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Prenatal genetic counseling for psychiatric disorders

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Abstract

Psychiatric disorders like schizophrenia, bipolar disorder, depression, anxiety, and obsessive compulsive disorder are common disorders with complex etiology. They can exact a heavy toll on the individual with the condition, and can have significant impact on family members too. Accordingly, psychiatric disorders can arise as a concern in the prenatal context – couples may be interested in learning about the chance for their child to develop the illness that manifests in the family, and may be interested in discussing options for prenatal testing. However, the complex nature of these conditions can present challenges for clinicians who seek to help families with these issues. We established the world's first specialist genetic counseling service of its kind in Vancouver, Canada in 2012, and to date, have provided counseling for ~500 families, and have demonstrated increases in patients' empowerment and self efficacy after genetic counseling. We draw on our accumulated clinical experience to outline the process by which we approach prenatal genetic counseling for psychiatric disorders, to assist other clinicians in providing thoughtful, comprehensive support to couples seeking out this service.

Keywords

schizophrenia; bipolar disorder; schizoaffective disorder; depression; risk counseling; postpartum depression

Introduction

Psychiatric disorders are common (1 in 4 individuals experiences a psychiatric condition at some point in their life[1]), and are a source of significant burden - both for the individual and their family, and economically.[2] The etiology of psychiatric disorders is complex and heterogeneous, and involves contributions of both genetic and environmental factors.[3,4] Genetic testing cannot establish, confirm or refine a psychiatric diagnosis, and at present, in most cases, determining the chance for a child to develop a psychiatric condition is usually based on analyzing a detailed 3-generation psychiatric family history.[5,6]

Studies have shown that people often overestimate the chances for future children to develop psychiatric illness, and that this can have an impact on child bearing decisions and provoke

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anxiety.[7,8] Further, individuals with psychiatric illness and their families often experience feelings of fear, guilt, shame, and stigma associated with the diagnosis, and often have misconceptions about the cause.[8–10] Accordingly, people with psychiatric problems and their families have expressed desire for prenatal genetic counseling and/or genetic testing to address their concerns about the risks of psychiatric illness for their children.[11–13]

Genetic counseling has been defined as the process of helping people to "understand and adapt to the medical psychological and familial implications of genetic contributions to disease."[14] Therefore, genetic counseling is neither solely concerned with genetic testing and/or discussions about risk for children to develop a condition that runs in the family, nor purely educational/informational; while information is a crucial component of the intervention, to achieve optimal patient outcomes[15] it is not simply delivered, but rather exchanged in the context of a psychotherapeutically oriented encounter.

In 2012, we established a specialist psychiatric genetic counseling (PGC) clinic in Vancouver, BC, Canada. The clinic provides genetic counseling to patients who have lived experience and/or a family history of psychiatric illness, and sees a range of adult, pediatric, and prenatal patients. Our research shows significant increases in empowerment and self-efficacy among patients one month after accessing the service.[16] Common indications for prenatal PGC include situations where a patient is interested in: 1) knowing the chance for the fetus to develop a psychiatric condition similar to the one they or their family member has experienced, and/or how to protect their child's mental health 2) obtaining prenatal genetic testing for psychiatric conditions, and 3) discussing use of psychotropic medication during pregnancy and/or the chance for postpartum mental health problems.

Since many clinicians who encounter patients in these contexts feel uncomfortable about how best to manage these complex patient concerns,[11,17–20] in this paper, we draw upon our accumulated experience to provide guidance to other healthcare professionals seeking to provide prenatal PGC.

Our discussion will focus on common complex psychiatric conditions (e.g. schizophrenia, bipolar disorder, schizoaffective disorder, depression, anxiety, obsessive compulsive disorder, eating disorders) rather than pervasive developmental disorders such as autism, which are squarely within the realm of conditions for which clinical genetics services are typically provided, and for which clinical guidelines for management already exist.[21–23]

Establishing psychiatric illness as a topic that needs to be addressed

In prenatal clinical encounters, the need to address psychiatric illness becomes self-evident when patients spontaneously and explicitly disclose their concerns, or when this is the primary reason for referral. However, psychiatric disorders rarely constitute the primary reason for referral for genetic counseling in generalist settings[24], and it is more typical for families to have difficulties articulating their worries related to this issue –sometimes even in the face of considerable concern.

