2018; **235**: 1915-1921 [PMID: 29589067 DOI: 10.1007/s00213-018-4881-0]
133 **Seeman MV**. Prevention of antipsychotic side effects in elderly populations. *J Ment Health Aging* 2018; **2**: 24-28
134 **Seeman MV**. Bilingualism and schizophrenia. *World J Psychiatry* 2016; **6**: 192-198 [PMID: 27354960 DOI: 10.5498/wjp.v6.i2.192]
135 **Ostrow L**, Nemec PB, Smith C. Self-employment for people with psychiatric disabilities: Advantages and strategies. *J Behav Health Serv Res* 2018 [PMID: 29845512 DOI: 10.1007/s11414-018-9625-8]
136 **Hammell KW**. Dimensions of meaning in the occupations of daily life. *Can J Occup Ther* 2004; **71**: 296-305 [PMID: 15633880 DOI: 10.1177/000841740407100509]
137 **Link BG**, Phelan JC. Conceptualizing stigma. *Ann Rev Sociol* 2001; **27**: 363-385 [DOI: 10.1146/annurev.soc.27.1.363]
138 **Khalifeh H**, Johnson S, Howard LM, Borschmann R, Osborn D, Dean K, Hart C, Hogg J, Moran P. Violent and non-violent crime against adults with severe mental illness. *Br J Psychiatry* 2015; **206**: 275-282 [PMID: 25698767 DOI: 10.1192/bjp.bp.114.147843]
139 **Desmarais SL**, Van Dorn RA, Johnson KL, Grimm KJ, Douglas KS, Swartz MS. Community violence perpetration and victimization among adults with mental illnesses. *Am J Public Health* 2014; **104**: 2342-2349 [PMID: 24524530 DOI: 10.2105/AJPH.2013.301680]
140 **Lamsma J**, Harte JM. Violence in psychosis: Conceptualizing its causal relationship with risk factors. *Aggress Violent Behav* 2015; **24**: 75-82 [DOI: 10.1016/j.avb.2015.05.003]
141 **Krumm S**, Checchia C, Badura-Lotter G, Kilian R, Becker T. The attitudes of mental health professionals towards patients' desire for children. *BMC Med Ethics* 2014; **15**: 18 [PMID: 24580889 DOI: 10.1186/1472-6939-15-18]
142 **Jeffery D**, Clement S, Corker E, Howard LM, Murray J, Thornicroft G. Discrimination in relation to parenthood reported by community psychiatric service users in the UK: a framework analysis. *BMC Psychiatry* 2013; **13**: 120 [PMID: 23601350 DOI: 10.1186/1471-244

