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BRIEF REPORT

Leveraging electronic health records to inform genetic counseling practice surrounding psychiatric disorders

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Abstract

Since nearly one-fifth of US adults have a psychiatric disorder, genetic counselors (GCs) will see many patients with these indications. However, GCs' reports of inadequate preparation and low confidence in providing care for patients with psychiatric disorders can limit their ability to meet patient's needs. How frequently psychiatric disorders present in GC sessions is currently unclear. Here, we used deidentified electronic health records (EHR) to estimate the prevalence of 16 psychiatric disorders. In 7,155 GC patients, 34% had a diagnostic code associated with a psychiatric disorder; 23% with anxiety/phobic disorders; 21% with mood disorder/depression; 5% with attention deficit hyperactivity disorder (ADHD); and 1% with psychotic disorders. Compared to 415,709 demographically matched controls, GC patients showed a significantly higher prevalence of psychiatric disorders (GC prevalence: 34%, matched prevalence: 30%, p-value < 0.0001) driven predominantly by anxiety disorder, major depressive disorder, generalized anxiety disorder, and ADHD. Within GC specialties (prenatal: $n = 2,674$, cancer: $n = 1,474$, pediatric: $n = 465$), only pediatric GC patients showed a significant increase in psychiatric disorder prevalence overall (pediatric GC prevalence: 28%, matched prevalence: 13%, p-value < 0.0001). However, significant evidence of increased prevalence existed for generalized anxiety disorder (prenatal GC prevalence 6.4%, matched prevalence: 4.9%, p-value < 0.0001), anxiety disorders (cancer GC prevalence: 26%, matched prevalence: 21%, p-value < 0.0001 and pediatric GC prevalence: 12%, matched prevalence: 5.5%), and ADHD (pediatric GC prevalence: 18%, matched prevalence: 7.9%, p-value < 0.0001). These results highlight the need for additional guidance around care for patients with psychiatric disorders and the value of EHR-based research in genetic counseling.

KEYWORDS
genetic counseling, genetic counselors, intervention, mental health, psychosocial

1 | INTRODUCTION

Mental health is a global public health concern with the cumulative impact of psychiatric disorder presentation being associated with injurious outcomes for individuals ranging from increased socioeconomic burdens to increased healthcare cost, poorer quality of life, and early mortality (Vigo et al., 2019). Multiple studies spanning several decades have provided information regarding the global prevalence of psychiatric disorders and have indicated 1 in 5 adults will present with psychiatric disorder symptoms in a given

year (Kessler et al., 2007; Steel et al., 2014). A large-scale global analysis completed by the World Health Organization in 2007, which included over 85,000 individuals from 18 countries, found estimates for the lifetime prevalence of mood disorders (20.8%), anxiety disorders (16.9%), substance abuse disorders (10.5%), and total lifetime prevalence of any psychiatric disorder to be 36.4% (Kessler et al., 2007). This retrospective study indicated that nearly one-third of the general population will present with a psychiatric disorder during their lifetime, but more recent prospective studies indicate a more accurate assessment might increase the number of individuals to nearly half of the population (Moffitt et al., 2010).

Clinical genetic counselors working across specialties see patients and disseminate diagnoses for genetic conditions with well-elucidated psychiatric disorder comorbidities. Of the more well established are neurodevelopmental psychiatric disorders resulting from genomic copy number variants (CNVs). A body of research has indicated patients with CNVs have an increased risk of developing both common psychiatric disorder phenotypes like anxiety and depression and more rare conditions like schizophrenia (as seen in patients with 22q11.2 deletions). This research also indicated clinical outcomes could improve with patients being counseled regarding potential psychiatric comorbidities (Martin et al., 2020; Moreno-De-Luca et al., 2013; Wain et al., 2021). Moreover, multiple systematic reviews and cross-sectional studies have demonstrated that patients with chronic conditions like neurofibromatosis type 1 or cystic fibrosis are more likely to present with anxiety and depression (Cohen et al., 2015; Quittner et al., 2016). For example, nearly 55% of adults in a population affected with NF1 scored above the threshold on the Center for Epidemiologic Studies Depression scale indicative of clinical depression (Cohen et al., 2015). Additionally, an international committee on mental health in cystic fibrosis found that not only were depression and anxiety seen at relatively higher rates in patients with cystic fibrosis, but also that a course for prevention of these disorders should be implemented upon diagnosis (Quittner et al., 2016).