Therefore, in order to deliver optimal patient care, clinicians must be equipped to identify patients who could benefit from PGC in a manner that is not dependent on the patient's

spontaneous self-identification of interest, or their unprompted volunteering of personal or family history of psychiatric illness. Specifically, by routinely asking all patients about a personal/family history of mental illness, and exploring potential associated concerns with them, clinicians can create an opportunity for patients to open up about their experiences, reduce feelings of stigma, and obtain the information that they need to ensure they are receiving appropriate support.

Exploring personal and family history of psychiatric illness

Research suggests that psychiatric disorders are rarely considered in genetic counseling settings during documentation of detailed family history for non-psychiatric indications.[25] However, questions regarding psychiatric illness can easily be appended to the targeted questions that would routinely be asked in relation to the patient's primary reason for referral, and documented using standard pedigree nomenclature.[26]

Simple approaches to initiating a conversation about psychiatric family history (such as asking patients: "Do you have any personal history of mental illness?") can be followed with inquiries about formal diagnoses, and other family members' experiences. Often patients may be uncertain about specific psychiatric diagnoses in family members, or, formal diagnoses may not have been made. But, rather than pursuing records to confirm diagnoses (which can change over time, and can prove time consuming and difficult to obtain), our clinical practice involves detailed exploration of patients' descriptions of the symptoms (for further discussion, see Inglis et al[16]). The Family Interview for Genetic Studies (FIGS; (National Institute of Mental Health, 2016) and the accompanying manual[27] can be used as to help collect and appraise information from the patient on family members' psychiatric symptoms. After systematic questioning about psychiatric history of individual family members, broad screening questions can help to ensure that different conceptualizations or indicators of psychiatric illness have not been overlooked (see Table I).

Once the presence of a personal or family history of psychiatric illness has been established, the clinician can explore whether the patient is interested in discussing its etiology and/or chances for recurrence for themselves and/or their fetus (see Table I). Depending on the initial reason for the appointment and time constraints, addressing the patient's needs in this area appropriately may require a separate appointment.

Establishing shared understanding and expectations for the session (contracting)

To ensure that the clinician and patient share a foundational understanding of the nature of the condition(s) to be discussed, it can be useful to begin by exploring the patient's experiences with the psychiatric illness in the family. Particularly for patients with limited exposure to or experience with psychiatric illness, this exploration may reveal a need to spend part of the session discussing the signs and symptoms of psychiatric illness and the variable nature of the spectrum of severity with which individuals can be impacted.

Actively encouraging the patient to explicitly articulate what they hope to gain from the session – at a level beyond the superficial - is crucial. Table II outlines some common presenting interests among patients in the prenatal PGC context, together with some of the deeper emotional motivations and key misconceptions that often drive these interests.

Our clinical experience shows that excellent patient outcomes can be achieved by founding all conversations about risk or prenatal genetic testing on an accurate understanding of the etiology of psychiatric illness, and framing the discussion around how etiology relates to recovery and ways to protect mental health.[16] Therefore, even if a patient expresses that their sole motivation for attending the session is to know the chance for the fetus to develop a psychiatric illness or to access a genetic test, we are careful to ensure that we address these needs in the context of a shared understanding of etiology, recovery, and strategies to protect mental health. A suggestion to help clinicians contract with patients to establish this plan is provided in Table I.

Emotional issues related to explanations for cause of illness are pervasive and impactful, therefore, if they do not come up spontaneously in the discussion around what the patient hopes to gain from the session, they should be explicitly explored. A suggestion for wording to open the topic for discussion is provided in Table I, but alternatively a tool like the Genetic Counseling Outcome scale, which contains items that address issues like guilt, can be used.[28] Though it was developed for research purposes, we have been using it with great success clinically[16] to facilitate contracting.

Once the patient's expectations and needs have been uncovered, the clinician can propose an outline for the session. Our clinical experience suggests that it can be helpful for the clinician to explicitly explain their own motivators for the session too (see Table I).

