Before the Nazi regime focused its efforts on the extermination of European Jewry, one of its early eugenics directives aimed at cleansing the gene pool of psychiatric disease. Thousands of mentally ill patients were either sterilized against their will or murdered as part of the German Racial Hygiene Movement. Shamefully, this movement was largely fueled by the research and ideologies of early psychiatric geneticists, such as Ernst Rudin [1].

Similar efforts were undertaken in the United States to prevent the reproduction of those deemed mentally insufficient. This practice was famously upheld by the Supreme Court in *Buck v. Bell* in 1927, with Justice Oliver Holmes Jr. concluding his argument by declaring that “Three generations of imbeciles are enough” in reference to the plaintiff Carrie Buck, her mother, and her daughter [2].

Given a past marred by such ethically deplorable behavior, it is vital for current medical professionals to have a thorough understanding of the ethical issues involved in psychiatric genetics and a structured framework with which to evaluate new psychiatric genetic tests. In “Ethical Considerations in Psychiatric Genetics,” Jinger Hoop provides a succinct introduction to this topic with practical suggestions on how to assess the ethical acceptability of psychiatric genetic tests.

**Summary of “Ethical Considerations in Psychiatric Genetics”**

In her review article, Dr. Hoop touches on four broad ethical issues in psychiatric genetics: (1) the use of genetic testing to predict future health outcomes, (2) the psychosocial consequences of genetic testing, (3) the effect of genetic testing on family members and communities, and (4) the ethics of the use of emerging genetic technologies [3].

She begins by describing how the landscape of clinical psychiatric genetics has changed from one focused on rare, monogenic disorders such as Huntington’s disease (HD) to one that will be dedicated increasingly to common, polygenic diseases, such as schizophrenia. In HD, the ethical debate concerns the risks and benefits of providing a patient with precise information about his or her medical future—if you have the HD gene, you will get the disease if you live until its onset, typically middle age. If little can be done to prevent the onset or mitigate the effects of the disease being tested for, is it ethical to test for the disease at all?
In contrast, hundreds or thousands of genes each confer a small increase in risk for developing schizophrenia. Testing a patient for such genes provides only an estimate of his or her increased risk for developing schizophrenia (e.g. 3 percent, when risk is 1 percent in the general population) with much uncertainty remaining. Hoop highlights the difficulty patients are likely to have in interpreting such results. Some patients may think they are completely free of risk if they test negative for a risk gene, while others may believe that they are destined to develop a disease if they test positive, when really they may have only a slightly greater-than-average risk.

Hoop identifies psychological consequences, insurance and employment discrimination, and social stigmatization as the three main psychosocial risks of psychiatric genetic testing. While genetic testing in general certainly has psychological consequences, the consequences of genetic testing for psychiatric disorders may be more profound. Many view the psyche as an inextricable component of one’s being. Thus, being told of a genetic “defect” in one’s psyche may be particularly distressing. The findings of several studies Hoop cites are consistent with this theory; they suggest that “learning one has a ‘good’ or ‘bad’ [psychiatric] genotype may have a more profound psychological impact than learning one’s absolute risk of illness”[4].

Another potential hazard of genetic testing in psychiatry is that employers, insurers, and the general public may discriminate against individuals based on their psychiatric genotypes. Hoop discusses a case of three young men who lost their jobs because their employer discovered that they had first-degree relatives with schizophrenia [4]. There is a risk that similar discrimination could occur based on one’s genotype, a risk that may be more likely to happen with mental than with physical disease. In hopes of limiting such discrimination, the United States Congress enacted the Genetic Information and Nondiscrimination Act of 2008 [5].

Genetic information can also have serious implications for relatives of a person being tested and for those who come from a similar ethnic background. For example, if a grandparent developed Alzheimer’s disease, his or her grandchild (of adult age) may wish to get tested for disease-related genes to determine the risk for developing Alzheimer’s. If the grandchild’s parent does not want to know his or her risk, an ethical dilemma arises in which the parent’s right to not to know must be weighed against the child’s right to know.

Similarly, ethical conflicts may arise during population-based genetic testing in reproductively isolated groups, such as the Amish or Ashkenazi Jews. Testing can have great public health benefits by identifying severe genetic conditions that are present in these groups. But this benefit must be carefully weighed against the risk that finding a genetic predisposition for illness, especially mental illness, could reinforce preexisting stigmas and provide a false basis for discrimination and bigotry.
At the time of Hoop’s writing, many candidate genes had been identified, but virtually no genes had been conclusively linked to psychiatric disease, with the exception of APOE for Alzheimer’s disease. Without a definitive link between gene and disease, genetic testing may be highly unethical. With significant advancements in the field, however, direct-to-consumer or physician-requested genetic testing will certainly play a future role in the management of psychiatric illness. It will fall to the clinician to interpret the results and advise patients on how to proceed. Unfortunately, data from the most recent studies published (up to 2008) [6] indicate that the vast majority of psychiatrists are insufficiently trained in genetics to provide this service and that there are too few genetic counselors to fill in the gaps.

Hoop then applies Burke et al.’s framework for categorizing ethical considerations of genetic tests to psychiatric testing specifically. According to Burke’s frameworks, the primary ethical consideration in psychiatric genetic testing is nonmaleficence, doing no harm, as few effective treatments can be provided based on test results and tests have low predictive power. Hoop proposes an expanded framework that includes additional factors, such as psychosocial risk, the level of stigma of the condition, and the newness of the test to provide a more robust evaluation of whether genetic tests for psychiatric disorders are ethical.

Lastly, Hoop emphasizes the importance of designing “prospective evaluations of the outcomes of psychiatric genetic counseling and testing…[to] complement empirical ethics research methods”[7]. She argues that the knowledge gained from such studies will help prevent genetic discrimination and improve public trust in psychiatric genetic research and testing.

Discussion
Hoop’s piece stands out in the field of bioethics not only as a review of important ethical issues in psychiatric genetics but also as a source of a novel, structured framework for evaluating the ethical nuances of new psychiatric genetic tests. This is a particularly timely contribution to the field, as our knowledge about the genetic underpinnings of mental illness has been advancing at a furious pace. For example, many genomic deletions and duplications have been detected in patients with autism spectrum disorders [8]. This has led to recent guideline changes recommending chromosomal microarray analysis as part of an initial work-up for children who display autistic-type behaviors [9]. Similar advances have been made in schizophrenia, with strong evidence for associations with vasoactive intestinal peptide receptor 2 (VIPR2), neurexin 1 (NRXN1), and transcription factor 4 (TCF4) [10].

Many more genes involved in psychiatric disease are likely to emerge in the near future, with the thousand-dollar genome, once a distant dream, now at our fingertips [11]. Furthermore, some genetically informed pharmacotherapies are now in development, from mGluR5 antagonists for fragile-X syndrome to PI3K inhibitors for schizophrenia [12, 13] With such advances, nonmaleficence will no longer be the prevailing ethical principle dictating psychiatric genetic testing. Instead, as Hoop
proposes, justice, respect for autonomy, psychosocial risk and stigma of disease will all have to be strongly considered before pursuing genetic testing for psychiatric illness.

References
4. Hoop, 328.
5. Hoop, 328-329.
6. Hoop, 331.

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