Crossing the Threshold: An Epigenetic Alternative to Dimensional Accounts of Mental Disorders

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Davide Serpico and Valentina Petrolini

Recent trends in psychiatry involve a transition from categorical to dimensional frameworks, in which the boundary between health and pathology is understood as a difference in degree rather than as a difference in kind. A major tenet of dimensional approaches is that no qualitative distinction can be made between health and pathology. As a consequence, these approaches tend to characterize such a threshold as pragmatic or conventional in nature. However, dimensional approaches to psychopathology raise several epistemological and ontological issues. First, we review major sources of evidence usually recruited in support of the dimensional trend (focusing on clinical observation and biological data), and we show that these are connected to different conceptualizations of how dimensional traits extend across health and pathology. Second, we criticize two unquestioned assumptions that stand at the core of the dimensional trend: (a) that there is continuity from health to pathology at the symptomatic level; (b) that such continuity reflects an underlying continuity in the genetic liability for pathological conditions. Third, we argue against the idea of a conventional threshold by showing that such a view implies a linear relationship between the genotype and the phenotype. Fourth, drawing on epigenetics and developmental biology, we offer a characterization of mental disorders as stable and dynamic constellations of multi-level variables that differ qualitatively from 'healthy states'. We conclude by showing that our account has several theoretical advantages over both categorical and dimensional approaches. Notably, it provides crucial insights into psychological development over time and individual differences, with major implications in terms of intervention and clinical decision-making.

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1. Introduction

The debate over the boundaries between mental health and pathology, and over the theoretical approach better suited to capture such boundaries, has flourished over the past decade in psychiatry and philosophy of science (Parnas and Kendler [2012]; Kincaid and

Sullivan [2014]; Keil et al. [2017]). The issue of determining what counts as pathological is obviously critical for psychiatric research and practice. Indeed, one of the main goals of psychiatry as a medical discipline lies in identifying as accurately and reliably as possible who is entitled to medical treatment. This also has important ethical and social consequences, given that receiving a psychiatric diagnosis affects one's life significantly in several ways (Keuck and Frances [2017]). Traditionally, two competing approaches have been put forward. Categorical approaches are committed to the idea that the gap between health and pathology should be conceived of as a difference in kind. On a strong reading of this position, healthy and pathological conditions would be comparable to different substances with specific chemical compositions, akin to natural kinds (Haslam [2014]). Dimensional approaches rather maintain that such a gap should be seen as a difference in degree, similar to a spectrum of colours fading into one another (Murphy [2006]; Banicki [2020]; Phillips [2020]).

Although these two approaches are usually contrasted as if they developed simultaneously, in the history of psychiatry we witness a clear trajectory from categorical to dimensional perspectives. At least until the DSM-4, standard approaches in Western psychiatry have been categorical in nature (Jablenski [2012]). It is only with the development of the DSM-5 (American Psychiatric Association [2013])—as well as with the numerous reactions against it (Cuthbert and Insel [2013]; Schumann et al. [2014]; Kotov et al. [2017])—that nosology has moved towards the identification of fewer disorder types and their distribution along dimensions or domains of functioning (Regier et al. [2010]).

Such a trend towards dimensional approaches has been mostly motivated by discontent with the categorical model. One prominent risk concerns essentialism (Jablensky [2012]; Banicki [2020]). From an ethical perspective, essentialism has been connected with the risk of stigma and harm against individuals diagnosed with mental conditions

(Haslam [2011]). Indeed, essentializing psychiatric disorders has been taken to encourage the representation of patients as 'categorically abnormal, immutably afflicted, and essentially different' (Haslam [2014], p. 25). Epistemically, the categorical approach makes room for over-simplifications that fail to accurately represent mental conditions in their complexity (Kendell [1975]; Kendell and Jablensky [2003]; Cooper [2013]). Clinically, discontinuous categories are often considered too rigid for the purposes of individualized diagnosis and effective treatment (Frances [2013]), because they encourage 'arbitrary and rigid thresholds' (Hyman [2021]). This becomes especially problematic when individuals do not fit neatly into one or the other category (not-otherwise-specified diagnoses) or exhibit multiple comorbidities (Petrolini and Vicente [2022]).

Despite the apparent endorsement of dimensional concepts, the dimensional trend does not come without controversies. From an ethical viewpoint, researchers, practitioners, and individuals diagnosed with a mental condition still disagree about whether psychiatric labels should be seen as harmful, humanizing, or liberating (Kenny et al. [2016]; Botha et al. [2020]). This calls into question the idea that dimensional frameworks should be regarded as more ethically desirable than categorical ones. Moreover, major epistemic and methodological issues have been identified (Meehl [1999]), and a significant portion of the DSM-5 ended up retaining the traditional categorical framework (Blashfield et al. [2014]).

In this article, we discuss open epistemological questions and conceptual limitations of dimensional approaches. We then outline a novel theoretical framework that better accommodates a wide range of features that we take to be distinctive of the health–pathology distinction, while at the same time avoiding the shortcomings that are usually associated with categorical and dimensional accounts.

In section 2, we show that the dimensional trend is far from being internally homogeneous, as it takes support from different sources (clinical observation, biological data) and involves different conceptualizations of how dimensional traits extend across health and pathology. By echoing some key open questions raised in the literature, we underscore the need of further refining dimensional accounts of mental disorders.

Throughout section 3 and section 4, we show that beneath the dimensional trend lies a set of fundamental assumptions: (a) there is continuity at the level of symptoms, that is, continuous variation at the populational level from healthy to pathological conditions; (b) such continuity reflects continuity in the underlying liability for pathological conditions—for instance, in terms of neurobiological and genetic factors. We then proceed to argue that both assumptions are problematic.[1]

In section 4, we criticize, in particular, the view that the threshold between health and pathology should be regarded as conventional or arbitrary. This is in fact a key component of some exemplifications of the dimensional trend, particularly those that understand the continuity between health and pathology as an ontological feature. On these readings, ontological continuity is believed to be what generates semantic vagueness and epistemic uncertainty in drawing the distinction. We argue that this problematic assumption is at the root of many theoretical issues.

In section 5, we outline a theoretical framework where the health–pathology threshold has an ontological basis, rather than an arbitrary one. Here, we draw on developmental biology, and more specifically on the conceptual architecture provided by Waddington's

[1] In our analysis, we mostly focus on continuity at the behavioural and genetic levels. We do so for the following reasons. First, empirical evidence in support of the dimensional trend mostly derives from clinical observation and behavioural genetics research, but this comes with major misconceptions. Second, analysing the biological complexity that lies between such two 'extremes' (for instance, neurobiological, endocrine, and immunological) exceeds what can be possibly done in one article. We thus select behavioural and genetic evidence as our reasonable starting point.

epigenetics, to characterize mental disorders as complex states that are qualitatively different from each other as well as from 'healthy states'. This approach acknowledges semantic vagueness and epistemic uncertainty in setting the threshold, while still regarding healthy and pathological states as ontologically discontinuous.

We argue that this account has several theoretical and clinical advantages over classical dimensional approaches, as it avoids: (a) the reduction of individual variability to single (or few) quantitative dimensions; (b) the idea that the genetics of mental disorders is additive; (c) the assumption of underlying ontological continuity between health and pathology based on the continuity observed at the behavioural level. Moreover, since it depicts mental disorders as dynamic but stable states, our framework also provides crucial insights on psychological development and individual differences, with major implications in terms of intervention and clinical decision-making. As we will explain, conceptualizing health and pathology as qualitatively different states, together with insights from epigenetics, has much explanatory and practical potential.

Our account can also be seen as a potential integration to contemporary network and cluster models of mental disorders, particularly regarding two aspects. First, our epigenetic model is centred around how to characterize individual differences in terms of their multi-level properties (biological, developmental, psychological, environmental). Second, the model focuses on how individual developmental trajectories evolve over time in response to internal and external factors. In this sense, our proposal directly incorporates the idea that mental disorders emerge from the interaction of multi-level variables over psychological and biological development.

2. The Dimensional Framework: Its Grounding and Pitfalls

The transition from categorical to dimensional approaches in psychiatry revolves around the observation that typical behaviours, symptoms, and biological factors associated with mental pathologies are continuously distributed in the general population, so that no sharp distinction can be drawn between health and pathology.

At the behavioural level, this is supported by the observation that traits that are typically found in clinical populations also extend to non-clinical ones at different degrees of intensity, frequency, and severity. For instance, several studies established that individuals without a psychiatric diagnosis experience auditory verbal hallucinations (AVH) (Johns and van Os [2001]; Alderson-Day et al. [2014]). Another example concerns the so-called broader autism phenotype (Sucksmith et al. [2011]), which refers to individuals—often family members of autistic individuals—who exhibit autistic traits at a subthreshold severity level. Delusions have also been shown to lie on the far end of the irrationality spectrum and to exhibit significant similarities with other forms of irrational beliefs, such as biases, superstitious beliefs, and conspiracy theories (Bortolotti [2010]).

The dimensional view is also supported by biological data. In a recent review of autism research, Happé and Frith ([2020]) consider dimensionality at various levels (cognitive, neuroanatomical, genetic).[2] At the genetic level, they argue that 'the genetics of autism is just like the genetics of height; [often] autism is the result of many common genetic variants, each of miniscule effect. We all carry many of these variants, and so, a

[2] Regarding neuroanatomical aspects, the authors claim that neuroimaging studies revealed few qualitative differences among neurotypical and autistic individuals but found evidence of quantitative ones. However, data on brain morphology and connectivity are inconsistent across studies, probably due to differences in nosology, aetiology, and inclusion criteria (this is suggested by the very same studies cited by Happé and Frith; see Pua et al. [2017]; van Rooiji et al. [2017]; Carmon et al. [2020]). Elton et al. ([2016]) identified both quantitative and qualitative differences, which testifies the complexity of autism (something that the dimensional trend risks obscuring; see sec. 3.1). Also due to this complexity, we do not focus on what lies between behavioural and genetic levels.

dimensional characterisation of autism is also plausible genetically' (p. 223). In quantitative genetics, models of psychopathology are based on data regarding the presence of alleles associated to diseases in the general population for a variety of conditions, including attention-deficit/hyperactivity disorder, autism spectrum disorder, personality disorders, and schizophrenia (Owen et al. [2007]; Riglin et al. [2016]; Robinson et al. [2016]).[3] For many scholars, these data testify that healthy and pathological states share a common genetic basis, and this would support the dimensional view (Jang [2005], p. 110). According to Knopik et al. ([2017], p. 240), it is an emerging rule in behavioural genetics 'that disorders are actually the quantitative extreme of a continuum of normal variation'.

Nonetheless, clinical practice and healthcare systems have been notoriously resistant to embrace fully dimensional models of psychopathology. A key concern stems from the eminently pragmatic nature of psychiatry as a medical discipline, where diagnosis is usually treated as binary, and intersubjective and efficient criteria are thus required to identify those individuals that are in need of treatment. As a consequence, researchers in psychiatry and philosophy of science have often accepted the necessity of drawing a line between health and pathology but embraced the idea that such distinction should be somewhat conventional or normative (Bolton [2008]; Haslam [2014]; Hyman [2021]). This has also become a defining feature of recent quantitative genetics models. For instance, Jang ([2005], p. 47) stated that 'disorder represents the extremes of the normal distribution of function. Illness is operationally defined by a threshold placed on the frequency dis-tribution of severity'. More recently, Knopik and colleagues ([2017], p. 37)

[3] Molecular genetics research on personality traits and disorders (such as neuroticism or antisocial behaviour) has received much less attention than research in other domains of psychiatry (Knopik et al. [2017], p. 272). Most dimensional models of genetics liability are based on family studies and on the assumption that personality traits are normally distributed due to their very nature: they are traits that all of us manifest in different forms or degrees (for some reviews, see Jang [2005]; Knopik et al. [2017]).

wrote: 'A continuum from normal to abnormal seems likely for common disorders such as depression and alcoholism […] Individuals diagnosed as depressed might be extreme cases that differ quantitatively, not qualitatively, from the rest of the population […] Even for less common disorders like schizophrenia [...] there may be no sharp threshold dividing the normal from the abnormal'.

2.1. Methodological and conceptual issues

Despite its popularity, the dimensional trend does not come without controversies. In this subsection, we introduce the major issues that motivate the present article, and more specifically the need to provide a novel framework that combines the advantages of categorical and dimensional approaches while avoiding their shortcomings.

One first set of problems of dimensional approaches concerns their practical limitations. Methodological issues stem from disagreements on how to assess subjective symptoms in quantitative terms through psychometric methods: many symptoms are shared across diagnostic categories, generating conceptual complications (Koi [2021], p. 59), which also concerns the number and nature of the relevant dimensions (Jablensky [2012], pp. 89–91). Addressing such questions requires considerable mathematical and statistical skills to adequately understand psychometric methods and multifactorial techniques (Frances [1982]; Banicki [2020]). So, in terms of everyday clinical practice, the dimensional framework comes with a high degree of complexity and technicalities.