X-13-120]
143 **Topor A**, Bøe TD, Larsen IB. Small things, micro-affirmations and helpful professionals everyday recovery-orientated practices according to persons with mental health problems. *Community Ment Health J* 2018 [PMID: 29423684 DOI: 10.1007/s10597-018-0245-9]
144 **Kaplan KJ**, Harrow M, Clews K. The twenty-year trajectory of suicidal activity among post-hospital psychiatric men and women with mood disorders and schizophrenia. *Arch Suicide Res* 2016; **20**: 336-348 [PMID: 26881891 DOI: 10.1080/13811118.2015.1033505]
145 **Seeman MV**. Suicide among women with schizophrenia spectrum disorders. *J Psychiatr Pract* 2009; **15**: 235-242 [PMID: 19461398 DOI: 10.1097/01.pra.0000351885.60507.1c]
146 **Seeman MV**. The marilyn monroe group and the werther effect. *Case Rep J* 2017; **1**: 4
147 **Seeman MV**. The impact of suicide on co-patients. *Psychiatr Q* 2015; **86**: 449-457 [PMID: 25618004 DOI: 10.1007/s11126-015-9346-6]
148 **Brodsky BS**, Spruch-Feiner A, Stanley B. The zero suicide model: applying evidence-based suicide prevention practices to clinical Care. *Front Psychiatry* 2018; **9**: 33 [PMID: 29527178 DOI: 10.3389/fpsyt.2018.00033]
149 **Brown S**, Birtwistle J, Roe L, Thompson C. The unhealthy lifestyle of people with schizophrenia. *Psychol Med* 1999; **29**: 697-701 [PMID: 10405091 DOI: 10.1017/S0033291798008186]
150 **Moradi H**, Harvey PD, Helldin L. Correlates of risk factors for reduced life expectancy in schizophrenia: Is it possible to develop a predictor profile? *Schizophr Res* 2018; [PMID: 29859858 DOI: 10.1016/j.schres.2018.05.035]
151 **Seeman MV**. An outcome measure in schizophrenia: mortality. *Can J Psychiatry* 2007; **52**: 55-60 [PMID: 17444079 DOI: 10.1177/070674370705200109]
152 **Martin CR**, Osadchiy V, Kalani A, Mayer EA. The brain-gut-microbiome axis. *Cell Mol Gastroenterol Hepatol* 2018; **6**: 133-148 [PMID: 30023410 DOI: 10.1016/j.jcmgh.2018.04.003]
153 **Severance EG**, Dickerson FB, Yolken RH. Autoimmune phenotypes in schizophrenia reveal novel treatment targets. *Pharmacol Ther* 2018; **189**: 184-198 [PMID: 29742478 DOI: 10.1016/j.pharmthera.2018.05.005]
154 **Bosworth B**. Increasing disparities in mortality by socioeconomic status. *Annu Rev Public Health* 2018; **39**: 237-251 [PMID: 29608870 DOI: 10.1146/annurev-publhealth-040617-014615]
155 **LePage JP**, Bradshaw LD, Cipher DJ, Crawford AM, Hoosyhar D. The effects of homelessness on Veterans' health care service use: an evaluation of independence from comorbidities. *Public Health* 2014; **128**: 985-992 [PMID: 25443100 DOI: 10.1016/j.puhe.2014.07.004]
156 **Cohen S**. Social relationships and health. *Am Psychol* 2004; **59**: 676-684 [PMID: 15554821 DOI: 10.1037/0003-066X.59.8.676]
157 **Butler-Jones D**, Wong T. Infectious disease, social determinants and the need for intersectoral action. *Can Commun Dis Rep* 2016; **42**: S118-S120 [PMID: 29770035 DOI: 10.14745/ccdr.v42is1a04]
158 **Teasdale SB**, Samaras K, Wade T, Jarman R, Ward PB. A review of the nutritional challenges experienced by people living with severe mental illness: a role for dietitians in addressing physical health gaps. *J Hum Nutr Diet* 2017; **30**: 545-553 [PMID: 28419586 DOI: 10.1111/jhn.12473]
159 **Dickey B**, Normand SL, Weiss RD, Drake RE, Azeni H. Medical morbidity, mental illness, and substance use disorders. *Psychiatr Serv* 2002; **53**: 861-867 [PMID: 12096170 DOI: 10.1176/appi.ps.53.7.861]
160 **Attar R**, Berg Johansen M, Valentin JB, Aagaard J, Jensen SE. Treatment following myocardial infarction in patients with schizophrenia. *PLoS One* 2017; **12**: e0189289 [PMID: 29236730 DOI: 10.1371/journal.pone.0189289]
161 **Holt RI**, Mitchell AJ. Diabetes mellitus and severe mental illness: mechanisms and clinical implications. *Nat Rev Endocrinol* 2015; **11**: 79-89 [PMID: 25445848 DOI: 10.1038/nrendo.2014.203]
162 **Lawrence D**, Kisely S. Inequalities in healthcare provision for people with severe mental illness. *J Psychopharmacol* 2010; **24**: 61-68 [PMID: 20923921 DOI: 10.1177/1359786810382058]
163 **Jayatilleke N**, Hayes RD, Dutta R, Shetty H, Hotopf M, Chang CK, Stewart R. Contributions of specific causes of death to lost life expectancy in severe mental illness. *Eur Psychiatry* 2017; **43**: 109-115 [PMID: 28391102 DOI: 10.1016/j.eurpsy.2017.02.487]
164 **de Boer MK**, Castelein S, Wiersma D, Schoevers RA, Knegtering H. The facts about sexual (Dys) function in schizophrenia: an overview of clinically relevant findings. *Schizophr Bull* 2015; **41**: 674-686 [PMID: 25721311 DOI: 10.1093/schbul/sbv001]
165 **Seeman MV**. Loss of libido in a woman with schizophrenia. *Am J Psychiatry* 2013; **170**: 471-475 [PMID: 23632833 DOI: 10.1176/appi.ajp.2012.12111475]
166 **Wong J**, Seeman MV. Prolactin, menstrual irregularities, quality of life. *Schizophr Res* 2007; **91**: 270-271 [PMID: 17198750 DOI: 10.1016/j.schres.2006.11.004]
167 **Seeman MV**. Antipsychotic-induced amenorrhea. *J Ment Health* 2011; **20**: 484-491 [PMID: 21942684 DOI: 10.3109/09638237.2011.586741]
168 **Vigod SN**, Seeman MV, Ray JG, Anderson GM, Dennis CL, Grigoriadis S, Gruneir A, Kurdyak PA, Rochon PA. Temporal trends in general and age-specific fertility rates among women with schizophrenia (1996-2009): a population-based study in Ontario, Canada. *Schizophr Res* 2012; **139**: 169-175 [PMID: 22658526 DOI: 10.1016/j.schres.2012.05.010]
169 **Miller LJ**. Sexuality, reproduction, and family planning in women with schizophrenia. *Schizophr Bull* 1997; **23**: 623-635 [PMID: 9365999 DOI: 10.1093/schbul/23.4.623]
170 **Vigod SN**, Rochon-Terry G, Fung K, Gruneir A, Dennis CL, Grigoriadis S, Kurdyak PA, Ray JG, Rochon P, Seeman MV. Factors associated with postpartum psychiatric admission in a population-based cohort of women with schizophrenia. *Acta Psychiatr Scand* 2016; **134**: 305-313 [PMID: 27437875 DOI: 10.1111/acps.12622]
171 **Whitworth AB**. Psychopharmacological treatment of schizophrenia during pregnancy and lactation. *Curr Opin Psychiatry* 2017; **30**: 184-190 [PMID: 28306564 DOI: 10.1097/YCO.0000000000000329]
172 **Seeman MV**. Women with schizophrenia as parents. *Primary Psychiatry* 2002; **9**: 39-42
173 **Seeman MV**. Assessing the effects of antipsychotics on parenting. *Womens Health Bull* 2018; **5**: e13409 [DOI: 10.5812/whb.13409]
174 **Seeman MV**, González-Rodríguez A. Use of psychotropic medication in women with psychotic disorders at menopause and beyond. *Curr Opin Psychiatry* 2018; **31**: 183-192 [PMID: 29528895 DOI: 10.1097/YCO.0000000000000410]
175 **Costantine MM**. Physiologic and pharmacokinetic changes in pregnancy. *Front Pharmacol* 2014; **5**: 65 [PMID: 24772083 DOI: 10.3389/fphar.2014.00065]
176 **Pariente G**, Leibson T, Carls A, Adams-Webber T, Ito S, Koren G. Pregnancy-associated changes in pharmacokinetics: A systematic review. *PLoS Med* 2016; **13**: e1002160 [PMID: 27802281 DOI: 10.1371/journal.pmed.1002160]
177 **Westin AA**, Brekke M, Molden E, Skogvoll E, Castberg I, Spigset O. Treatment with antipsychotics in pregnancy: Changes in drug disposition. *Clin Pharmacol Ther* 2018; **103**: 477-484 [PMID: 28643331 DOI: 10.1002/cpt.770]
178 **Murphy SM**, Irving CB, Adams CE, Waqar M. Crisis intervention for people with severe mental illnesses. *Cochrane Database Syst Rev* 2015; CD001087 [PMID: 26633650 DOI: 10.1002/14651858.CD001087.pub5]
179 **Seeman MV**. Sleepwalking, a possible side effect of antipsychotic medication. *Psychiatr Q* 2011; **82**: 59-67 [PMID: 20734137 DOI: 10.1007/s11126-010-9149-8]
180 **Seeman MV**. Diagnosis and treatment of sleep apnoea in women with schizophrenia. *J Ment Health* 2014; **23**: 191-196 [PMID: 24433147 DOI: 10.3109/09638237.2013.869572]
181 **Seeman MV**. Sleep, nightmares and schizophrenia. *J Sleep Disord Manag* 2017; **3**: 1-7 [DOI: 10.23937/2572-4053.1510017]
182 **Seeman MV**. Antipsychotic-induced somnolence in mothers with schizophrenia. *Psychiatr Q* 2012; **83**: 83-89 [PMID: 21739299 DOI: 10.1007/s11126-011-9185-z]
183 **Waddell A**, Ross L, Ladd L, Seeman MV. Safe Minds - Perceptions of safety in a rehabilitation clinic for serious persistent mental illness. *Int J Psychosocial Rehab* 2006; **11**: 4-10
184 **Goering PN**, Streiner DL, Adair C, Aubry T, Barker J, Distasio