Discussing etiology of psychiatric illness

Rather than simply providing information in a unidirectional manner (from clinician to patient), the goal when discussing etiology of psychiatric disorders with patients is to achieve a shared understanding of cause. This necessitates engaging in a bidirectional exchange of information to uncover the patient's existing explanation for cause of illness (suggestions for asking patients about this in Table I). Without this step, patients may not apply the new information provided in the context of the clinical encounter to themselves, especially if the new information is incompatible with their existing beliefs.[29] It is important to note that while a patient may know intellectually, or have been told that the etiology of psychiatric illness is complex, they may feel that in their own family, for example, it is entirely genetic. Similarly, they may see the etiology of their own condition as fundamentally different from that of a relative, e.g. "mine is a situational depression, while Aunt Rose was just always depressed, hers was genetic". Elements from the patient's narrative can be drawn into the discussion of research findings regarding the etiology of psychiatric illness, to individualize the information and help the patient to make personal meaning from it. During this discussion it is critically important to emphasize the key messages in Table III.

These discussions are facilitated by the use of visual aids (contact corresponding author for full set of visual counseling aids) representing how genes and environmental factors work together to contribute to the development of psychiatric illness, and how protective factors can be employed.

It is important to personalize the discussion about illness etiology to the patient's own unique circumstance and experience. For example, it can be helpful to show the patient that their parent experienced psychiatric illness (if applicable), and to talk about how this may have contributed to their own increased genetic vulnerability. Or, if there are no other affected family members, it can help to discuss how people can have genetic vulnerability, without a positive family history. Similarly, in addition to sharing information about some of the environmental factors that – according to research -can increase vulnerability (like childhood head injury[30]) it is useful to ask the patient if any of the examples resonated for them, or if they had other experiences that they were wondering about.

Discussing protective factors/self-management strategies

When talking with patients about strategies for recovery and protecting mental health, the principles of personalizing the discussion should again be applied. This can involve exploring sleep, social support, current exercise and nutrition practices [31–34], and other strategies/activities that the patient finds help them cope when they feel stressed or unwell. The clinician can ensure that patients are aware that these strategies will not only be of value for taking care of their own mental health during the pregnancy and postpartum (when they may be more vulnerable themselves, particularly if they have a personal history of psychiatric illness,[35–38] see "managing issues related to maternal psychiatric problems," below), but that they can also encourage and model these self management strategies with their children to help protect their mental health, too.[31–34] However, our clinical experience reveals that patients can feel guilty about not doing as much as they feel that they "should" to take care of their own mental health, and this can be debilitating. Therefore, it can be helpful to explicitly acknowledge that these self-management strategies can be difficult to do consistently for most people–and that celebrating ones successes in this regard is important.

Further, patients who are seeking to identify ways to support their children's mental health can be encouraged to talk with them to create an environment in which psychiatric illness is not a taboo subject, and in which their child feels comfortable to let them know if they are struggling. Given that avoiding cannabis and crystal meth can be particularly important for those with increased vulnerability to psychosis,[39–41] patients can also find it helpful to discuss how to talk about avoidance of street drugs with children.

Communicating about risk for children to develop psychiatric illness

The discussion about risk for children to develop psychiatric illness should be handled in the same way as the discussion of etiology. Specifically, after discussing etiology, it is important to check in with the patient about whether knowing specific chances is of interest – even if this was their primary presenting interest. In our experience, many patients who present requesting to know chances for their children to develop psychiatric illness actually *decline*

to discuss specific probabilities after a thorough discussion of the etiology of psychiatric illness. It seems that patients are often sufficiently reassured by their new understanding that it is not a foregone conclusion that their child will develop a psychiatric illness, and that there are things that can be done to protect mental health, to the point that knowledge of specific probabilities is no longer attractive.

For patients who are interested in a discussion of probabilities, the clinician can first explore whether they are interested in discussing probabilities for all psychiatric diagnoses in the family (if there are multiple), or if there is one in particular that they are most concerned about that they would like to focus on. The clinician should also open a discussion with the patient about whether they have an existing idea about what the chance for their fetus to develop psychiatric illness might be, where this impression comes from, and whether the discussion of these numbers is important to them in terms of how they manage the pregnancy, or prepare for the future. It can also be helpful to ask the patient about their perceptions of whether, to them, there are chances that would feel “high” or “low”.