A major conceptual problem regards the very notions of 'dimension', 'spectrum', and 'continuity', which have been conceptualized in different ways (Koi [2021]) thereby giving rise to several over-simplifications (Meehl [1992]). For instance, such notions can be applied intra-categorically (when we assess levels of severity) or inter-categorically (when we claim that a given trait grades continuously across clinical and non-clinical

populations). The specific way in which dimensional accounts may be implemented also varies depending on nosological versus research purposes, for example, the DSM-5 aims to integrate categories with dimensions (Jablensky [2012]; American Psychiatric Association [2013]), while the research domain criteria framework (RDoC) endorses a stronger view where dimensional constructs are meant to replace categories altogether (Cuthbert [2014]; Fernandez [2019]).[4]

Another conceptual problem concerns the semantic vagueness of terms like health and disease, which carries much practical importance as it generates epistemic uncertainty in medical decision-making. If the threshold between health and pathology is taken to be pragmatic or conventional, we need some criteria for determining where to set the threshold. Given that many threshold values are pragmatically or conventionally determined (for instance, symptoms lasting at least for fourteen days, or five out of nine criteria out of a checklist), one may legitimately wonder whether the distinction is just arbitrary (Keil et al. [2017]; Keil and Stoecker [2017]). In other words, one may wonder if there is any actual difference between two individuals that present five and six diagnostic criteria, respectively, or between individuals who experience a given symptom for thirteen and fourteen days. According to Keil and Stoecker ([2017], p. 55), introducing notions such as subthreshold disorders and prodromal phases does not solve the issue as it ends up creating two thresholds instead of one (the one between healthy and vulnerable, and the one between vulnerable and diseased).

[4] As we mention above, the shift towards dimensionality in DSM-5 may be characterized as uneven at best. Some categories, such as autism, have undergone major changes with the DSM-5 revision reducing many separate disorders to a spectrum defined in terms of two dimensions that extend into the general population, that is, social communication and interaction; restrictive and repetitive behaviour (for a review, see Amoretti et al. [2021]). Other categories, such as schizophrenia spectrum and other psychotic disorders, maintain several independent nosological entities (as in DSM-4). Personality disorders may be seen as an in-between case: initially supposed to transition to a fully dimensional classification but then relegated to section 3 of the manual (Blashfield et al. [2014]).

A debated aspect is whether such vagueness has epistemic or ontological origins. Many believe that it follows from the 'immaturity' of psychiatry and that the advancement of biological knowledge will increase diagnostic clarity (Hucklebroich [2017]). Others have suggested that in many (or even most) cases, vagueness might have an ontological basis. On this view, 'psychiatric concepts are vague because the reality that they aim to capture is continuous rather than discrete' (Keil et al. [2017], pp. 8–9; see also Hauswald and Keuck [2017]).

We go back to this debate in section 4, where we introduce a more principled distinction between pragmatic and conventional ways of understanding thresholds in psychiatry. As we will see, the idea that continuity is an ontological feature of the relationship between health and disease is an essential tenet of some exemplifications of the dimensional trend. Indeed, much of the dimensional trend—at least in its theoretical component—originated from the view that there are no distinct natural kinds in psychiatry (Kendell [1975]; Kincaid and Sullivan [2014]; Zachar [2000]; Hyman [2021]).[5] Within this trend, the dimensionality observed at the behavioural and biological levels is attributed to how the world is and 'does not depend on semantics' (Keil et al. [2017], p. 10). In this sense, apart from very special cases that behave more categorically (such as Huntington's disease), semantic vagueness and epistemic uncertainty are generated by the very nature of the phenomena under investigation. The difficulty to draw a line between health and pathology is not just due to imperfect scientific theories, limited biological knowledge, or any other contingent reasons.

[5] Interestingly, a similar view characterized the transition from Mendelian to quantitative genetics, where the latter is considered a better framework to account for real-world phenotypic complexity (Kendler [2006]). This suggests that both in psychiatry and genetics the trend towards dimensionality is at least partially motivated by ontological concerns.

The considerations above tie together the various methodological, practical, and ontological issues discussed so far: the general picture is that semantic vagueness and epistemic uncertainty are inevitable prices to pay if health and pathology are in fact ontologically continuous. If dimensional models better capture the reality of most (if not all) psychopathologies, it will be a practical problem to translate the dimensional framework into a more tractable tool for psychiatry practice. Ontology alone justifies the framework.

In the next sections, we question this idea by discussing major—albeit insufficiently explored—issues with the dimensional framework. Our general concern is that the dimensional framework over-simplifies the distinction between health and pathology based on misleading interpretation of two main sources of evidence: clinical observation and genetic data.

3. Unpacking Continuity

In this section, we spell out our concerns with respect to unwarranted over-simplifications surrounding the health–pathology distinction in dimensional frameworks. At the level of observable symptoms, typically, this over-simplification is exemplified by claims such as 'we all are a little bit x'—for instance, we are all a bit autistic, we are all (occasionally) depressed, and so on. Within the dimensional trend, these claims can be taken to reflect a commitment to some sort of ontological continuity, rather than just semantic vagueness or epistemic uncertainty. Indeed, as we shall show, at the behavioural level, the claim can imply that all individuals exhibit mental conditions to different degrees (sec. 3.1), while at the genetic level one can jump to a similar conclusion from the genetic overlap between clinical and non-clinical cases (sec. 3.2).

3.1. From behaviour to dimensional operationalization

As we explained in section 2, epidemiological and clinical studies support the idea that many symptoms and traits may be detected in varying degrees across clinical and non-clinical populations. This is usually taken as evidence in favour of continuity between healthy and pathological states. However, we should carefully distinguish between such observations and the claim that normal and pathological states are ontologically continuous. Indeed, part of the continuity observed may depend on how we conceptualize or measure psychological traits. Meehl ([1992], [1999]) makes a similar point in his work on taxometry: the fact that symptoms come in degrees should not rule out the underlying presence of a genuine disease entity. The parallel with somatic medicine makes this more apparent, given that many infectious diseases are diagnosed through the observation of quantitative symptoms, such as fever and blood sugar levels (Meehl [1992], p. 154).

Yet, operationalizing psychological and psychiatric constructs is notoriously difficult due to the very nature of these disciplines, as human thoughts and behaviour present themselves as unwieldy and inherently resistant to being captured precisely through scientific inquiry (Bridgman [1927]; Hurlburt [2011]). Due to the uncertainty surrounding the aetiology and biomarkers of mental conditions (Aragona [2009]), psychiatry and clinical psychology have developed indirect measures to assess mental conditions—such as interviews, checklists, scales, questionnaires, and behavioural tests. Operationalizing psychological traits through such measures, we suggest, can artificially generate the observation of continuity between healthy and pathological states.

Although clinicians overwhelmingly disagree with the idea that mental conditions could be reduced to single dimensions and instead grant that mental disorders are multidimensional entities (Maung [2016]), psychometric tools and factor analytic techniques routinely reduce heterogeneous constellations of traits to quantitative, unidimensional

variables. This assimilates mental conditions to quantitative traits that are usually taken to be unidimensional in nature, such as weight and height (Banicki [2020]), thereby allowing for quantitative inter-individual comparisons.

To better understand how this plays out in clinical research, let us take two commonly used measures of autism: Baron-Cohen's autism spectrum quotient (or AQ; Baron-Cohen et al. [2001]) and the autism diagnostic observation schedule (or ADOS-2; Lord et al. [2012]). Although they reflect different conceptualizations of dimensionality, both of them ultimately allow for a quantitative characterization of autism. The former tool, the AQ, is often used to assess autistic traits as a continuum across clinical and non-clinical populations (for a review, see Ruzich et al. [2015]). In this sense, it reflects what Koi ([2021]) has dubbed simple spectrum or far end models, where conditions are placed on a single phenotypic continuum that extends throughout the general population. In a recent article, Happé and Frith ([2020], p. 223) defend a similar view: 'Autistic trait measures [...] show a smooth continuum between diagnosed autism and subclinical individual differences; there is a normal distribution of traits [...] it does appear that, at the behavioral level at least, one can be "a bit autistic"'. However, the fact that the severity of autism-related traits can be understood as a matter of degree and as extending to non-clinical populations does not imply that humans differ from each other along a spectrum between non-autistic and autistic *qua* conditions. Indeed, autism involves a heterogeneous constellation of traits, such as difficulties in social-emotional reciprocity and in non-verbal communication; difficulties in developing, maintaining, and understanding relationships; stereotyped or repetitive motor movements or speech; inflexibility; routines or ritualized behavioural patterns; and unusual reactivity to sensory inputs. Individuals in both clinical

and non-clinical populations may present various forms of such traits, without implying that autism itself varies continuously.[6]

More structured diagnostic tools, such as the ADOS-2 (Lord et al. [2012]), rather reflect a multidimensional view where autism arises from the intersection of more dimensions (social communication and interaction; stereotyped behaviour and restricted interests). Here, the construct is not taken to extend across non-clinical populations. Although borderline scores are possible, anyone who scores below the cut-off of a given ADOS module qualifies as non-autistic for diagnostic purposes. Similarly, psychometric tests of intelligence—such as IQ tests—assess individual intelligence through a single score. In this sense, IQ represents a single dimension along which individuals can be compared, and factor analysis can distillate a general dimension that summarizes test variance, widely known as g-factor. However, such dimension does not correspond to a single cognitive phenomenon; rather, individual differences in IQ depend on a constellation of neurocognitive processes, including verbal, mathematical, and visuo-spatial skills, as well as working memory, processing speed, and metacognition (van der Maas et al. [2006]; Kovacs and Conway [2016]; Serpico [2018]).[7]

Yet, even multidimensional measures such as the ADOS or IQ tests rely on a picture where different dimensions are assessed separately and then combined in a single score. In these cases, an individual is tested on a variety of tasks designed to tap into specific abilities; each dimension is then scored separately and added to the others, giving rise to a global score that is thought to be diagnostic of the underlying construct, be it autism or

[6] For a similar point, see (Chown and Leatherland [2021]). We develop this idea further in section 3.2.

[7] Other relevant examples are biometric traits like body-mass index (Serpico and Borghini [2021]), scales measuring various aspects of mood to assess degrees of depression, internalization versus externalization measures, and tests to detect the big five personality traits (BFPT).

intelligence. As a result, variation in constellations of traits can be represented as variation along a single dimension, but it is important to stress that this is mostly a consequence of how we operationalize phenotypic complexity.

This reduction of multidimensional complexity often depends on pragmatic factors, such as making complex traits more tractable in public-health service and policies. However, as we explain later in the article (sec. 4), this has metaphysical implications that should not be overlooked. As we see it, complex conditions such as mental disorders are better understood as constellations of multi-level variables that interact with one another (sec. 5). The more internally complex and multidimensional a psychological construct is, the less informative quantitative characterizations of individual differences within such a construct would be, that is, characterizations in terms of continuum or degrees—be they unidimensional or multidimensional.

There is also a second, potentially misleading way that a trait can be conceptualized as varying continuously as a consequence of how we operationalize it. In diagnostic checklists, clinicians often use terms such as frequency or duration to determine whether a person crosses the threshold of clinical significance. For instance, in order to receive a DSM-5 diagnosis of depression, a subset of the relevant symptoms have to be experienced for at least two weeks (duration). Similarly, symptoms for schizophrenia have to be experienced for a significant portion of time (frequency). Other factors, such as intensity, are used comparatively in diagnostic tools designed to assess depressed mood or affective states more generally (see, for instance, the Hamilton scale). Although these phenomena may be seen as quantitative in some sense, as they are subjectively experienced as coming in degrees, we propose a principled distinction between them and quantitative phenomena.

Quantifiable phenomena include, for instance, the increase (or decrease) in frequency, intensity, or duration, delineated above. Despite their pragmatic value as behavioural proxies of severity, these factors should not be understood as inherently quantitative. Quantitative phenomena rather involve quantifiable biological variables that have an additive structure (on a similar distinction, see Hibberd [2014]). Hucklenbroich ([2017]) calls this type of variables 'objectively measurable functional parameters', such as blood pressure (measured in millimetres of mercury or torr) for determining the degree of hypertension. Notably, to consider behavioural proxies as quantitative, as opposed to quantifiable, they would have to be realized by lower-level mechanisms in such a way that their increase (or decrease) in intensity and frequency would be directly correlated with changes in the relevant underlying quantitative variable(s). For instance, for low mood to be considered as a quantitative phenomenon, it would not suffice to assess it through countable factors, but it also would need to increase linearly with the increase or decrease of some relevant neurobiological variable (such as serotonin reuptake).

To draw a parallel with the discussion on IQ, intelligence would be a quantitative phenomenon if there was a latent quantitative dimension that varies among individuals and that generated the observed continuous variation in behaviour. Scholars have argued that the reduction of intelligence to a single quantitative variable is empirically untenable (see above). Such a reduction also raises problems for metaphysical reasons as the internal structure of human intelligence cannot be considered as inherently quantitative or additive: intelligence is not comparable to quantitative properties like length, weight, mass, and temperature (on this point, see Michell [2012]). In other words, a manifest variable (like IQ) can be quantitative, though the latent variable it tries to capture (for instance, intelligence) may not be (De Boeck et al. [2005], p. 129).