Genetic counselors have also self-reported hesitancy in providing psychiatric genetic counseling with concerns ranging from lack of preparedness in training, to scant risk assessment data, lack of genetic testing options, and overall discomfort navigating the complexities of psychosocial counseling when patients have psychiatric disorders (Low et al., 2018; Monaco et al., 2010). However, patients and families have reported eagerness to receive care in psychiatric genetic counseling, and psychiatrists have emphasized the usefulness of genetic counseling in psychiatry practices (Hippman et al., 2013; Martorell et al., 2019; Quinn et al., 2014). These findings highlight the need for better understanding of GC patient populations with psychiatric diagnoses to better enable optimal care.

Although more information is needed to understand the propensity for psychiatric comorbidities across many additional genetic conditions, decades of research has shown that those suffering from any chronic illness are at a higher risk of psychiatric disorder presentation (Delamater et al., 2017). Policy changes favoring interventional and integrated behavioral healthcare strategies might be of great use in addressing and overcoming barriers regarding mental health care for patients (Austin & Honer, 2007). Genetic counselors are trained to provide integrated psychotherapeutic counseling and can do so within multiple medical disciplines. However, more information is needed to better understand within what specialty, and how frequently patients might present with a psychiatric disorder.

GC research regarding psychosocial concerns and counseling surrounding psychiatric disorders has provided tremendous insight to increase the efficacy of attending to behavioral healthcare needs for patients and recognizing necessity for referral (Austin & Honer, 2007; Cunningham et al., 2018; Hippman et al., 2013). However, until now, epidemiological research for the GC patient population has been restricted to smaller cohort studies, and to our knowledge this is the first study to assess the frequency of psychiatric disorders in the genetic counseling patient population using large-scale electronic health record (EHR) data.

What is known about this topic

Since nearly one-fifth of US adults have a psychiatric disorder, genetic counselors (GCs) will see many patients with these indications. However, GCs' reports of inadequate preparation and low confidence in providing care for patients with psychiatric disorders can limit their ability to meet patient's needs.

What this paper adds to the topic

This study assesses the frequency of psychiatric disorders in the genetic counseling patient population using large-scale electronic health record (EHR) data.

2 | METHODS

Statistical analyses were performed to calculate prevalence of psychiatric disorders among patients having at least one genetic counseling visit. Data were acquired from the Vanderbilt University Synthetic Derivative (*SD*) which is a deidentified version of the electronic health record (EHR) (Roden et al., 2008) consisting of roughly 2.8 million individuals. Patients were included if considered a "frequent visitor" to the Vanderbilt University Medical Center (VUMC) defined as having two unique visits over a four-year span. The remaining 845,423 patients were then queried for at least one instance of the Genetic Counseling services CPT Code 96040, which yielded a GC patient population of 7,155 individuals. Prevalences of psychiatric disorders were calculated based on patients having at least one or at least two instances of 16 phecodes (phecodes, version 1.2) associated with psychiatric disorders (Figure 1) (Denny et al., 2013). Location of care data was used to identify in what specialty the genetic counseling patients received care. Of the 7,155 patients seen by a genetic counselor, location of care provided the attributable

specialty for 4,671 GC patients. 2,371 patients were excluded where the site of care data did not provide conclusive evidence to whether the patient was seen at a location where a GC provided care. 2,674 patients were seen by prenatal GCs, 1,474 patients by cancer GCs, and 465 patients by pediatric GCs. The prevalences of psychiatric disorder phecodes were then calculated for the patient populations within these specialties.