Deriving estimates of probabilities for children to develop psychiatric illness

Currently, determining chances for children to develop psychiatric illness is typically not based on genetic testing, but rather is typically based on detailed assessment of a three generation psychiatric family history.[5,6] In fact, there are currently no evidence-based clinical practice guidelines regarding the use of genetic testing in the context of psychiatric illness (N.B. as described above, we are excluding pervasive developmental disorders like autism from this discussion, for which practice guidelines for testing do exist)[21], and no recommendations about using these tests in the context of pregnancy. As a result, clinical practice regarding genetic testing for psychiatric illnesses varies at the levels of individual healthcare professional and institution. In our own clinical practice, we typically only consider prenatal genetic testing when the family history suggests that the psychiatric disorder in the family is associated with a genetic syndrome (e.g. 22q11.2 deletion syndrome). Despite this, and importantly, our analysis of patient outcomes of PGC *in the absence of genetic testing* revealed meaningful patient benefits.[16] We outline how clinicians might discuss different genetic testing strategies and their limitations in the context of psychiatric disorders in Box 1.

Box 1

Discussing genetic testing to predict offspring psychiatric illness

Patients typically arrive for themselves at the conclusion that genetic testing will not be able to tell them definitively whether or not their child will develop psychiatric illness during the discussion about etiology of illness. However, it is important for clinicians to help all patients to appreciate that there are at present, no genetic tests that can establish, confirm or refine a psychiatric diagnosis, and therefore the best that any genetic testing can offer when applied pre-symptomatically is probabilistic (rather than categorical or definitive) information.

Testing for copy number variations

Several CNVs have been identified that can contribute to development of psychiatric disorders[62,64–66] and they can be detected using different testing techniques including chromosomal microarray, and next generation sequencing methods. However, no CNV has yet been identified that directly causes psychiatric illness in a fully penetrant manner.[22,67] For example, 22q11.2 deletion syndrome carries one of the highest likelihood ratios of developing some form of psychiatric illness[68], including a ~30% chance of schizophrenia spectrum disorders, but even for this CNV penetrance for psychiatric disorders seems to be incomplete.[46,68] Cumulatively, CNVs are common in the population, and are not necessarily pathogenic, thus the relevance to the etiology of psychiatric illness of most that can be detected is uncertain.

Testing for single nucleotide polymorphisms

Though it is likely that we have yet to identify all single nucleotide polymorphisms (SNPs) that are associated with psychiatric illness, there are many that have already been described.[62,69] SNPs can be detected using strategies including next generation sequencing methods and panel based testing. Typically each SNP individually confers only a very small contribution to vulnerability to psychiatric illness so testing for individual variants of this kind is of minimal clinical utility. However, the derivation of polygenic risk scores (combining information for as many associated SNPs as possible) for psychiatric disorders is an area of increasing interest.[70,71] At present, these approaches have predictive values comparable to analysis of a detailed three generation psychiatric family history, but ultimately, as and when they surpass this threshold, may be used more clinically.

In many encounters, clinicians may find themselves providing estimates of the probability for a patient's child to develop psychiatric illness using empiric data. Though empiric data regarding probabilities of recurrence exist for many of the common conditions such as schizophrenia, bipolar disorder, depression, obsessive compulsive disorder,[5,42–44] these have important limitations (for example, family histories of psychiatric illness are often considerably more complex than family structures for which empiric recurrence data exist), and should be used only with careful clinical judgment, as described elsewhere.[5] It is not uncommon for the best estimate of chance for a child to develop a psychiatric disorder to take the form of a relatively broad range (e.g. 15 – 50%). Though research shows that clinicians question the value of providing ranges like these and can feel uncomfortable doing so,[25] patients can not only understand and tolerate the inherent uncertainty, but also feel satisfied with this kind of information.[45] When providing ranges of probability, we always provide an open explanation of the upper and lower limits (for suggested wording, see Table I), and find that patients tend to respond well to this.