It seems to us that similar considerations apply to most behaviours and psychological traits. If so, symptomatic dimensions of mental disorders cannot be taken to be quantitative properties, strictly speaking. We invite reflection on this point although we acknowledge that, in principle, the representation of a construct is independent from its metaphysics. In psychometric and clinical practice, scholars may represent a multidimensional condition as a quantitative trait while being aware of the caveats of this interpretation—in fact, practitioners routinely determine diagnostic status through additional factors, including in-depth interviews. However, this awareness is easily lost, especially in research, with the consequence that a practically useful quantitative index of individual differences can be mistaken as a 'metaphysical description'. For instance, quantitative measures of symptoms across scales, or scores obtained through diagnostic tools such as ADOS-2, are often taken to be sufficient to include a given individual in the clinical group for the purposes of conducting a case-control study (Petrolini and Vicente [2022]). Likewise, it seems to us that when behavioural geneticists try to identify the additive genetic architecture of intelligence and account for individual differences in terms of single-nucleotide polymorphisms (SNPs), they embrace a realist interpretation of quantitative psychological constructs (we return to genetics research in section 3.2). Several scholars made a similar point about how measurement in psychology may imply a realist, quantitative reading. For instance, Michell ([1997]) points out that measurement always presupposes a theory according to which a given attribute is quantitative, but this is a contingent, empirical hypothesis that, in principle, may be false. However, the history of psychology testifies that instrumental concerns—such as the practical need to assess individual differences—have led researchers to focus more on the development of measurement tools than on the justification of the quantitative theory of psychological traits

(see also Hibberd [2014]; Uher [2021]). Philosophical work about realism and operationalism in psychometrics suggests similar considerations—for instance, Borsboom et al. ([2004]) show that much work on validity in psychometrics requires a realist interpretation.[8]

To summarize, dimensionality observed at the behavioural level does not imply that healthy and pathological states are continuous in any strong, ontological sense. Although we can operationalize mental disorders in terms of quantitative dimensions, we should not mistake them as inherently quantitative traits or phenomena. That is, we should resist the idea that constellations of traits—rather than traits themselves—vary continuously in populations. In section 4 and section 5, we will offer a finer-grained account of the relation between health and pathology, focusing on mental conditions as complex states or constellations. In the next subsection, we question whether the available evidence actually grounds continuity at an underlying (biological) level.

3.2. From genetics data to the quantitative framing of psychopathologies

An important source of evidence motivating the dimensional framework derives from behavioural genetics. There are several reasons why scholars have turned to genetics to ground the dimensional view. For instance, Happé and Frith ([2021]) acknowledge that the behavioural level can be 'tricky', while biological data can be more persuasive. The appeal to genetic evidence is also motivated by non-epistemic factors, as explorations of continuity within advocacy movements can involve 'the aim of probing to what extent

[8] For an introduction on realism and operationalism in psychometrics, see (Vessonen [2019]). On non-epistemic values in psychometrics that guided the adoption of a quantitative view of individual differences, see (Wijsen et al. [2021]).

autism and ADHD are continuous with—or amount to—normal human variation' (Koi [2021], p. 54).

In the last few decades, researchers identified the presence of disease-associated alleles in the general population for a variety of conditions, suggesting that health and pathology share in part the same biological basis. Such data are taken as naturally implying the continuity thesis and led many to conceptualize mental disorders as quantitative traits (see sec. 2). But do data actually support the ontological interpretation of continuity? To address this question, we need to consider how psychopathologies fit the general explanatory framework of quantitative genetics (for an introduction, see Serpico et al. [2023]). We will show that the presence of disease-associated alleles in the general population does not imply that the genetics of mental disorders is continuously distributed across health and pathology. Moreover, we argue, understanding mental disorders as quantitative traits is conceptually misleading as it takes them to be characters instead of character-states.[9] Let us proceed step by step.

Typical examples of quantitative traits are stature, skin colour, and blood pressure, but also multifaceted traits that are operationalized in metric terms (BMI as an index of fat metabolism; IQ as an index of cognitive abilities). The distinctive mark of such traits is that, phenotypically, they vary continuously: in any given population, we can observe all values or gradations within a certain range—for instance, the height values of different individuals can be ordered on a single scale or dimension. A fully developed account of the genetics of quantitative traits is usually attributed to Fisher ([1918]), who understood that the continuity observed at the phenotypic level could not be accounted for by variation in single genes as in the case of qualitative, Mendelian traits. He hypothesized that

[9] We borrow this distinction from (Serpico [2020]; Serpico and Borghini [2021]).

phenotypic continuity depends on several genes, each of which has a small, additive effect on the phenotype; this would explain why phenotypes vary continuously in populations.

Fisher's model became the cornerstone of quantitative genetics, but the typical way of modelling pathologies quantitatively derives from Falconer ([1965]), who applied Fisher's model to traits that appear to vary discontinuously, like pathologies (Génin and Clerget-Darpoux [2016]). Falconer ([1965], p. 52) introduced a theoretical concept called liability denoting 'an underlying gradation of some attribute immediately related to the causation of the disease. If we could measure this attribute, it would give us a graded scale of the degree of affectedness or of normality, and we should find that all individuals above a certain value exhibited the disease and all below it did not'. So, Falconer assumed that liability is normally distributed, but it is important to stress that he made this assumption for the sake of modelling. In his own words, he did not make any 'unwarranted assumption about the real nature of the liability: [such notion] simply specifies that in order to express the degree of liability we shall choose a scale of measurement which, if we could measure the liability, would yield a normal distribution' (p. 53).[10]

If we look closely at Fisher's and Falconer's models, we see that the assumption of the normal distribution of genetic risk is a theoretical idealization; more importantly, we see that such assumption is guided by the observation that phenotype values vary continuously in populations. Both such models aim to provide a plausible, though admittedly idealized, hypothesis on the genetic architecture of complex traits and pathologies, respectively, together with an explanation of how underlying genetic variability can generate phenotypic continuity.

[10] Note that Falconer aimed to provide a quantitative interpretation of the genetics of discontinuous traits to allow the application of quantitative genetics methods (such as heritability analyses) to diseases.

The upshot is that the inference of continuity is not made from the genotype to the phenotype level, as the data may suggest, but the other way around: geneticists started out from the phenotypic observation that some traits varied continuously and built a genetic model that would reflect such distribution. Such a direction of inference from phenotypes to genotypes is evident also in more recent discussions. Knopik and colleagues are arguably making such an inference when they say:

> […] theoretically, there should be a continuum of genetic risk, from people having none of the alleles that increase risk for schizophrenia to those having most of the alleles that increase risk. Most people should fall between these extremes, with only a moderate susceptibility to schizophrenia. (Knopik et al. [2017], p. 36)

> These findings […] suggest that common disorders [...] are merely the low end of the normal distribution [fitting the] quantitative genetic model, which assumes that genetic influence for complex traits is due to many genes of small effect size that contribute to a normal quantitative trait distribution. (Knopik et al. [2017], pp. 205–206)

Let us now consider a second limitation of genetic explanations of continuity, which lies in the description of pathologies as quantitative traits.

A well-acknowledged feature of quantitative traits is that they are shared by most (if not all) the individuals of a given species. For instance, *qua* humans, we all instantiate a given value of height and BMI. So, if we take seriously the possibility that mental disorders are quantitative traits, we should accept that each human would exhibit pathological traits to a certain degree. Indeed, this interpretation is more or less explicitly endorsed by the dimensional trend and is reflected by what Koi ([2021], p. 56) calls the phenotypic simple spectrum model (see also 3.1.), according to which ‘a gradient of the disability

[...] extends across the human population. A value of autism or ADHD can be thus ascribed to any person, similarly to blood pressure'. A similar view also emerges from claims like: 'at the behavioural level at least, one can be "a bit autistic". At the genetic level too, it appears that the genetic influences on subclinical traits largely overlap with those on diagnosed autism' (Happé and Frith [2020], p. 223). We dub this idea 'universal pathologization', as mental disorders—like quantitative traits—are taken to extend into the general population to different degrees.[11]

In section 3.1, we uncovered one potential issue associated with this view, namely, the risks connected with the reduction of multidimensional phenomena to single dimensions. Here, we focus on a drawback more related to genetics and biology: the idea that each human exhibits pathological traits to a certain degree risks misinterpreting mental disorders as characters, while they are probably character-states.

In our vocabulary, characters are general phenotypic characteristics with no determinate value, while character-states are specific values or forms that characters can take in concrete individual organisms. For instance, skin colour, height, BMI, and IQ are characters: they are 'abstract', species-specific characteristics that can be observed in any human being—each of us has some skin pigmentation and some height value. Likewise, a BMI and an IQ value could be calculated for every human. By contrast, specific skin colours and values of stature, BMI, and IQ are character-states, namely, 'concrete' instances of characters. And the same applies to non-metrical characterizations of such

[11] Although theorists in psychiatry may not endorse such a view fully, if one defines pathology as a 'biological or genetic dysfunction' and defers to behavioural genetics with respect to the investigation of the 'deeper' biology of mental disorders, one may end up endorsing a position that 'universalizes' pathology in the way described above.

characters (leanness versus obesity, intellectual disability versus 'normal' IQ, short versus tall stature).[12]

We argue that mental disorders should be understood as character-states (or constellations of character-states) rather than characters, namely, they are concrete forms or states that a character can take. In the case of autism, it looks reasonable to think that traits relating to it (repetitive behaviour, difficulties in social communication) are general human traits that in some specific states can fall outside a 'normal range' (however defined) and thus come to be associated with an autism diagnosis.[13] To simplify, traits such as 'difficulties in social communication' would be character-states of the character 'social communication' that are instantiated by some individuals of our species but not others (those other individuals would instantiate other forms or states of the very same characters, for instance, 'good social communication skills').

If so, mental disorders (and autism specifically) are not universal human traits, because only characters are 'universal' in some sense. How do genetic data fit this picture? The presence of genetic variants associated with autism in the general population does not imply that mental disorders are quantitative traits or that anybody is autistic 'to some degree'. Such data should simply be taken to mean that autism (as any mental disorder)

[12] In metaphysical terms, characters can be seen as determinables, while character-states are determinates (for more details, see Serpico and Borghini [2021]).

[13] Several authors make similar considerations. For instance, Chown and Leatherland ([2021], p. 749) suggest that what look like 'autistic traits' are human traits that 'when presented in a cluster that "significantly impairs" a person's life in certain areas, are considered justification for a diagnosis of autism [...] exhibiting some of these traits, individually or in combination, does not make a person "a bit autistic" [...] a person is either autistic or not autistic'. Koi ([2021]) considers the notion of a complex spectrum of endophenotypes as better suited to account for variability in conditions like autism. One of us (Serpico [2020]) suggests that many phenotypic traits might be reframed as character-states and that a quantitative characterization of human variation in such traits has serious limitations. All these works refocus the attention on multidimensional human variability more broadly and on the relationship between 'pathological traits' and other human traits. Our suggestion that mental disorders are character-states has similar purposes.

involves some typically human traits that vary among individuals, and their variation is associated with genetic variation in any given population. On this view, it is unsurprising that there are statistical associations between genetic variation and variation in such traits in both the clinical and non-clinical population.

To summarize, the equation 'mental disorders = quantitative traits' is usually justified by: (a) the observation that symptoms are continuously distributed in populations; (b) data on the presence of disease-associated alleles in the general population. As regards (a), since mental disorders show the same patterns of population variation as quantitative traits, the dimensional trend (in its ontological reading) assumes that they have the same type of genetic architecture. This seems to follow naturally from classical genetics models, but such interpretation is unwarranted: as we argued, the continuity observed (or rather postulated) at the genetic level does not imply that the phenotype is quantitative all the way up to behaviour.[14] As regards (b), genetic data are compatible with alternative explanations, our own being that mental disorders are specific states of characters that are observed across the whole human species.

Equipped with the theoretical clarifications offered in this section, we now turn to how the dimensional trend construes the concept of threshold between health and pathology.

[14] Mental disorders are by no means comparable to Mendelian diseases, but this does not imply that they are quantitative instead. For Plomin et al. ([2009], p. 877), evidence of polygenicity seems enough to conclude that a trait is quantitative. In our understanding, such data indicate that individual variability is due to many genes but do not imply that genetic variability is normally distributed. The assumption seems to be that if a trait is not qualitative, then it should be quantitative. However, recent theorizing makes sense of complex traits beyond a quantitative characterization (see Boyle et al. [2017]; Serpico [2020]).

4. The Conventional-Threshold View

In the previous section, we analysed behavioural and genetic evidence usually recruited in support of the dimensional framework and introduced some key distinctions to uncover unwarranted inferences that are often based on such evidence. We made the case that the available data do not justify the view that health and pathology are ontologically continuous, but are rather open to alternative interpretations. In this section, we focus more closely on the notion of threshold between health and pathology, which is another core aspect of the dimensional trend reflected in the continuity thesis (sec. 2).

As we showed in section 2.1, recent theorizing in the dimensional trend has suggested that, in many cases, semantic vagueness and epistemic uncertainty may have an ontological basis. As a consequence, any distinction between health and pathology will always require some conventional, pragmatic, or normative way to set a threshold. However, the view that no sharp threshold exists between health and pathology can take various forms that are worth differentiating from each other. In what follows, we discuss two ways of understanding thresholds. We distinguish between cases where a cut-off point between health and pathology is established for pragmatic reasons, to serve heuristic purposes in clinical practice (without any strong ontological commitment regarding the nature of the underlying phenomenon), and cases where the distinction is believed to be conventional because of specific ontological beliefs. Then, in section 4.1, we will show that the latter account (which we call the 'conventional-threshold view') raises some important issues both at the psychological and at the genetic level.