J, Hwang SW, Komaroff J, Latimer E, Somers J, Zabkiewicz DM. The At Home/Chez Soi trial protocol: a pragmatic, multi-site, randomised controlled trial of a Housing First intervention for homeless individuals with mental illness in five Canadian cities. *BMJ Open* 2011; **1**: e000323 [PMID: 22102645 DOI: 10.1136/bmjopen-2011-000323]

185 **Piva M**, Santarelli E, Vivarelli M. The skill bias effect of technological and organisational change: Evidence and policy implications. *Res Policy* 2005; **34**: 141-157 [DOI: 10.1016/j.respol.2004.11.005]

186 **Vos J**, Craig M, Cooper M. Existential therapies: a meta-analysis of their effects on psychological outcomes. *J Consult Clin Psychol* 2015; **83**: 115-128 [PMID: 25045907 DOI: 10.1037/a0037167]

187 **Mushkin P**, Band-Winterstein T, Avieli H. "Like every normal person?!" The paradoxical effect of aging with schizophrenia. *Qual Health Res* 2018; **28**: 977-986 [PMID: 29577846 DOI: 10.1177/1049732318764389]

188 **Chochinov HM**, Hassard T, McClement S, Hack T, Kristjanson LJ, Harlos M, Sinclair S, Murray A. The landscape of distress in the terminally ill. *J Pain Symptom Manage* 2009; **38**: 641-649 [PMID: 19713069 DOI: 10.1016/j.jpainsymman.2009.04.021]

189 **Kaczkurkin AN**, Raznahan A, Satterthwaite TD. Sex differences in the developing brain: insights from multimodal neuroimaging. *Neuropsychopharmacology* 2018 [PMID: 29930385 DOI: 10.1038/s41386-018-0111-z]

190 **Arnold AP**. A general theory of sexual differentiation. *J Neurosci Res* 2017; **95**: 291-300 [PMID: 27870435 DOI: 10.1002/jnr.23884]

P- Reviewer: Hicks PB, Rajkowska G, Sobanski T **S- Editor**: Ji FF
L- Editor: Filipodia **E- Editor**: Wu YXJ

Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com