



ETHICS & MEDICS

A COMMENTARY OF THE NATIONAL CATHOLIC BIOETHICS CENTER ON HEALTH

JULY 2023 † VOLUME 48, NUMBER 7

Also in this issue: "Force-Feeding a Prisoner on a Hunger Strike" by Gerald Coleman

THE GENETIC CONTRIBUTION TO MENTAL ILLNESS

David Chen and Kevin Shaw

April 14, 2023, marked the twentieth year since the completion of the Human Genome Project (HGP) (1990–2003).¹ The HGP completed the total mapping of more than three billion DNA base-pairs found in the human genome. This is the biological basis for the transmission of human traits by procreation from parents to the child, also known as heritability. HGP would usher progress in genomic science that would lead to genome-wide association studies in 2005 and next-generation whole-exome sequencing in 2009. With the whole genome next-generation sequencing readily available these days, HGP has confirmed a good amount of our understanding of human trait heritability originally elucidated via human twin studies.

For more than seventy years before the start of HGP, human heritability of traits has been estimated using twin studies comparing similarities between identical twin pairs who should share 100 percent of their genetics versus fraternal twin pairs who do not share genetics more than an average sibling pair.² The logic in these early twin studies was simple and elegant. For any trait studied, one could determine how closely tied to genetics or biology that trait could be by comparing the likelihood the trait is shared by identical twin pairs versus fraternal twin pairs. Both types of twin pairs should, in theory, share 100 percent of their environment. This would include all environmental factors that could cause a trait of interest. However, only identical twin pairs would share 100 percent of their genetics that could cause a trait of interest. So, for a trait of interest, by examining the difference in the rates of this trait shared by identical twins compared to fraternal (non-identical) twins, straightforward subtraction mathematics would reveal an estimation of its genetic heritability. This is the definition of heritability (h^2) or narrow-sense heritability. In other words, since the 1920s, we have been able to estimate the genetic heritability of many traits using twin studies. In recent years via the fruits of the HGP, we have been able to confirm a good portion of these early findings.

Today for individuals suffering from mental illnesses, there is still confusion over how much is due to environmental factors versus genetic heritable causes.³ Types of mental illnesses or psychiatric disorders afflicting individuals can vary quite a lot in terms of their genetic heritability. There is also quite a bit of variation on how prevalent each illness or disorder is in our society.⁴ All this is to say that we generally talk about mental illness with confusion. To alleviate the confusion, this present article will describe published genetic heritability of most major categories of mental illnesses. This article will also describe the published lifetime prevalence rates of these major mental illnesses in our society and our nation. Using published data on any psychiatric disorder as defined by Kessler et al. (2007), this article will describe a novel estimation on the

genetically heritability of mental illness as a whole. This novel estimation will be calculated using two approaches: conditional probability versus weighted average. This article will conclude that regardless of genetic causal assumptions, mental illness as a whole is roughly 69 to 80 percent genetic. In other words, mental illness is caused in majority by genetic heritability and not by the environment. This report can also be understood as defining by quantification the material and efficient causality of mental illness as a whole. Bioethical and applicational implications of these findings are discussed later in this paper.

Methods

Heritability and prevalence data for individual psychiatric illnesses have been previously published for the United States and worldwide.⁵ For the variable “drug dependence and abuse,” heritability was determined using a simple mathematical average. For “Anorexia/Bulimia/Binge Eating,” heritability was determined using a simple mathematical average, and the prevalence rate was determined via a sum of individual prevalence.⁶ Apart from these two exceptions, all other heritability and prevalence rates were reported as per published data.⁷ The main lifetime prevalence rate for “any psychiatric illness” was published by Kessler et al. in 2005. The heritability of any psychiatric illness was determined using two approaches: weighted average approach and conditional probability.

The use of the weighted-average approach would assume some level of genetic pleiotropy, defined as one gene or gene set having several effects manifesting as independent traits. For example, anxiety disorder and depression might share a common genetic cause. Therefore, where anxiety and depression each play a part in the whole, the common genetic cause should be counted more than once when we are estimating total genetic contribution to mental illness as a whole. Weighted average approach was used to determine the overall heritability (h^2) for mental illness as a whole via the cumulative proportional contribution of heritability (h^2) of each type of psychiatric disorder. As heritability (h^2) is understood within the field of human genetics to represent the genetic contribution, we are therefore reporting the genetic material and efficient causality of any psychiatric illness. Proportional contribution was defined as the odds of encountering a particular type of psychiatric illness among other types of psychiatric illness prevalent in the population multiplied by the heritability (h^2) of that particular type of psychiatric illness. In other words, weighting was determined by the portion of the overall prevalence rate of mental illness as a whole contributed by each psychiatric disorder. Plainly, we determined the contribution of genetic heritability to mental illness as a whole that is not caused by general environmental factors by adding together the weighted average genetic heritability of each individual type of psychiatric disorder. We quantified the causal material that can be passed from one generation to another for any psychiatric illness. We excluded psychiatric illness secondary due to a primary medical condition or as an effect of medication. An example of these excluded types of illness would include bipolar disorder secondarily resulting from taking steroids for lupus. Other examples would include