The former view may be taken to describe the practical uses of thresholds in clinical practice, where most practitioners have no explicit interest in (or commitment to) ontological claims about the nature of the health–pathology distinction. In other words, the use of pragmatic thresholds does not imply the existence of an ontological threshold (nor

the lack thereof). This view is widely applied in psychiatric practice as a consequence of the pragmatic nature of the discipline. Although psychiatric diagnoses may be unable to pick out distinctive causal entities that fully explain the symptoms, a diagnosis is still necessary to assess how to allocate healthcare resources and may still be epistemically useful, for instance, because it contributes to excluding some causes, or to offering partial information on possible relations among symptoms (Maung [2016]).

Although no thick ontological view is involved here, setting a practical threshold may not be entirely arbitrary, as the decision often results from some consensus among experts based on clinical and empirical considerations. For instance, cut-offs like those adopted in the DSM may appear to be *prima facie* arbitrary, but they originated from complex negotiations in the writing of the manual and can be based on pragmatic concerns or empirical indicators. In the philosophical literature, this pragmatic view of thresholds would correspond to the notion of practical kinds (Zachar [2000]; Haslam [2014]), according to which, 'it is sometimes possible to define a cut-point on the continuum that is not arbitrary [based on] some external criterion that is pragmatically relevant in the clinical context' (Haslam [2014], p. 14). Typical examples of pragmatic, non-arbitrary thresholds in medicine include blood-pressure values for diagnosing hypertension and BMI values for obesity, which can be selected 'because they roughly correspond to levels at which adverse health consequences become more likely or health risks begin to accelerate' (Haslam [2014], p. 14).

Our main critical targets are rather accounts that take a stronger ontological stance and embrace the continuity thesis more decisively, thereby rejecting qualitative differences between health and pathology altogether, both epistemically and ontologically. Such accounts take dimensionality (intended as the absence of thresholds) as an ontolog-

ical feature and/or claim that the dimensional approach does a better job than its alternatives in capturing actual mental functioning and dynamics. In terms of existing categorizations, this interpretation of the continuity thesis would correspond to Haslam's notion of dimensions: on this view, stating that health and pathology are dimensional means that 'there is not a delimited condition at all [and] for the sake of convenience, a cut-point may be defined on the dimension so that the quantitative variation is simplified into a dichotomous diagnosis. However, its placement is arbitrary' (Haslam [2014], p. 14). A classic formulation of the continuity thesis as intended above may be found in Freud ([2003], p. 81): 'It is not scientifically feasible to draw a line of demarcation between what is psychically normal and abnormal; so that distinction, in spite of all its practical importance, possesses only a conventional value'.

There are two sets of sources that exemplify this type of perspective. The first set includes diagnostic manuals and research programmes in psychiatry. For instance, the DSM-5 makes the point that the transition towards the dimensional framework would increase the validity of the manual's categories. Here, the manual appears to endorse a (partial) shift towards a dimensional view that would allow for a more realistic and empirically informed picture of mental disorders.[15] The shift towards dimensional explanations is also at times framed as a move from utility to accuracy (Phillips [2020], p. 664).

[15] For instance: 'A growing body of scientific evidence favours dimensional concepts in the diagnosis of mental disorders. The limitations of a categorical approach to diagnosis include the fail-ure to find zones of rarity between diagnoses (i.e., delineation of mental disorders from one another by natural boundaries), the need for intermediate categories like schizoaffective dis-order, high rates of comorbidity, frequent not-otherwise-specified (NOS) diagnoses, relative lack of utility in furthering the identification of unique antecedent validators for most men-tal disorders, and lack of treatment specificity for the various diagnostic categories' (American Psychiatric Association [2013], p. 733).

The second set of sources includes claims by researchers in genetics, psychiatry, and philosophy. As we discussed throughout the article, several scientists (particularly geneticists, but also neuroscientists and psychiatrists themselves) make claims in support of the continuity between mental health and pathology. Meehl refers to this view as the 'no types, only dimensions dogma', citing Donald Paterson's lectures in applied psychology: 'categorical terminology (e.g., "introvert," "bright," "thin") is merely a convenient—and sometimes careless—way of demarcating rough regions on what are in reality quantitative traits, dimensions, or factors' (Meehl [1992], p. 117). Similarly, the no-joints-to-be-found argument (Kendell [1975], p. 131) is thought to be supported by epidemiological and behavioural findings on the continuous distribution of symptoms and impairments in non-clinical populations, 'with no evidence of discontinuities between affected and unaffected individuals' (Hyman [2021], p. 12). Evidence from genetics is also routinely recruited in support of this point (see sec. 2 and sec. 3.2). In this respect, dimensional models are thought to capture phenotypic variation more accurately and precisely through quantitative measures (Banicki [2020], p. 224). This move towards accuracy also lies behind initiatives such as the RDoC, aimed at identifying relevant dimensions of functioning at various levels (from genetic to subjective self-report) and at validating them as to inform future nosological revisions (Cuthbert [2014]). Finally, various philosophers of psychiatry (Keil et al. [2017]) suggest that the continuity between health and pathology may be a feature of the outside world, that is, an ontological aspect that generates epistemic uncertainty in drawing the distinction.

In the conventional-threshold view, we find the assumption that a dimensional understanding is ontologically and empirically more accurate than a categorical one. This suggests the embracement of an ontological stance towards continuity rather than a merely pragmatic one. Indeed, this use of thresholds reflects the commitment to a certain view

of the health–pathology relationship—that is, the view that there is no sharp, clear-cut distinction between the two.

It should be noted that the difference between pragmatic and conventional uses of thresholds may be subtle. Although the pragmatic view may involve only a small ontological component, clinical and philosophical issues have important interconnections—particularly in psychiatry. As a consequence, even the view that the threshold is pragmatic is not completely neutral in philosophical terms. On the one hand, epistemological issues can impact how practitioners behave: for instance, they may tend to adopt a pragmatic view of the health–pathology distinction as a consequence of uncertainty at the epistemic level. This might be due to the practical difficulty of drawing a line between health and pathology or to sparse data on the aetiology of mental conditions (Murphy [2006]; Aragona [2009]). Pragmatic uses of thresholds may also reflect 'theoretical choices' and a specific interpretation of the data within a dimensional framework (see sec. 3.1 and sec. 3.2). On the other hand, it is plausible that (some aspects of) the view of thresholds as pragmatic tools originated in the practice itself and then influenced theorizing. In this sense, both the conventional-threshold view as well as its more pragmatic counterpart tend to be connected to one type of ontological claim over others—take, for instance, claims such as 'no thresholds exist beyond those that we adopt for conventional reasons'.

As we argue in the next subsection, the conventional-threshold view—intended as a stronger, ontological thesis—raises several problems.

4.1. Theoretical issues of the conventional-threshold view

As we discussed in section 2.1, the view that health and pathology are ontologically continuous implies that typical ways of setting the threshold are somewhat arbitrary. For

instance, the thresholds and cut-offs adopted in the DSM involve the duration of symptoms or the number of diagnostic criteria out of a checklist, and one may question whether there is any actual difference between two individuals that present five or six diagnostic criteria, for instance, or between individuals experiencing a given symptom for thirteen or fourteen days. As we argued in section 3.1, these worries seem more plausible in cases where a unidimensional, quantitative characterization does not raise significant concerns, as in the case of unidimensional variables like blood pressure, BMI, or height. For instance, one could say that there is no ontological, sharp divide between individuals with a BMI of twenty-four or twenty-five, although they are categorized as healthy and overweight, respectively.

Yet, when we consider multidimensional and highly heterogeneous constructs like mental disorders, the conventional-threshold view risks failing to grasp individual differences properly insofar as it takes 'pathological' forms of traits, as well as normality and pathology, as extremes of a continuum. In such cases, the view that health and pathology are continuous depends, at least in part, from the widespread practice of operationalizing multidimensional collections of traits as single scores or comprehensive quantitative traits (see sec. 3.1).

From the perspective of genetics research, the conventional-threshold account seems to make perfect sense given the presence of disease-associated alleles in the general population (see sec. 3.2). Although pathologies are usually diagnosed binarily, behavioural genetics models interpret their genetic architecture as quantitative. On this view, the fact that pathologies vary discontinuously in populations is considered a pragmatic necessity or a clinical contingency but, ontologically speaking, phenotypes and genotypes are thought to be continuously distributed. However, we argued in section 3.2 that this interpretation is unwarranted as continuity at the genetic level tends to be postulated rather

than observed. Moreover, the data recruited to support dimensionality are open to alternative explanations—ones that do not require seeing mental disorders as quantitative traits.

Here we aim to take a step further and show that the conventional-threshold view is also biologically implausible. In particular, we argue that to accept the ontological continuity based on genetic data, it is necessary to assume that the relationship between the genotype and the phenotype is to an important extent linear, so that genetic liability is reflected linearly at the phenotypic level. This assumption, however, proves to be too strong. Let us see why and what this implies.

Generally speaking, the idea of genotype–phenotype linearity is that genes have one-to-one effects on the phenotype. Although in classical experiments and in rare Mendelian diseases we can observe such a simple relationship, scholars unanimously reject the idea that linearity could characterize complex traits involving pleiotropic effects, epistasis, and gene-environment interactions (Griffiths and Stotz [2013]; DiFrisco and Jaeger [2019]; Lynch [2021]).[16] Notably, beyond psychiatry, linearity is a widespread assumption in quantitative genetics models that attracted various criticisms (Nelson et al. [2013]; Génin and Clerget-Darpoux [2016]; Huang and MacKay [2016]; Serpico [2020]; Koi [2021]), but these are admittedly idealized models that should not be taken literally.[17]

[16] Mendel's data pointed at one-to-one associations between variation in single genes and variation in traits (as in green versus yellow pea seeds). However, such a simple genotype–phenotype relationship depended on the use of cross-breeding techniques aimed at manipulating the genetic composition of populations of organisms: such techniques allow geneticists to get organisms that are genetically identical (or similar enough) to each other except for one gene; if such organisms are then exposed to equal environmental conditions, variation in one gene can happen to make a difference at the level of the phenotype (see Waters [2007]; Burian and Kampourakis [2013]; Griffiths and Stotz [2013]; Lynch [2021]). Early geneticists (such as Morgan et al. [1915]) were aware that in natural populations, the development of phenotypic traits is rather due to the interaction between many genetic and environmental effects.

[17] In early models like Fisher's ([1918]), the linearity assumption was made to make sense of Mendel's data in the analysis of quantitative traits (this was an explicit aim of various scholars working at the

Although the linearity of genetic effects has been questioned on multiple grounds, the linearity assumption seems to lie at the heart of the conventional-threshold view. Indeed, this view requires to postulate a direct relationship between genetic liability (and genetic variation more generally) and variation in the severity of symptoms, so that (a) at the individual level, the higher the genetic liability—the more disease-associated alleles one has—the more severe the clinical condition, and (b) at the population level, the higher the genetic liability—the more disease-associated alleles one has—the more 'extreme' (far from average values) the phenotype value on a bell curve.

In other words, the conventional-threshold view (and genetics models more generally) sees the 'position' that individuals occupy on the 'curve of symptomatology' as determined by their position in the 'curve of liability'. Being on the far end of the distribution at the genetic level would then cause being on the far end at the phenotypic level. Likewise, people with symptoms severity around the mean in any given pathology would carry an average number of alleles associated with such pathology (fig. 1).

crossroad of biometrics and Mendelism). Here, the one-to-one effects detected by Mendel were reinterpreted in the context of polygenic systems, where phenotypes are determined by many genes with additive effects (see sec. 3.2). Thus, linearity came to involve additive changes at the phenotypic level caused by additive genetic effects, as we represent in figure 1.

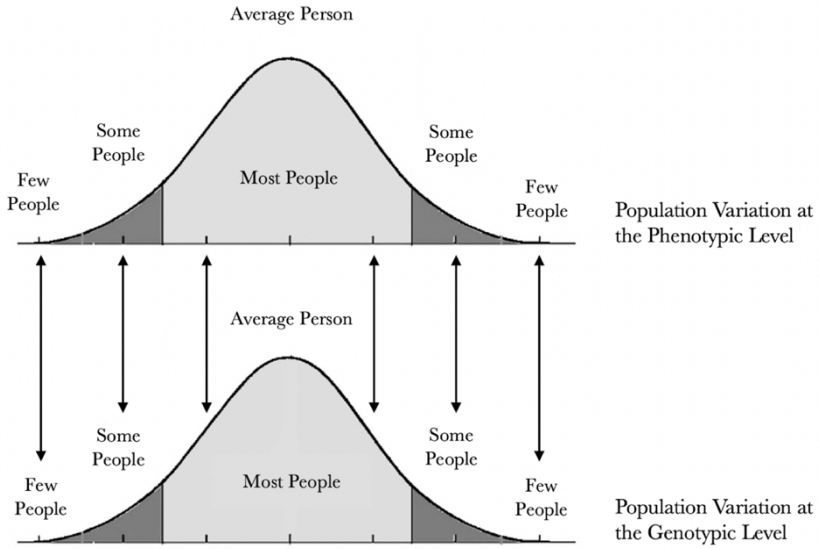

Figure 1. A graphical representation of the relationship between phenotypic variation (top) and genetic variation (bottom) under the assumption that symptoms and alleles are normally distributed. If the genotype-phenotype relationship is linear, it can be assumed that the position that different individuals occupy on the 'phenotypic curve' is determined by their position on the 'genotype curve' (the arrows represent this relationship between individuals' position on the two curves). For instance, individuals on the right (or left) end of the genotype distribution—that is, individuals carrying more (or less) disease-associated alleles—will also be on the right (or left) end of the phenotype distribution—that is, they will have more (or less) severe symptoms.