The 7,155 GC patients were matched with 838,268 frequent visitor controls in order to compare prevalences to a non-GC sample. For each GC patient, controls were considered a match if they had the exact same age in years, reported sex, reported race, and number of unique years in which they visited VUMC. In total, 7,088 GC patients could be matched to at least one of 415,709 controls. For testing differences in prevalences, we randomly selected a single matched control for each case and calculated the prevalence among those 7,088 random controls. This selection process was performed 10,000 times, which allowed for direct assessment of statistical significance after correcting for 64 tests, and a *p*-value was calculated empirically based on how often the permuted control sample had a prevalence equal to or higher than the GC sample.

We repeated the same procedure for each of the GC specialty patient populations that included 2,674 prenatal GC patients matched to 151,814 controls, 1,474 cancer GC patients matched to 180,832 controls, and 465 pediatric GC patients matched to 78,205 controls. Additionally, given that pediatric genetic counselors at VUMC also see adult patients in general genetics, we defined our pediatric patient population to reflect that of the American Academy of Pediatrics (patients being under the age of 21 at the time of their first genetic counseling visit).

3 | RESULTS

We identified 7,155 GC patients at VUMC including 6,448 females, and 707 males, with a mean age of 40 years (81% White, 11% Black, 3% Asian, 2% unknown, 3% other) (Figure 1, Figure S1). Among this set, 2,415 (34%) had at least one of 16 psychiatric disorder diagnoses. In total, 1,654 patients (23%) were diagnosed with anxiety/phobic disorders, 1,521 mood disorder/depression (21%), 329 attention deficit hyperactivity disorder (5%), and 102 with psychotic disorders (1%) (Table S1). After demographically matching to controls based on age, sex, race, and record length (see Methods), we had 7,088 GC patients and 415,709 matched controls in which to test for differences in prevalence of psychiatric disorders. We identified a significantly lower average psychiatric disorder prevalence in our matched controls (30%, p-value < 0.00001) after 10,000 permutations where