Once the probabilities have been disclosed, the clinician should explore the patient's reaction to the information, and whether it is in line with their expectations. The clinician can watch for patient cues and take opportunities as appropriate to acknowledge the difficulty of living with the worry of raising a child who may have a higher chance for psychiatric illness, and of the uncertainty around whether an emerging behavior is one

typical of adolescence or symptoms of emerging psychiatric problems. In the context of this discussion, patients can find it helpful to hear that while their potential future child may have higher chances for psychiatric illness than others, the family's experience with psychiatric illness provides them with the knowledge of what emerging symptoms of psychiatric problems might look like. This knowledge can allow the family to access appropriate help in a timely manner if it is needed, and research shows that early intervention promotes optimal long-term prognosis.[46–49]

When providing consult reports to patients' referring physicians, our practice (developed in consultation with our clinical ethics program) is to indicate that specific probabilities were discussed without documenting the numbers themselves (because they reflect personal information about someone other than the individual to whom the chart relates). [50]

Special circumstances: managing issues related to maternal psychiatric problems

Guidelines suggest that all healthcare professionals who come into contact with pregnant women should screen their patients for mental health problems[51], but this becomes particularly important in the context of prenatal PGC when the patient has a personal history of psychiatric illness, as they are at increased risk for relapse in the perinatal period.[31–34,52] Perinatal psychiatric illness can have profound consequences: suicide is the leading cause of maternal death during the first year postpartum, and women with a history of mood or psychotic disorders have an increased chance to develop postpartum psychosis, which is considered a psychiatric emergency.[33,34,53–55]

Screening for current mental health issues can be accomplished through simple questioning about whether they are currently noticing any of the symptoms that they have experienced in the past, but ideally involves using a validated tool like the Edinburgh Postpartum Depression Scale (EPDS).[51] This 10 item scale has been validated for use both in pregnancy and the postpartum, is available in several languages and takes about five minutes to complete,[56–58] and so can easily be incorporated into the beginning of a prenatal PGC appointment.

For patients who are currently experiencing mental health problems, the clinician can ask about their supports, whether they are receiving any treatment, and whether the healthcare professional who is following their pregnancy is aware and arrange for communication and referral (e.g. ideally to a perinatal mental health specialist) as necessary. For patients about whom the clinician is particularly concerned, following a protocol outlined in a suicide assessment checklist can be helpful (e.g. from the Substance Abuse and Mental Health Services Administration).[59] Regardless of whether the patient is currently actively experiencing mental health problems, if there is a history of these issues, the clinician should explore whether they currently have someone following them for their mental health and discuss the fact that while there is an elevated risk of experiencing a relapse of psychiatric illness during the postpartum period, it is not a guarantee. It is important for women to know that they have an increased risk for relapse during the postpartum period so that they can get the appropriate supports and plan (including regarding the use of psychotropic

medications[60]) in place. The clinician can discuss with the patient that while it can be hard to fully engage in protective/self-management strategies (as discussed above), particularly with a newborn, they can be employed to protect mental health during the pregnancy and postpartum, and that social support is particularly important. Some women also find it helpful to complete a "Ulysses Agreement" (or advance directive [61]) outlining what they would like to happen for themselves and for their children in the event that they become unwell – the communication process with family and healthcare providers in developing this plan can provide peace of mind and be experienced as empowering.

Summary

Psychiatric disorders are common, and are of relevance to many patients in the prenatal setting. It is important for clinicians to routinely ask their patients about personal and family history of psychiatric illness in order to identify individuals who could benefit from genetic counseling targeted to this issue and referral for support. By using the strategies outlined herein (and more fully detailed elsewhere[32]) to engage patients in psychotherapeutically oriented discussions around etiology of psychiatric illness and techniques for managing mental health issues, and risk, clinicians are ideally placed to help patients to feel empowered.

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Table I

Suggestions for how clinicians might approach various aspects of the prenatal psychiatric genetic counseling session.