Within the dimensional trend, many scholars seem to assume this sort of linearity across the various levels of organisms. For instance, apart from Knopik et al. ([2017]) (already cited in sec. 3.2.), according to Plomin and colleagues (Plomin et al. [2009], p. 874), 'quantitative traits need not be limited to symptoms of the diagnosed disorder but can occur at any level of analysis […] from gene expression profiles, to other "-omic" levels of analysis, to physiology and often to the structure and function of the brain'. Recently, Hyman ([2021], pp. 10–13) stressed a similar point: 'Higher levels of genetic loading for a disorder are associated with increasing severity (and thus increased likelihood of being above threshold for a diagnosis), greater persistence of symptoms, and perhaps earlier onset'. Recall that in section 3.2 we argued that it is unwarranted to infer phenotypic continuity from the continuity identified (or postulated) at the genetic level.

In other words, it does not follow from genetic continuity that the phenotype is quantitative all the way up to behaviour. In this section, we have shown that the same applies the other way around: from the continuity observed at the symptoms level, it does not follow that biology is quantitative all the way down to genes, unless one makes the very problematic assumption of genotype–phenotype linearity.

5. The Ontological-Threshold Model

We have argued that the conventional-threshold view (namely, the idea that there is ontological continuity between health and disease) is vulnerable to several conceptual problems. In a nutshell: (a) it gives rise to demarcation issues, (b) it encourages a reductive view of complex pathologies that end up being operationalized along single (or few) dimensions, (c) it obscures the distinction between quantifiable and quantitative phenomena, and (d) it implies linearity between genetic liability and symptoms severity.

Our aim in this final section is to propose a theoretical framework that avoids such downsides. At the same time, we aim to accommodate the evidence usually marshalled in favour of dimensional models, such as behavioural data on symptom distribution and genetic data on disease-associated alleles (sec. 2 and sec. 3). To meet this range of desiderata, we provide a characterization of mental disorders as complex states that are qualitatively—rather than quantitatively—different from healthy ones. To illustrate and ground our proposal, we draw on Waddington's metaphor of the epigenetic landscape.

Before we delve deeper into our view of ontological thresholds, in the next subsection we start out by providing a characterization of mental disorders as constellations. We also position our model with respect to two prominent metaphysical frameworks of mental disorders and we explain how our proposal depicts the relationship between biological, psychological, and environmental variables.

5.1. Mental disorders as constellations

Our theory borrows the term 'constellation' from Freud ([2000]) to describe individual profiles as multidimensional states that include multi-level variables (symptoms, environmental factors, biological underpinnings). This view of mental disorders naturally fits our view since we aim to avoid the reduction of mental disorders to one or a few quantitative dimensions. One way to visualize mental disorders as constellations draws on systems biology, where biological systems are represented as 'clouds of variables' or networks of multi-level causal interactions and statistical associations.[18] Mental disorders as constellations are thus complex states where individual differences are determined through the relevant biological and psychological characteristics (namely, through the individual-specific group of variables).

Our notion of constellation has important similarities with contemporary cluster and network theories that describe the causal and statistical relationships between the variables associated with mental disorders. Our model predicts that some variables may be absent in some individuals, or present themselves in different forms in different individuals. In this respect, homeostatic property cluster (HPC) models of mental disorders (Kendler et al. [2011]; Hauswald and Keuck [2017]) fit our representation of mental disorders as heterogeneous constellations where no single variable is individually necessary. The 'homeostatic nature' of constellations clarifies that different individuals may be diagnosed with the same mental disorder while sharing only some of their properties. More specifically, a cluster-like framework that nicely fits our model is Slater's ([2015]) stable

[18] Recently, Olthof et al. ([unpublished]) provided a characterization of mental disorders based on the vocabulary of complex systems theory that nicely complements our analysis. We will mention some relevant similarities between their framework and ours in section 5.3.

property cluster (SPC) theory, which accounts for the statistical interconnection of variables in property clusters—while also accommodating the explanation of the interconnection among symptoms provided by network models (such as the fact that some symptoms can generate other symptoms).[19]

Remarkably, SPC provides a metaphysically neutral account that avoids reference to causal notions that would explain why or how properties cluster together.[20] This neutrality is important for our purposes as regards the identification of what variables are relevant for the definition of the constellation that represents a mental disorder. What matters, to us, is the stable and statistically relevant interconnection of the variables that constitute a constellation. In this sense, assessing what variables should be included in a cloud for it to be deemed as pathological is a question beyond the aims of our model; this will depend on clinical considerations and empirical data (including data from neuroendocrine research, for instance).[21]

Likewise, our account is neutral as to whether a given constellation qualifies as 'healthy' or 'pathological' or to what framework (naturalism or conventionalism) would better capture the distinction between health and pathology. We subscribe to a pluralist

[19] Network models similarly characterize mental disorders as arising from interactions between symptoms, as opposed to seeing them as effects of a common cause or latent variable (Borsboom [2017]; Borsboom et al. [2019]; Robinaugh et al. [2020]) and loss of concentration tend to co-occur and self-sustain over time through positive feedback mechanisms (insomnia → fatigue → loss of concentration); see (Cramer and Borsboom [2015]).

[20] Indeed, SPC can be seen as an interpretation of Boyd's ([1999]) formulation of HPC according to which a homeostatic mechanism may be unnecessary to account for the stability of clusters (see Slater's notion of cliquish stability).

[21] Like our model, most network and cluster theories are quite 'liberal' in terms of their empirical content and thus abstract away from details on the actual realization of symptoms. For instance, Borsboom et al. ([2019]) target the robust patterns of covariation among symptoms, regardless of their underlying causes, while other network models (Fried et al. [2017]; Bringmann et al. [2022]) assign different weights to the connections among symptoms and focus on how networks change dynamically over time (for a comparison of causal versus non-causal cluster theories, see Onishi and Serpico [2022]). Recent approaches devoted to analysing multi-level complexity, such as computational psychiatry (Huys et al. [2016]), may provide useful insights as regards the identification of the relevant variables in a constellation.

view according to which the definition of health and pathology involves several factors (biological, psychological, social, practical), also connected to highly contextual considerations about what counts as harm (Cooper [2005]), the role played by socio-political movements (Kapp and Ne'eman [2020]), and normative judgements aimed at avoiding negative social or clinical outcomes (Cooper [2015]; Zachar [2015]; Solomon [2017]). In this sense, our model is not tied to any specific nosology: each reliable and valid psychiatry category can be seen as a distinct cloud of variables that includes any symptoms, psychosocial, developmental, and biological factors that may been found to be relevant for the definition of a constellation associated to pathological states.

Although both network and cluster frameworks are compatible with our proposal that mental disorders are constellations (rather than single traits or dimensions), there are two additional aspects that our model aims to account for: the multi-level nature of mental disorders and the key role played by the time variable.

Let us start with a few considerations on the first aspect. In classic formulations, network models rest on the assumption that symptoms should be taken as the relevant unit of analysis (Borsboom [2017], p. 7). This assumption has been criticized for multiple reasons, including disregard for aetiology and risk of reductionism (Elbau et al. [2019]; Ward and Fisher [2019]). Since then, other versions of network models have attempted to address these criticisms by broadening their focus to variables other than symptoms, such as degree of functional impairment, life events, and so on (Fried and Cramer [2017]). Although we welcome these developments, our model starts out from a more holistic perspective that characterizes individual differences in terms of their multi-level properties, be they biological, developmental, environmental, or behavioural (namely, any variable that is relevant for the temporal development of a constellation). By embracing an epigenetic approach more decisively (see below), our model need not make a

principled decision about which unit of analysis we deem to be central, as constellations emerge—by definition—from the complex interaction of multi-level factors.

Second, our model offers a way to think about healthy and pathological states that sheds light on their development, placing the time variable at the core of the model. In this respect, it combines some aspects of cluster models—specifically, the idea of mental disorders as SPC kinds—with epigenetics. As it will become clear in section 5.2 and section 5.3, embracing a time-sensitive, epigenetic perspective represents a key conceptual shift that, in our view, should be integral to an account of mental disorders.[22] Through the notions of canalization and plasticity, our model provides a vision of how constellations associated with a given diagnosis tend to develop over time and what implications this has for clinical practice and theorizing.

In the next subsection, we provide a clearer characterization of our model that encompasses all the aspects discussed above. In our view, mental disorders are constellations embedded in an epigenetics framework, where they dynamically develop over time and in response to biological, psychological, and environmental changes.

5.2. Mental disorders as stable and dynamic qualitative states

Besides the advantages listed above, embracing an epigenetic framework for mental disorders allows us to address some of the theoretical problems generated by the conventional-threshold view (see sec. 4.1). Specifically, rather than placing arbitrary thresholds

[22] Although network models shift the focus from a static to a dynamic view of mental disorders (Wichers et al. [2017]), their classic representation as structures with nodes and edges does not directly incorporate the time variable in any strong sense. As a consequence, network theories seem to be more suited to capture some disorders—such as episodic or chronic conditions with a more or less well-delineated onset—but accommodate less obviously conditions that include rapid transitions (manic episodes) and much slower trajectories (autism) (Borsboom [2017]; but see Deserno et al. [2018]). For more recent discussions on how to incorporate the appropriate timescales in network models, see (Robinaugh et al. [2020]; Bringmann [2021]).

on a continuum of genetic risk, it is worth considering the possibility that thresholds are 'genuine' ontological features. Genetics textbooks sometimes discuss this hypothesis as the view that although liability is normally distributed, a disorder only occurs when a certain threshold of liability is exceeded (Knopik et al. [2017]; Pierce [2017]). In this sense, thresholds can be described as 'switch-points' where the accumulation of risk factors brings about a systemic change from health to pathology. However, for most conditions, qualitative changes from health to pathology are unlikely reducible to genetic factors, as such systemic changes require the interaction of genetic, epigenetic, and environmental effects. Therefore, an account limited to the genetic level would fail to capture the appropriate degree of complexity.

Beyond genetics, the ontological interpretation of thresholds is still underexplored in the literature (for some exceptions, see Serpico [2020]; Koi [2021]; Mottron [2021]).[23] In what follows, we propose a comprehensive way of framing the notion of ontological threshold by availing ourselves of the conceptual architecture described by Waddington's epigenetics (Waddington [1941], [2008]). In his renowned epigenetic landscape (fig. 2),

[23] Threshold traits are mostly investigated in the study of sexual and morphological development and environmental stress tolerance (Roff et al. [1997]; Ostrowski et al. [2000]; Milton et al. [2006]).

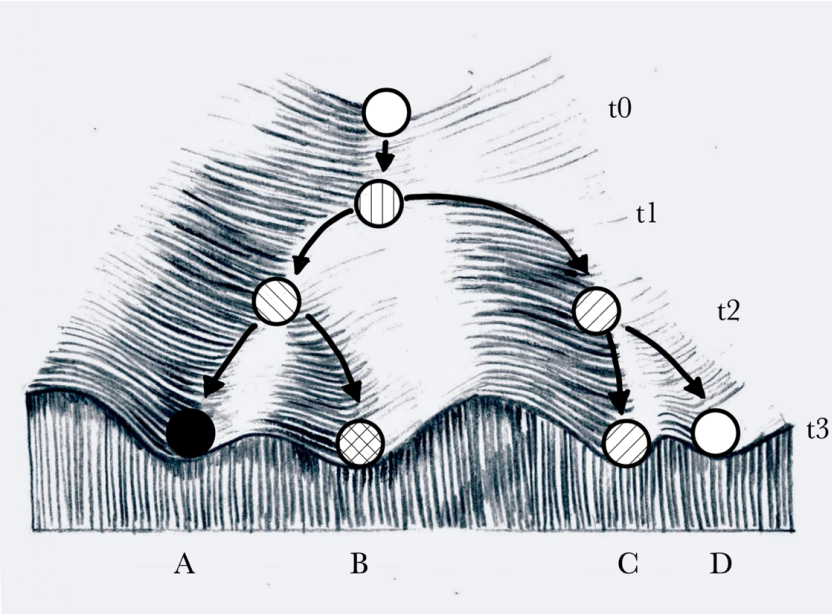

Figure 2. A representation of the epigenetic landscape with additional details to illustrate our ontological-threshold view. Different balls and arrows represent alternative developmental trajectories that an organism can take. At various developmental stages (t1, t2), we can observe bifurcations in the trajectory that represent ontological thresholds. Letters represent alternative endpoints of such trajectories: in our proposal, each letter corresponds to a state of the system that can be associated with healthy or pathological conditions.

Waddington depicted biological development as a process where a ball rolls down a sequence of valleys (which he called 'chreods'), where each sequence represents a given developmental trajectory.

In this framework, different phenotypic variants can be conceptualized in terms of bifurcations that create alternative pathways in a given trajectory, that is, branching points where the organism can take one path or another. We suggest that ontological thresholds between healthy and disordered states may be characterized as bifurcations of this sort.[24] A threshold would be the location where a branching point is created (in fig.