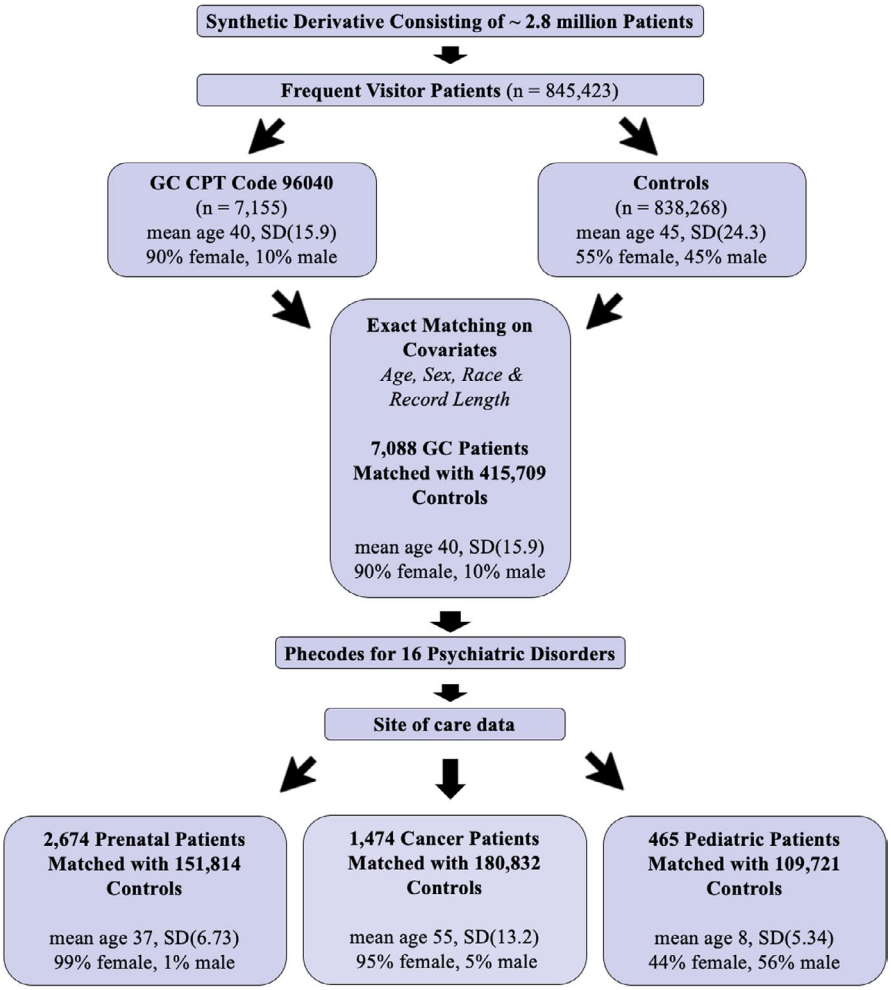

FIGURE 1 Analytical steps and samples used to calculate prevalence of psychiatric disorder diagnoses in patients seen by genetic counselors and matched controls. Mean age and standard deviation represent age at time of data analysis

we randomly selected one matched control for each GC patient. Among specific psychiatric disorders, we saw increased prevalences of major depressive disorder, anxiety disorder, generalized anxiety disorder, phobias, and ADHD among the GC patients (Figure 2, Table S2).

Performing the same matching analysis within three GC specialties resulted in 2,674 prenatal GC patients and 151,817 matched controls, 1,474 cancer GC patients and 180,832 matched controls, and 465 pediatric GC patients and 78,205 matched controls. Only the pediatric GC population had a significantly increased prevalence of all psychiatric disorders combined (28%) compared to 13% in the matched controls (p-value < 0.0001) (mean age of 8 years, *SD* 5.34). Both the prenatal (31% compared to 30% in matched controls, p-value = 0.121) and cancer (38% compared to 36% in matched controls, p-value = 0.026) GC populations had higher overall prevalences of psychiatric disorders compared to the matched controls but neither surpassed Bonferroni multiple test correction for all 64 tests (p-value = 0.0078).

Despite a lack of significant difference in total prevalence in patients seen in prenatal and cancer settings, there were specific disorders with significant differences in prevalence within the specialties. The prenatal GC patients had a significant increased prevalence of generalized anxiety disorder compared to the matched controls (6.4% versus 4.9% respectively, p-value = 0.0001) (Table S3). The cancer GC population showed a significant increase in anxiety disorder diagnoses (26% versus 21% in matched controls, p-value<0.0001, Table S4). The primary drivers for the increased prevalence of psychiatric disorders in the pediatric population were attention deficit hyperactivity disorder (18% versus 7.9% in the matched controls, p-value < 0.0001) and anxiety disorder (12% versus 5.5% in the matched controls, p-value < 0.0001, Table S5). Nominal significance ($p < .05$) was also seen among mood disorders and major depressive disorder in the prenatal population, major depressive disorder and phobia among the cancer population and generalized anxiety disorder, anxiety, phobic and dissociative disorders, and phobia in the pediatric population. Requiring at least two phecodes rather than one produced lower prevalences but the same significant differences in GC patients compared to the matched controls (Table S6).

In an attempt to better understand significant differences in psychiatric disorder presentation within specialties, we calculated the time interval between the first generalized anxiety disorder diagnostic code entered and the date of the first GC visit for those patients seen by prenatal GCs who had at least one phecode associated with a generalized anxiety disorder diagnosis (n = 182, 100% female, 86% White, 9% Black 2% Asian, 2% other, 1% unknown). On average, patients had their first entry of a generalized anxiety disorder phecode 85 days prior to their first GC visit which was not significantly different from expectation (p-value = 0.140, Wilcoxon signed rank test, Figure S3). The average age at initial entry of the diagnostic code was 32 years, and the average age at the genetic counseling visit was 37 years , Table S7). Requiring that patients had longer EHR records prior to GC visit had no impact on those results (Table S7).