Issue	Suggested wording
Broad screening questions for eliciting a psychiatric family history (suggestions from the FIGS)[27]	*"Has anyone ever been hospitalized for a "nervous breakdown?"* *"Has anyone in the family attempted suicide?"* *"Has anyone received electroconvulsive therapy or ECT?"* *"Is there anyone in the family who has had noticeable symptoms of: paranoia/hearing or seeing things that are not there/depression/anxiety/checking/hoarding?"* *"Has anyone in the family taken medications for their "nerves" or medicines like lithium or Prozac?"*
Exploring a patient's interest in discussing implications of their psychiatric family history	"*Thank you for sharing the information about the family history of psychiatric illness. Would you be interested in having a conversation with me about what we know from research about the things that can contribute to the development of these conditions, chances for children to develop a psychiatric problem, and what sorts of things might be done to protect mental health?"*
Contracting: situations when a patient expresses interest in discussing chance for illness recurrence only	*"I hear that what you really want to know about is the chance for your future child to develop schizophrenia. We can certainly talk about that. What I propose to do first, is to provide you with some context for the numbers. We can talk a bit about what we know from research about the causes of psychiatric illness and how this relates to your/your family members experiences. We can also talk about how this relates to how people recover, and what we can do to protect mental health. Would that be alright? I find that having this context tends to really help people to get the most out of the conversation about the numbers."*
Contracting: Opening emotional issues as a topic for discussion	*"Sometimes people have feelings of guilt around their personal experience with/family history of psychiatric illness, and/or they can sometimes feel judged for wanting to be a parent despite having a history of psychiatric problems, and these can be helpful things to talk about - have you experienced anything like this?"*
Contracting: Explicit statement of clinician's goals for the session	*"I want to thoroughly addresses the needs and questions that you have, so that you leave feeling that you got something meaningful and important from our conversation today. To make this session as helpful for you as it can be, I'd like to invite you to share your thoughts and questions with me as we go – does that sound ok?"*
Exploring patient's existing explanation for cause of illness	"*Can you tell me what you think contributed to the development of your own illness?* *"What was going on for you around the time you experienced your first episode?"*
Discussing probability for illness recurrence in children: explaining ranges	*"I am basing this range on the family history information that you provided for me. Studies have shown that if someone has a single first degree relative (like a parent) with schizophrenia, then their chance to develop the same condition themselves is around 15%. But, in this situation, in addition to having a parent who has experienced schizophrenia, your future child also has an uncle, a grandparent, and a great grandparent all on the same side of the family, and all with (what sounds like) schizophrenia. A greater the number of affected relatives suggests a greater chance of recurrence in the family. If we assume that your own parent and grandparent did indeed have schizophrenia or something like it, then the upper end of the range of chance is likely to be around 50%. So in this situation the chance for your child is somewhere between 15 and 50%"*

Table II

Examples of patients' presenting interests, their deeper emotional motivations and associated key misconceptions.

Presenting (stated) interest	Deeper emotional motivation	Key misconception
Genetic testing	Guilt about passing on "bad genes", and/or fear, need for control	Genetic testing will provide definitive answer
Probability for child to develop psychiatric illness	Fear, need for control	Overestimation of probability
	Guilt around being a "bad parent" due to need to take psychotropic medication during pregnancy	That all women should stop taking medications during pregnancy to protect the fetus

Table III

Key messages to convey to patients during a psychiatric genetic counselling appointment

Key messages to convey in psychiatric genetic counseling
Genetic factors work together with environmental factors (or our experiences) to contribute to the development of a mental illness.
We cannot control the genes that we pass along to our children.
We all have some genetic vulnerability to mental illness[62], but we vary in how much.
Those with higher genetic vulnerability to mental illness can thrive under the right circumstances.[63]
Mental illness is not genetically determined. Indeed there is no single factor that is necessary and sufficient to cause someone to develop a psychiatric disorder (see Box 1 for more discussion).
We do not inherit mental illness itself, but we can inherit a vulnerability to mental illness.
There are things that we can do to protect mental health: sleep, nutrition, exercise, social support, finding effective ways to manage stress, avoiding street drugs[35–38], but there is no such thing as “perfect parenting” and we cannot definitively prevent mental illness.
Stress is a subjective experience that is: a) not always negative in valence (e.g. a planned and wanted pregnancy can still be stressful), and b) need not be classifiable as trauma to contribute to mental illness vulnerability.
Mental illness is not a moral failing, and it is not anyone’s fault.