[24] Although we contend that such a view captures most mental disorders as we currently know them, we are open to the possibility that—at least for some conditions—a conventional-threshold approach may be more appropriate. This is obviously an empirical question, whose answer would hinge on whether the underlying lower-level mechanisms—such as serotonin reuptake—would be directly and linearly correlated with relevant increase (or decrease) in terms of intensity, frequency, and/or duration of symptoms. In such a scenario, a mental disorder would be more amenable to a truly quantitative explanation (see

2, t1 and t2), from which we could observe a discontinuity between alternative states of a biological system. In our vocabulary, this would be the point where a different constellation has emerged. Crossing a threshold would thus imply entering a specific state (metaphorically, entering a new chreod) that differs qualitatively—rather than quantitatively—from others. For example, a clinically relevant threshold is crossed when we observe the change from the prodromal phase of psychosis to the onset of a frank psychotic episode, or from occasional depressive episodes to the chronicization of a depressive disorder.

By embedding the notion of constellation within Waddington's epigenetic framework, our model depicts mental disorders as complex states that are both stable and dynamic, which in turn facilitates a time-sensitive description of psychological transitions. As we mentioned in section 5.1, following the development of constellations over time is what allows us to capture the relevant transitions between healthy and disordered states, as well as the trajectories that bring about clinically relevant changes. On the one hand, since organisms are robust systems, constellations are stable. As Waddington clarifies, development becomes canalized over time within specific trajectories of steady states (metaphorically, sequences of chreods). A clinical example here would be neurodevelopmental conditions, like autism, that become canalized at an early age and significantly constrain further development in core areas such as cognition and language.[25] On the other hand, since organisms are also flexible systems, constellations constantly develop and change in response to environmental stimuli and epigenetic interactions. In many

sec. 3.1) and the threshold between health and pathology could be drawn conventionally (similarly to what happens, for instance, with blood pressure).

[25] Barring special cases such as loss of diagnosis (Fein et al. [2013]), autism seems to exemplify a trajectory that exhibits specific constraints. For example, if a child does not develop language by the age of five, it is unlikely that they would do so as time progresses.

cases, recovery from mental disorders is possible, pharmacological and psychological treatments are fairly effective, and life events may exercise a key role in pushing an individual across the relevant threshold in one sense or another—that is, they may enhance risk or provide protection (Petrolini [2021]). Given the characteristics above, psychological development can be understood as a 'stabilized flow' of transitions from one constellation to another (see Waddington's ([2008]) notion of homeorhesis). This allows for a significant degree of individual heterogeneity to co-exist with a sufficient degree of stability. As we explain further in section 5.3, such stability supports clinically relevant inferences and generalizations, both in terms of between- and within-individual comparisons. This can occur despite the heterogeneity in constellations, that is, the fact that clouds of variables can vary across individuals or in the same individual over time.

Another key aspect of our proposal is that health and pathology are better understood as qualitatively different states rather than as states varying on a continuum. Although constellations, as we described them, are composed of individual elements that are likely to include both quantitative and binary variables (quantifiable symptoms or dimensions, and variables that are either present or not), two arguments prevent us from seeing whole constellations as quantitatively different from one another.

First, as we explained in section 3.1, mental disorders are likely to be too complex to be aptly captured by quantitative characterizations of individual differences in terms of continuum or degrees—be they unidimensional or multidimensional. Although diagnostic or psychometric tools may be used to pragmatically assess individual symptoms and global constellations quantitatively (take ADOS-2 scores), this does not imply that mental disorders are inherently quantitative. To exemplify, let us consider an ADOS-2 test including items assessing two variables: communication and social interaction, and restricted and repetitive behaviours. To obtain the general ADOS score, the individual

scores are combined into a single one. Individual differences would thus be represented through variation in such a single score. Yet, two individuals may have similar ADOS scores, but still very different profiles in terms of social abilities and repetitive behaviours. In cases of this sort, information about the individual profiles will get lost if we limit our analysis to the quantitative variation in one single score. The complexity skyrockets if more than just two variables are considered, as it is usually the case in real-world scenarios where we have dozens of abilities involved.

Second, a continuous phenotypic distribution would imply a quite liberal and continuous transition from one chreod to another, regardless of the 'topological distance' (metaphorically speaking) between each chreod. This would be misleading because, as we will argue in more detail in section 5.3, the transition from one complex state to another is often significantly constrained (see the example of autism above). In fact, such transitions tend to involve only chreods that are 'closer' to each other and occur only through the generation of new pathways (which, if we are correct, requires stable qualitative changes in a system). Indeed, transitions from one state to another arguably require durable and high-impact changes in the relevant constellation that are better described in non-continuous terms.

As a consequence, despite the heterogeneous composition of each constellation, the general distinction between one constellation and another—that is, between two alternative states of a system—is better understood as qualitative.[26] A purely quantitative description thus seems unable to satisfactorily capture variation in such complex traits. This does not imply that our model rejects the idea of quantitative differences wholesale, as quantitative differences are probably involved at the level of single variables. But if we

[26] For a similar conception, see the notion of phase transition in (Olthof et al. [unpublished]).

consider a whole constellation—that is, a complex state that can be associated with mental illness—our point is that (most) individual differences are better described as qualitative (but see footnotes 25 and 27). If this is correct, it would be misleading to compare health and pathology quantitatively, for instance, by saying, 'I am more depressed now than I was when I was healthy'. We acknowledge that this vocabulary may be—and often is—used as a rough heuristic, but it risks mischaracterizing the underlying dynamics at play. We also acknowledge that, in many cases, quantitative measures and assessment tools are used pragmatically and without strong ontological commitments. Our proposal is compatible with quantitative methods still being employed methodologically, with an increased awareness of their features and implications. For example, tools such as the ADOS should not be presented and communicated as the be-all-and-end-all when it comes to diagnosis, but rather they should be seen as components of a complex constellation that includes a multiplicity of variables.

Finally, our proposal is compatible with the idea that assessing individual differences may generate epistemic uncertainty and involve pragmatic aspects. Yet, ontologically speaking, capturing the difference between healthy and pathological states requires reference to qualitative, systemic changes. We now move on to fleshing out the clinical significance and implications of our model.

5.3. Clinical implications: individual differences and individual development

As we mentioned above, in our model psychological development can be understood as a 'stabilized flow' of transitions from one constellation to another. Such a framework allows us to comprehensively describe both between-individual differences and within-individual development. These aspects are clearly important in clinical settings: while

between-individual variation provides us with tools to think about disorders in epidemiological terms, within-individual development allows us to better understand a disorder's trajectory and assess degrees of individual risk, as well as to predict relevant transitions in terms of vulnerability, relapse, and recovery.

With respect to between-individual variation, our view predicts that in some cases the chreods of different individuals will be sufficiently similar to ground epidemiological and statistical comparisons. This is crucial when it comes to comparing individuals who exhibit similar clinical profiles and who are therefore likely to receive the same diagnosis. Indeed, people who are diagnosed with a given condition are more likely to share specific symptoms and/or biomarkers, and some states can be frequently associated with each other (as in the case of comorbidities). For instance, agoraphobia might be more similar to social anxiety disorder than to major depression.

Theoretically speaking, a good model of mental disorders should be able to capture different instances of a given condition ('autism spectrum disorder', for instance) when they present themselves in ways that are qualitatively similar to each other. Our model nicely meets such a generalization criterion based on the study of similarities among the constellations of different individuals. Starting from individual constellations, we can make generalizations and identify statistical regularities. For instance, two constellations may be more alike one another than others, as two chreods in the epigenetic landscape can—metaphorically speaking—be spatially closer to one another, generating similarities between the associated endpoint states (in fig. 2, A is closer to B than to C, for instance).[27]

[27] Our use of spatial concepts like closeness and distance—when we say that two disorders can be 'topologically closer' than others—plays a metaphorical role in our model. When we think about psychological profiles, beyond the graphical representation of the epigenetic landscape, better suited concepts are those of similarity and difference.

This would account for the differences and similarities that we observe in clinical symptoms, but also for the overlapping distribution of biomarkers and genetic risk factors across categories. Such similarities would also allow for fruitful comparisons among patients with similar profiles and guide clinical decisions in terms of diagnosis, treatment, and prevention.[28]

One may wonder, however, how to make sense of between-individual variability in any given constellation that is associated with a psychiatric diagnosis, especially if each individual follows a 'unique' developmental trajectory. Indeed, as we construed constellations in our model, each healthy and pathological state corresponds to a specific configuration of a group of variables that stabilizes over time due to an individual's epigenetic history. Similar questions have plagued psychiatry since its birth. The field deals with very individualized problems, such as internal feelings and personal narratives, and yet it sets out to draw general conclusions, thus seeking to identify regularities and similarities among individuals that can inform nosology, diagnosis, and treatment. Our model acknowledges that phenotypic development is extremely individualized, meaning that each individual can be subject to a unique epigenetic history (intended here as the interaction between contingent genetic characteristics, environmental exposures, and experiences). However, through the notion of robustness, flexibility, and canalization, the

[28] Although our model does not take a definite stance with respect to nosological changes (see sec. 5.1), at least in its initial applications, our framework would provide clinicians with a way to better systematize individual differences (in terms of quantitative and qualitative changes) and track them over time. Once a substantial amount of data will have been collected, and statistical regularities among individuals will be identified, we would be in a better position to determine whether a given condition is better captured by a categorical or dimensional description. Robust and stable discontinuities in the relevant Waddington-like landscapes would point towards categorical descriptions, whereas their absence would suggest continuity with non-clinical manifestations. In the latter scenario, nosology could also be revised accordingly, for instance, by adopting a dimensional outlook on disorders that are now conceived of categorically, or by expunging these disorders from classification manuals in virtue of their continuity with healthy states.

model meets the generalizations demands delineated above. Waddington himself analysed the problem of between-individual differences through the notions of species-level developmental canalization and robustness, which denote the ability of an organism to bypass minor genetic and environmental perturbations and develop as a typical individual of its species under a normal set of conditions (Debat and David [2001]). On this view, different individuals of the same species may end up being phenotypically similar to one other despite their developmental trajectory differing to some degree. In this sense, some phenotypic traits supervene on the specific epigenetic story that generates them or, in other words, traits are multiply realizable not just at the molecular level but in epigenetic terms more broadly. Likewise, the fact that each individual has a personal epigenetic story does not imply that constellations are incommensurable: rather, they are somewhat stable and generalizable because mental conditions—like any phenotypic trait—involve some degree of species-level canalization and multiple realizability. For instance, different individuals can end up with similar psychological states (intended as end points in the developmental trajectory) even if they do not share the very same environmental influences, experiences, biological features, and genetic aetiologies.

Let us now turn to within-individual variation. An intriguing application of our model concerns the analysis of psychological development over time (what we call 'trajectory'). Conceiving of health and pathology as qualitatively different states helps us reframe various aspects of individual development, including an individual's history, biological makeup, environmental influences, and so on. Moreover, our model allows us to bring into sharper focus a crucial aspect of psychological development, namely, the dynamic transition from one state to another. Below we consider two types of transitions: from at-risk states to pathological ones (vulnerability) and from pathology to health (recovery).

Within the dimensional trend, at-risk states are usually considered transitional conditions that differ from pathology only quantitatively. Indeed, individuals in such states may look, for instance, 'less depressed' than their clinical counterparts, while at the same time appearing 'less healthy' than not-at-risk individuals. As we mentioned in section 2.1, such states thus give rise to several demarcation issues—for instance, Keil and Stoecker ([2017]) talk about vagueness of 'grey areas' between health and disease. As we now explain, our model could sidestep these issues.

Our view is that health and pathology are states that are both stable and dynamic. Thanks to such 'robust flexibility', it is possible to observe relatively stable transitions between one state and another where individuals may stay 'on the brink' for longer periods of time (Petrolini [2021]); we dub such conditions brink states (fig. 3). Although brink states are certainly transitional, they are also sufficiently stable to be regarded as states in their own right, intended as specific configurations of the epigenetic landscape at a given time, which differ significantly from those associated with healthy and disordered ones.

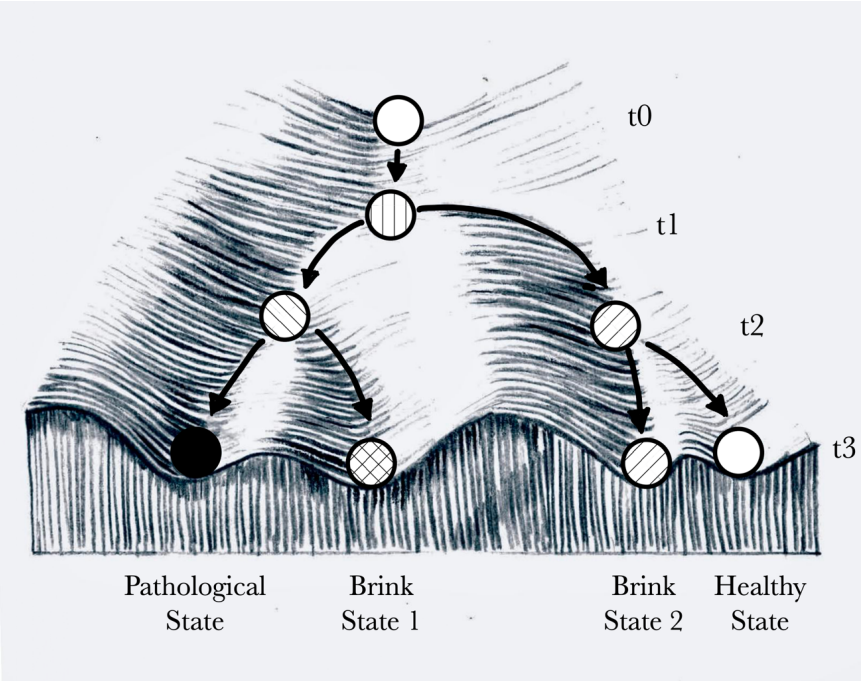

Figure 3. A representation of an epigenetic landscape involving at-risk states. Brink state 1 represents a state that is 'closer' to a pathological state and is thus more likely to gravitate towards it depending on external circumstances, at a subsequent bifurcation that is not represented in the picture. By contrast, brink state 2 is 'closer' to a healthy state.