Next, we assessed the temporal relationship concerning the statistically significant anxiety disorder prevalence in patients seen by cancer genetic counselors with the same methodology as used above (n = 378, 97% female & 3% male, 93% white, 6% black, 0.05% Asian, 0.05% unknown). Patients seen in a cancer setting were significantly more likely to receive their first anxiety disorder diagnostic code prior to their genetic counseling session by an average of 754 days (p-value = 5.023e-12, Wilcoxon signed rank test, Figure S4, Table S8), The average age at the first cancer genetic counseling visit was 51 years (*SD* = 12.3).

Finally, we assessed the timing of diagnosis in pediatric patients presenting with ADHD and anxiety disorder. Of the 18% of pediatric patients with at least one phecode associated with ADHD (n = 86, 66% male, 34% female, 82% White, 10% Black, 3.5% Asian, 3.5% unknown, 1% other), the mean age of the first diagnostic code entry was 8 years (*SD* = 3.59) (Table S9). Stratifying the population by sex indicated no significant difference in mean age of diagnosis at 8.6 years (*SD* = 3.51) for females and 8.4 years (*SD* 3.66) for males (p-value = 0.6511, Wilcoxon signed rank test). Notably, 81% (n = 70) of pediatric patients with an ADHD phecode had their first entry before the age of 12. Additionally, of the 12% of pediatric patients with anxiety disorder diagnoses (n = 57, 49% female, 50% male, 93% White, 3.5% Black, 3.5% Asian) the mean age at diagnosis was 11 (*SD* = 4.54) years with 56% of that population being diagnosed before the age of 12.

4 | DISCUSSION

We find that patients seen in a GC setting are more likely to have been diagnosed with an anxiety disorder, major depressive disorder, generalized anxiety disorder, and attention deficit hyperactivity disorder than matched controls. Thus, clinical GCs should be aware which psychiatric disorders will be more commonly observed within their specialties and implement interventional strategies and techniques aimed at mitigating associated symptoms. The significant evidence of increased prevalence for generalized anxiety disorder within a prenatal setting, anxiety disorders in cancer and pediatric cohorts, and attention deficit hyperactivity disorder specific to the pediatric population provide a good preliminary overview of the diagnoses GCs will commonly face in routine practice.

More specifically, our data reveal that patients seen in prenatal and cancer settings will have a higher prevalence of anxiety disorders, the presentation of which may be in part situational, given the stressors surrounding pregnancy/reproductive health, or the emotional impact of having a personal or family history of cancer. The temporal analysis regarding these populations indicated that although the propensity for anxiety was enriched in both populations, only patients seen in a cancer setting would be more likely to have a diagnosis prior to a GC visit. This information could aid in the provision of psychosocial support for these populations and substantiate referral to the appropriate behavioral health providers when necessary.

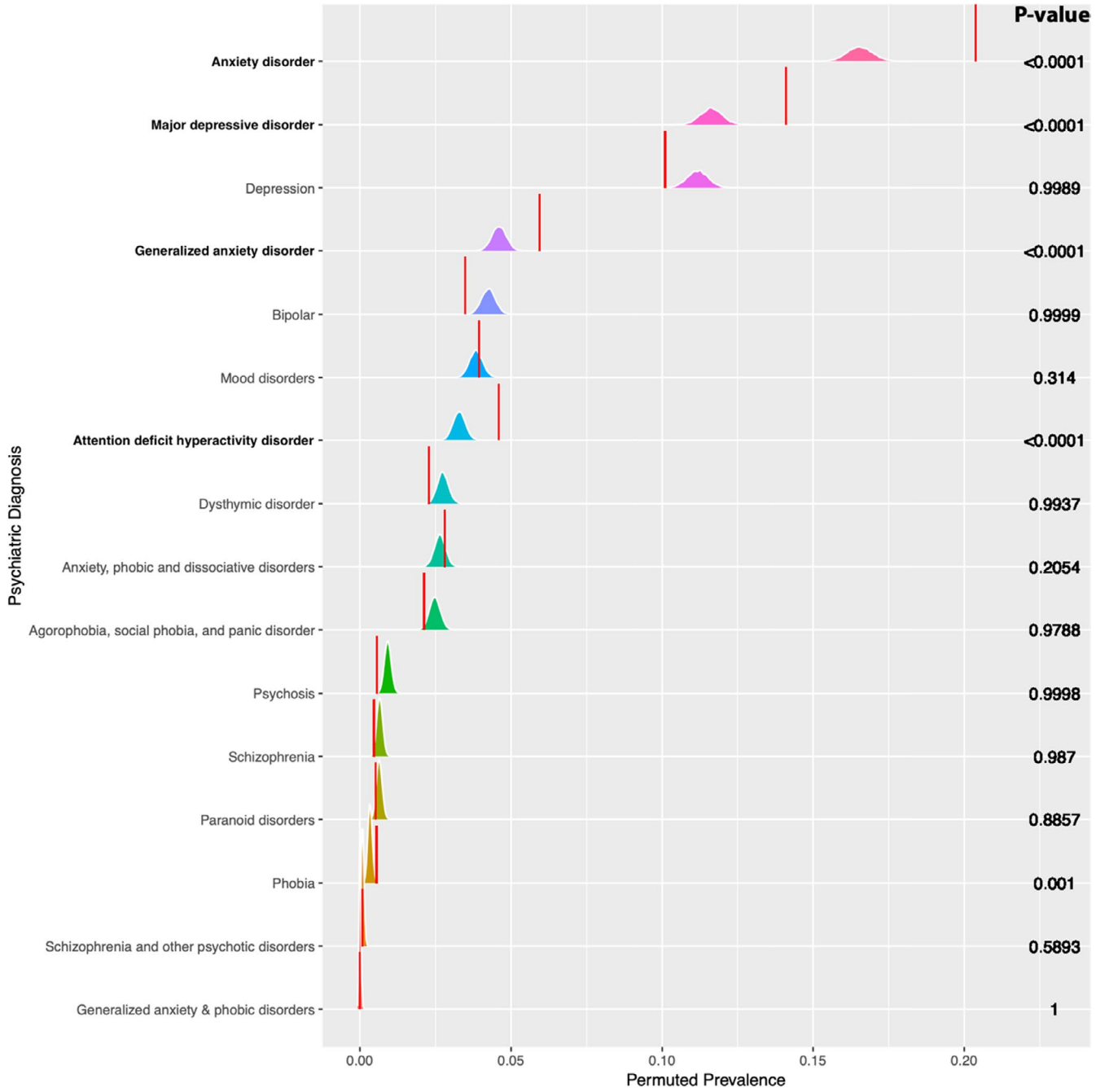

FIGURE 2 Empirical prevalence distribution of matched controls from 10,000 permutations (colored density distributions) compared to the prevalence of psychiatric disorders in the genetic counseling patient population (red line). Empirical *p*-values are listed on the right, bolded diagnosis indicates significance after multiple-test correction

The overall increased prevalence of psychiatric disorders in the pediatric population is likely in part founded upon the increased prevalence of neurodevelopmental comorbid psychiatric phenotypes as has been established in research concerning CNVs and other mendelian conditions like NF1 where learning disabilities and psychiatric disorders occur as part of the natural history of known genetic disorders (Cohen et al., 2015; Martin et al., 2020; Moreno-De-Luca et al., 2013; Wain et al., 2021). It is important to note that one might expect an increase in the prevalence of not only the significant anxiety disorder diagnoses as pediatric patients age, but also the more rare and nominally significant conditions like generalized anxiety disorder, anxiety phobic and dissociative disorders, and phobia. Together, this information might aid in an appropriate risk estimate for patients allowing for patients and families to better anticipate symptoms, optimize the opportunity for enhanced clinical outcomes, and enhance psychotherapeutic approaches (Wain et al., 2021).

Genetic counselors have a unique opportunity to counsel patients regarding psychosocial concerns that arise within a clinical setting. The multifactorial continuum of psychiatric illness

presentation requires individualized strategies for intervention, referral, and mitigation which can be daunting for providers who are not trained to implement behavioral health practices. Additionally, genetic counselors have self-reported inadequate training and decreased self-efficacy in their ability to navigate the intricacies necessary to provide care for patients regarding psychiatric illness (Low et al., 2018). This initial assessment indicates patterns of psychiatric disorder presentation within genetic counseling subspecialties and calls for effective facilitation of training for GCs to navigate the impact of psychiatric disorders on decision making and coping in their patients regardless of their indication for referral.