Such a conceptualization of vulnerability is also corroborated by data on 'at risk', 'ultra-high risk', and 'clinical high risk' mental states (Fusar-Poli et al. [2016]). Although these constructs are successful in identifying segments of populations that are more liable to develop clinically relevant conditions (Broome et al. [2005]; McGorry et al. [2006]), they also include individuals who fail to develop a psychiatric disorder in the following two to three years (Ajnakina et al. [2019]). In other words, it looks like some individuals go from being vulnerable to developing a fully-fledged psychiatric condition—they cross the threshold from vulnerability to a pathological state; while others stay vulnerable indefinitely or revert to a condition of mental health—they cross the threshold from vulnerability to a healthy state. This suggests that brink states are to some extent independent of healthy and pathological ones, as they are able to branch into both depending on the individual's circumstances. Moreover, the fact that at-risk states may last for months or

years speaks to their robustness, especially when contrasted with intermittent experiences of psychiatric symptoms that may be due to local causes (such as experiencing low mood due to sleep deprivation or drug-induced manic states). We should thus see brink states as qualitatively different from non-brink states—that is, states that we usually associate with health or well-established diagnoses—as opposed to conceptualizing them as grey areas.

The distinction between brink and non-brink states may be further refined through the notion of attractor state. In the terminology of dynamical systems theory, some configurations of a system are more stable over time, more robust, and—most importantly—more capable of attracting a system towards themselves. In our framework, health and disease work like attractor states: in virtue of their internal characteristics, they have the potential of attracting an individual towards a given developmental trajectory.[29] When an individual is 'on the brink' of depression, for instance, any relevant factor (environmental triggers or life events) may tilt the trajectory towards the 'closer' and more stable attractor state in the vicinity. The nature of the transition—from at-risk to clinically relevant, or from at-risk to out-of-risk—is then determined by whether the relevant attractor state is a healthy or a pathological one (fig. 3).

This characterization of risk states avoids the demarcation issues and the double-thresholds problems discussed in section 2.1. Indeed, brink states may be understood as sufficiently stable states rather than attenuated versions of pathological states, although

[29] A similar notion is provided by Huang ([2012]), who defines stable attractors as distinct epigenetic states and analyses them within the mathematics of network dynamics and molecular biology. See also the notion of stable regimes in (Jaeger and Monk [2014]) and the similar construct of 'tipping point' in (van de Leemput et al. [2014]); and for a recent proposal on health and pathology as attractor states, see (Olthof et al. [unpublished]).

they are likely to gravitate towards more robust states such as healthy and pathological ones.

Let us turn to the transition from pathology to health, namely, recovery. Conceptualizing mental disorders as stable states that develop over time has major implications for intervention and treatment. Since development follows the time arrow, the range of developmental potentials narrows down over time. In other words, one never truly goes back from the present state (t3 in fig. 3) to a previous one (t1 or t2) where there was a bifurcation of development, pushing the individual towards pathological states. This suggests that, depending on the individual's developmental stage, interventions may not have 'unlimited power' in shaping the future path. We already saw, through the example of neurodevelopmental conditions, that some mental disorders are significantly canalized and particularly resistant to radical changes in trajectory.

In this sense, the key role played by time in our model also provides insights on how to understand the role of healthcare in patients' treatment and recovery processes. In our framework, achieving or retrieving health should be conceptualized in terms of the generation of novel states or constellations (metaphorically, new chreods), rather than as the return to previous healthy states.[30] Such newly generated states are—again—qualitatively different both from disordered and from previously held healthy states. This does justice to a powerful observation in clinical practice: if a patient effortfully achieves a relatively healthy state after having experienced a disordered one, their state will differ from that exhibited by a person who had never fallen ill in the first place. This may be connected with data on high risk of relapse for many mental disorders (depression and

[30] Olhof et al. ([unpublished]) suggest a similar idea, according to which, 'interventions are not necessarily aimed at 'reversing' the processes that caused psychopathology in the first place'.

addiction are prime candidates here), as well as contribute to explaining why some psychiatric conditions are remarkably resistant to treatment. After all, the generation and maintenance of a novel qualitative state requires bringing about significant and stable changes.

6. Conclusions

In this article, we explored major shortcomings of the dimensional trend in psychiatry and proposed an alternative framework that regards mental disorders as constellations of multi-level variables that are qualitatively different from healthy states. First, we showed that the dimensional trend is motivated by the observation of continuity between health and pathology at different levels of analysis—we focused specifically on behavioural, symptomatic, and genetic levels. Such heterogeneity, together with unaddressed philosophical questions, leaves the door open for remarkable over-simplifications regarding how to characterize the distinction between health and pathology. Second, we argued that the idea of ontological continuity (and the related thesis that the health–pathology threshold is conventional) relies on an interpretation of the nature of psychological traits that although widespread, comes with important misunderstandings of quantitative data from various sources—ranging from clinical observation, to psychometrics, to behavioural genetics models. Finally, we introduced a theoretical model that takes the threshold between health and pathology to be ontological rather than conventional or pragmatic. Our proposal is embedded within the general framework of cluster and network theories of mental disorders. However, it complements these models with insights from developmental biology and epigenetics, particularly regarding the characterization of individual differences in terms of their multi-level properties and the centrality of time in the analysis of psychological development.

The model we propose has some important advantages over both categorical and dimensional approaches. *Contra* traditional categorical approaches, it avoids essentialist labels and stigma. Indeed, the fact that mental disorders are qualitatively different from healthy states does not imply that they fall outside the range of human variation. Rather, we see mental disorders as dynamic and individualized states that cannot be reduced to empty and potentially dehumanizing labels. Moreover, our model does justice to the dynamic and diachronic nature of psychological development. In Waddington's framework, the valleys of the epigenetic landscape develop over time and contextually in response to epigenetic regulation of environmental stimuli and experience. In this sense, the developmental trajectory is not predetermined, but is rather construed 'in the present moment' through a constant flow of multi-level interacting processes. This allows us to make sense of the influence that life events—along with several other factors—exercise on health and pathology by modifying the path in significant ways.

As regards dimensional approaches, our model does justice to the idea that symptom severity varies quantitatively along some relevant dimensions. Yet, it avoids potential downsides of dimensional frameworks, such as the reduction of individual variability to one or a few quantitative dimensions, the idea that mental disorders are normally distributed in the general population, and serious demarcation issues.

In terms of clinical implications, one of the main benefits of our model is that it allows us to make sense of the robustness of clinical conditions that we observe in many real-world scenarios. As we explained above, a continuity view would imply that an individual can change its development trajectory on a continuum (from one condition to another). Although we do not deny that such transitions may occur in some cases, they are much more difficult to achieve when it comes to more canalized (temporally stable) con-

ditions. As we argued, this means that some developmental pathways might be unavailable from a given starting point, and that recovery always implies creating new states as opposed to reverting to previous ones.

One last benefit of defining health and pathologies in qualitative terms concerns pragmatic aspects that force clinicians into binary decisions. Within the dimensional trend, binary diagnosis is sometimes perceived as an inescapable burden that forces clinicians to set up thresholds in the absence of any 'natural' discontinuities. We provided some epistemological, non-pragmatic reasons to retain a binary system: if pathologies are qualitatively different from health, and if they are states that get more stable over time, then the diagnostic process maps individual-level dynamics more accurately than the alternative. If we are correct, a psychiatric diagnosis would indeed capture something important about a person's profile, for instance, that they have entered a state that is qualitatively different from others. In this sense, binary diagnoses would better reflect the functioning of complex systems as described by developmental biology.

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References

Ajnakina, O., David, A. S. and Murray, R. M. [2019]: '"At Risk Mental State" Clinics for Psychosis—an Idea Whose Time Has Come—and Gone!', *Psychological Medicine*, **49**, pp. 529–34.

Alderson-Day, B., McCarthy-Jones, S., Bedford, S., Collins, H., Dunne, H., Rooke, C. and Fernyhough, C. [2014]: 'Shot through with Voices: Dissociation Mediates the Relationship between Varieties of Inner Speech and Auditory Hallucination Proneness', *Consciousness and Cognition*, **27**, pp. 288–96.

American Psychiatric Association [1994]: *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Washington, DC: American Psychiatric Publishing.

American Psychiatric Association [2013]: *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, Washington, DC: American Psychiatric Publishing.

Amoretti, M. C., Lalumera, E. and Serpico, D. [2021]: 'The DSM-5 Introduction of the Social (Pragmatic) Communication Disorder as a New Mental Disorder: A Philosophical Review', *History and Philosophy of the Life Sciences,* **43**, pp. 1–31.

Aragona, M. [2009]: 'About and beyond Comorbidity: Does the Crisis of the DSM Bring on a Radical Rethinking of Descriptive Psychopathology?', *Philosophy, Psychiatry, and Psychology*, **16**, pp. 29–33.

Banicki, K. [2020]: 'Beyond the Categorical–Dimensional Dichotomy: An Exercise of Conceptual Geography in the Domain of Personality Disorders', *Journal of Theoretical and Philosophical Psychology*, **40**, pp. 219–39.

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J. and Clubley, E. [2001]: 'The Autism-Spectrum Quotient (AQ): Evidence from Asperger Syndrome/High-Functioning Autism, Males and Females, Scientists and Mathematicians', *Journal of Autism and Developmental Disorders*, **31**, pp. 5–17.

Blashfield, R. K., Keeley, J. W., Flanagan, E. H. and Miles, S. R. [2014]: 'The Cycle of Classification: DSM-I through DSM-5', *Annual Review of Clinical Psychology*, **10**, pp. 25–51.

Bolton, D. [2008]: *What Is Mental Disorder? An Essay in Philosophy, Science, and Values*, Oxford: Oxford University Press.

Borsboom, D., Cramer, A. O. and Kalis, A. [2019]: 'Brain Disorders? Not Really: Why Network Structures Block Reductionism in Psychopathology Research', *Behavioral and Brain Sciences*, **42**, pp. 1–63.

Borsboom, D. [2017]: 'A Network Theory of Mental Disorders', *World Psychiatry*, **16**, pp. 5–13.

Borsboom, D., Mellenbergh, G. J. and Van Heerden, J. [2004]: 'The Concept of Validity', *Psychological Review*, **111**, pp. 1061–71.

Bortolotti, L. [2009]: *Delusions and Other Irrational Beliefs*, Oxford: Oxford University Press.

Botha, M., Dibb, B. and Frost, D. M. [2020]: '"Autism Is Me": An Investigation of How Autistic Individuals Make Sense of Autism and Stigma', *Disability and Society*, **37**, pp. 427–53.

Boyd, R. [1999]: 'Homeostasis, Species, and Higher Taxa' in R. Wilson (*ed.*), *Species: New Interdisciplinary Essays*, Cambridge, MA: MIT Press, pp. 141–85.

Boyle, E. A., Li, Y. I. and Pritchard, J. K. [2017]: 'An Expanded View of Complex Traits: From Polygenic to Omnigenic', *Cell*, **169**, pp. 1177–86.

Bridgman, P. W. [1927]: *The Logic of Modern Physics*, New York: Macmillan.

Bringmann, L. F. [2021]: 'Person-Specific Networks in Psychopathology: Past, Present, and Future', *Current Opinion in Psychology*, **41**, pp. 59–64.

Bringmann, L. F., Albers, C., Bockting, C., et al. [2022]: 'Psychopathological Networks: Theory, Methods, and Practice', *Behaviour Research and Therapy*, **149**, pp. 1–15.

Broome, M. R., Woolley, J. B., Johns, L. C., Valmaggia, L. R., Tabraham, P., Gafoor, R., Bramon, E. and McGuire, P. K. [2005]: 'Outreach and Support in South London (OASIS): Implementation of a Clinical Service for Prodromal Psychosis and the At-Risk Mental State', *European Psychiatry*, **20**, pp. 372–78.

Carmon, J., Heege, J., Necus, J. H., Owen, T. W., Pipa, G., Kaiser, M., Taylor, P. N. and Wang, Y. [2020]: 'Reliability and Comparability of Human Brain Structural Covariance Networks', *NeuroImage*, **220**, pp. 1–13.

Chown, N. and Leatherland, J. [2021]: 'Can a Person Be 'a Bit Autistic'? A Response to Francesca Happé and Uta Frith', *Journal of Autism and Developmental Disorders*, **51**, pp. 749–51.

Cooper, R. [2005]: *Classifying Madness*, Dordrecht: Springer.

Cooper, R. [2013]: 'Avoiding False Positives: Zones of Rarity, the Threshold Problem, and the DSM Clinical Significance Criterion', *The Canadian Journal of Psychiatry*, **58**, pp. 606–11.

Cooper, R. [2015]: *Diagnosing the Diagnostic and Statistical Manual of Mental Disorders*, Abingdon: Routledge.