We recognize several limitations to the interpretation of this work. One is the vast overrepresentation of female patients, which is exacerbated by the number of patients seen at the VUMC seeking reproductive genetic counseling services in addition to women seeking counseling with either a personal or family history of cancer. Also, the use of diagnostic codes to capture individuals with a psychiatric disorder is limited as these are billing codes and not directly equivalent to a clinical diagnosis; however, more stringent definitions did not change overall results. Patients records are incomplete and represent visits only to VUMC-affiliated providers and some patients might seek behavioral health services outside of the VUMC network. We matched patients based on demographic information and record length to account for this issue but record length is only proxy for healthcare utilization and even after matching on record length GC patients have more diagnostic codes than the comparison groups. This could indicate a difference in the extensiveness of medical care or history recorded for the GC patients compared to controls and in turn lead to an underrepresentation of psychiatric phecodes in the control population. Additionally, individual providers may vary in diagnostic documentation practices where patients with psychiatric disorders presenting with other comorbidities like intellectual disability may remain undiagnosed and in turn lead to an underrepresentation of diagnoses in the GC patient population.

To our knowledge, this is the first paper to assess psychiatric disorder presentation in the GC patient population using large-scale EHR data. We show that GCs are likely to encounter patients with psychiatric disorders more frequently than seen in the general population and that specific disorders may be overrepresented among certain GC specialties. Leveraging EHR data could be of great use for future directions of GC research to aid in elucidating patterns of referral, prevalence of phenotypes within subpopulations, and has the potential to reach well beyond psychiatric disorders in attempt to address patient needs. Methodology utilizing EHR data with predictive modeling is becoming increasingly recognized as a powerful tool to enhance patient care with potential to optimize screening protocols for patients needing referral for cancer genetic counseling, predicting pediatric patients at risk of genetic disease, and even aid in interventions as clinical decision support tools for patients at risk for self- harm (Morley et al., 2021; Sin et al., 2018; Walsh et al., 2018). Ultimately, we hope these findings could be used to inform policy changes allowing for increased efficacy in training and genetic counseling surrounding psychiatric disorders.

AUTHOR CONTRIBUTIONS

Conceptualization: L.R., D.R., G.H., H.P., N.C.; Data curation: L.R., T.M.; Formal Analysis: L.R.; Investigation: L.R.; Methodology: D.R., L.R.; Validation: D.R.; Visualization: L.R.; Writing—original draft: L.R.; Writing—review & editing: L.R., G.H., H.P., N.C., D.R.

D.R. confirms that they had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All of the authors gave final approval of this version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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COMPLIANCE WITH ETHICAL STANDARDS

CONFLICTS OF INTEREST

L.R., T.M., H.P., N.C., and D.R. declare that they have no conflict of interest. G.H. is a paid employee of Concert Genetics and serves on the Board of Directors for MyGene Counsel, for which she is compensated with stock.

HUMAN STUDIES AND INFORMED CONSENT

This study was reviewed by the Vanderbilt University Medical Center IRB #200339. No informed consent was required from subjects as data were anonymously extracted from the Vanderbilt University Medical Center Synthetic Derivative. All procedures followed were in accordance with US Federal Policy for the Protection of Human Subjects.

ANIMAL STUDIES

No non-human animal studies were carried out by the authors for this article.

DATA SHARING AND DATA ACCESSIBILITY

Summary level data regarding prevalence of psychiatric disorder diagnostic codes and age at entry of the first diagnostic phecode are presented in Tables S3–S6 and S9. All requests for raw (for

example phecode matrices for cases and controls) data are reviewed by Vanderbilt University Medical Center to determine whether the request is subject to any intellectual property or confidentiality obligations. For example, patient-related data not included in the paper may be subject to patient confidentiality. Any such data and materials that can be shared will be released via a material transfer agreement.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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