Cramer, A. O. and Borsboom, D. [2015]: 'Problems Attract Problems: A Network Perspective on Mental Disorders', in R. Scott and S. Kosslyn (*eds*), *Emerging Trends in the Social and Behavioral Sciences*, Hoboken, NJ: Wiley, pp. 1–15.

Cuthbert, B. N. [2014]: 'The RDoC Framework: Facilitating Transition from ICD/DSM to Dimensional Approaches that Integrate Neuroscience and Psychopathology', *World Psychiatry*, **13**, pp. 28–35.

Cuthbert, B. N. and Insel, T. R. [2013]: 'Toward the Future of Psychiatric Diagnosis: The Seven Pillars of RDoC', *BMC Medicine*, **11**, pp. 1–8.

De Boeck, P., Wilson, M. and Acton, G. S. [2005]: 'A Conceptual and Psychometric Framework for Distinguishing Categories and Dimensions', *Psychological Review*, **112**, pp. 129–58.

Debat, V. and David, P. [2001]: 'Mapping Phenotypes: Canalization, Plasticity, and Developmental Stability', *Trends in Ecology and Evolution*, **16**, pp. 555–61.

Deserno, M. K., Borsboom, D., Begeer, S. and Geurts, H. M. [2018]: 'Relating ASD Symptoms to Well-Being: Moving across Different Construct Levels', *Psychological Medicine*, **48**, pp. 1179–89.

Elbau, I. G., Binder, E. B. and Spoormaker, V. I. [2019]: 'Symptoms Are Not the Solution but the Problem: Why Psychiatric Research Should Focus on Processes Rather Than Symptoms', *Behavioral and Brain Sciences*, **42**, pp. 16–17.

Elton, A., Di Martino, A., Hazlett, H. C. and Gao, W. [2016]: 'Neural Connectivity Evidence for a Categorical-Dimensional Hybrid Model of Autism Spectrum Disorder', *Biological Psychiatry*, **80**, pp. 120–28.

Falconer, D. S. [1965]: 'The Inheritance of Liability to Certain Diseases, Estimated from the Incidence among Relatives', *Annals of Human Genetics*, **29**, pp. 51–76.

Fein, D., Barton, M., Eigsti, I. M., Kelley, E., Naigles, L., Schultz, R. T., ... and Tyson, K. [2013]: 'Optimal Outcome in Individuals with a History of Autism', *Journal of Child Psychology and Psychiatry*, **54**, pp. 195–205.

Fernandez, A. V. [2019]: 'Phenomenology and Dimensional Approaches to Psychiatric Research and Classification', *Philosophy, Psychiatry, and Psychology*, **26**, pp. 65–75.

Fisher, R. A. [1918]: 'The Correlation between Relatives on the Supposition of Mendelian Inheritance', *Transactions of the Royal Society of Edinburgh,* **52***,* pp. 399–433.

Frances, A. [1982]: 'Categorical and Dimensional Systems of Personality Diagnosis: A Comparison', *Comprehensive Psychiatry*, **23**, pp. 516–27.

Frances, A. [2013]: 'Saving Normal: An Insider's Revolt against Out-of-Control Psychiatric Diagnosis, DSM-5, Big Pharma, and the Medicalization of Ordinary Life', *Psychotherapy in Australia*, **19**, pp. 14–8.

Freud, S. [2000]: *Studies on Hysteria*, New York: Hachette.

Freud, S. [2003]: *An Outline of Psychoanalysis*, London: Penguin.

Fried, E. I. and Cramer, A. O. [2017]: 'Moving Forward: Challenges and Directions for Psychopathological Network Theory and Methodology', *Perspectives on Psychological Science*, **12**, pp. 999–1020.

Fried, E. I., van Borkulo, C. D., Cramer, A. O., Boschloo, L., Schoevers, R. A. and Borsboom, D. [2017]: 'Mental Disorders as Networks of Problems: A Review of Recent Insights', *Social Psychiatry and Psychiatric Epidemiology*, **52**, pp. 1–10.

Fusar-Poli, P., Rutigliano, G., Stahl, D., Davies, C., De Micheli, A., Ramella-Cravaro, V., Bonoldi, I. and McGuire, P. [2016]: 'Long-Term Validity of the At Risk Mental State (ARMS) for Predicting Psychotic and Non-psychotic Mental Disorders', *European Psychiatry*, **42**, pp. 49–54.

Génin, E. and Clerget-Darpoux, F. [2015]: 'Revisiting the Polygenic Additive Liability Model through the Example of Diabetes Mellitus', *Human Heredity,* **80**, pp. 171–77.

Griffiths, P. and Stotz, K. [2013]: *Genetics and Philosophy: An Introduction*, Cambridge: Cambridge University Press.

Happé, F. and Frith, U. [2020]: 'Annual Research Review: Looking Back to Look Forward—Changes in the Concept of Autism and Implications for Future Research', *Journal of Child Psychology and Psychiatry*, **61**, pp. 218–32.

Happé, F. and Frith, U. [2021]: 'Dimensional or Categorical Approaches to Autism? Both Are Needed: A Reply to Nick Chown and Julia Leatherland', *Journal of Autism and Developmental Disorders*, **51**, pp. 752–53.

Haslam, N. [2011]: 'Genetic Essentialism, Neuroessentialism, and Stigma: Commentary on Dar-Nimrod and Heine', *Psychological Bulletin,* **137**, pp. 819–24.

Haslam, N. [2014]: 'Natural Kinds in Psychiatry: Conceptually Implausible, Empirically Questionable, and Stigmatizing', in H. Kincaid and J. A. Sullivan (*eds*), *Classifying Psychopathology: Mental Kinds and Natural Kinds*, Cambridge, MA: MIT Press, pp. 11–28.

Hauswald, R. and Keuck, L. [2017]: 'Indeterminacy in Medical Classification: On Continuity, Uncertainty, and Vagueness', in G. Keil, L. Keuck and R. Hauswald (*eds*), *Vagueness in Psychiatry*, Oxford: Oxford University Press, pp. 93–116.

Hibberd, F. J. [2014]: 'The Metaphysical Basis of a Process Psychology', *Journal of Theoretical and Philosophical Psychology*, **34**, pp. 161–86.

Huang, S. [2012]: 'The Molecular and Mathematical Basis of Waddington's Epigenetic Landscape: A Framework for Post-Darwinian Biology?', *Bioessays*, **34**, pp. 149–57.

Huang, W. and Mackay, T. F. [2016]: 'The Genetic Architecture of Quantitative Traits Cannot Be Inferred from Variance Component Analysis', *PLOS Genetics*, **12**, available at <https://doi.org/10.1371/journal.pgen.1006421>.

Hucklenbroich, P. [2017]: 'Disease Entities and the Borderline between Health and Disease: Where Is the Place of Gradations', in G. Keil, L. Keuck and R. Hauswald (*eds*)., *Vagueness in Psychiatry*, Oxford: Oxford University Press, pp. 75–92.

Hurlburt, R. T. [2011]: *Investigating Pristine Inner Experience: Moments of Truth*, Cambridge: Cambridge University Press.

Huys, Q. J., Maia, T. V. and Frank, M. J. [2016]: 'Computational Psychiatry as a Bridge from Neuroscience to Clinical Applications', *Nature Neuroscience*, **19**, pp. 404–13.

Hyman, S. E. [2021]: 'Psychiatric Disorders: Grounded in Human Biology but Not Natural Kinds', *Perspectives in Biology and Medicine*, **64**, pp. 6–28.

Jablensky, A. [2012]: 'The Nosological Entity in Psychiatry: A Historical Illusion or a Moving Target', in J. Parnas and K. S. Kendler (*eds*), *Philosophical Issues in Psychiatry, II: Nosology*, Oxford: Oxford University Press, pp. 77–94.

Jaeger, J. and Monk, N. [2014]: 'Bioattractors: Dynamical Systems Theory and the Evolution of Regulatory Processes', *The Journal of Physiology*, **592**, pp. 2267–81.

Jang, K. L. [2005]: *The Behavioral Genetics of Psychopathology: A Clinical Guide*, Mahwah, NJ: Erlbaum.

Johns, L. C. and Van Os, J. [2001]: 'The Continuity of Psychotic Experiences in the General Population', *Clinical Psychology Review*, **21**, pp. 1125–41.

Kapp, S. K. and Ne'eman, A. [2020]: 'Lobbying Autism's Diagnostic Revision in the DSM-5', in S. K. Kapp (*ed.*), *Autistic Community and the Neurodiversity Movement*, Singapore: Palgrave Macmillan, pp. 167–194.

Keil, G. and Stoecker, R. [2017]: 'Disease as a Vague and Thick Cluster Concept', in G. Keil, L. Keuck and R. Hauswald (*eds*), *Vagueness in Psychiatry*, Oxford: Oxford University Press, pp. 46–74.

Keil, G., Keuck, L. and Hauswald, R. [2017]: *Vagueness in Psychiatry*, Oxford: Oxford University Press.

Kendell, R. E. [1975]: 'The Concept of Disease and Its Implications for Psychiatry', *British Journal of Psychiatry* **127**, pp. 305–15.

Kendell, R. and Jablensky, A. [2003]: 'Distinguishing between the Validity and Utility of Psychiatric Diagnoses', *American Journal of Psychiatry*, **160**, pp. 4–12.

Kendler, K. S. [2006]: 'Reflections on the Relationship between Psychiatric Genetics and Psychiatric Nosology', *American Journal of Psychiatry,* **163**, pp. 1138–46.

Kendler, K. S., Zachar, P. and Craver, C. [2011]: 'What Kinds of Things Are Psychiatric Disorders?', *Psychological Medicine*, **41**, pp. 1143–50.

Kenny, L., Hattersley, C., Molins, B., Buckley, C., Povey, C. and Pellicano, E. [2016]: 'Which Terms Should Be Used to Describe Autism? Perspectives from the UK Autism Community', *Autism*, **20**, pp. 442–62.

Keuck, L. and Frances, A. [2017]: 'Reflections on What Is Normal, What Is Not, and Fuzzy Boundaries in Psychiatric Classification', in G. Keil, L. Keuck and R. Hauswald (*eds*), *Vagueness in Psychiatry*, Oxford: Oxford University Press, pp. 152–68.

Kincaid, H. and Sullivan, J. A. [2014]: *Classifying Psychopathology: Mental Kinds and Natural Kinds*, Cambridge, MA: MIT Press.

Knopik, V. S., Neiderhiser, J. M., DeFries, J. C. and Plomin, R. [2017]: *Behavioral Genetics*, New York: Worth.

Koi, P. [2021]: 'Genetics on the Neurodiversity Spectrum: Genetic, Phenotypic, and Endophenotypic Continua in Autism and ADHD', *Studies in History and Philosophy of Science*, **89**, pp. 52–62.

Kotov, R., Krueger, R. F., Watson, D., et al. [2017]: 'The Hierarchical Taxonomy of Psychopathology (HiTOP): A Dimensional Alternative to Traditional Nosologies', *Journal of Abnormal Psychology*, **126**, pp. 454–77.

Kovacs, K. and Conway, A. R. [2016]: 'Process Overlap Theory: A Unified Account of the General Factor of Intelligence', *Psychological Inquiry*, **27**, pp. 151–77.

Lord, C., Rutter, M. DiLavore, P.C., Risi, S., Luyster, R.J., Gotham, K., Bishop, S.L. and Guthrie, W. [2012]: *Autism Diagnostic Observation Schedule*, Torrance, CA: Western Psychological Services.

Lynch, K. E. [2021]: 'The Meaning of "Cause" in Genetics', *Cold Spring Harbor Perspectives in Medicine*, **11**, available at <https://10.1101/cshperspect.a040519>.

Maj, M. [2011]: 'Psychiatric Diagnosis: Pros and Cons of Prototypes vs. Operational Criteria', *World Psychiatry*, **10**, pp. 81–2.

Maung, H. H. [2016]: 'Diagnosis and Causal Explanation in Psychiatry', *Studies in History and Philosophy of Biological and Biomedical Sciences*, **60**, pp. 15–24.

McGorry, P. D., Hickie, I. B., Yung, A. R., Pantelis, C. and Jackson, H. J. [2006]: 'Clinical Staging of Psychiatric Disorders: A Heuristic Framework for Choosing Earlier, Safer, and More Effective Interventions', *Australian and New Zealand Journal of Psychiatry*, **40**, pp. 616–22.

Meehl, P. E. [1992]: 'Factors and Taxa, Traits and Types, Differences of Degree and Differences in Kind', *Journal of Personality*, **60**, pp. 117–74.

Meehl, P. E. [1999]: 'Clarifications about Taxometric Method', *Applied and Preventive Psychology*, **8**, pp. 165–74.

Michell, J. [1997]: 'Quantitative Science and the Definition of Measurement in Psychology', *British Journal of Psychology*, **88**, pp. 355–83.

Michell, J. [2012]: 'Alfred Binet and the Concept of Heterogeneous Orders', *Frontiers in psychology*, **3**, pp. 1–15.

Milton, C. C., Ulane, C. M. and Rutherford, S. [2006]: 'Control of Canalization and Evolvability by Hsp90', *PLOS One*, **1**, available at <https://doi.org/10.1371/journal.pone.0000075>.

Mottron, L. [2021]: 'Progress in Autism Research Requires Several Recognition–Definition–Investigation Cycles', *Autism Research*, **14**, pp. 2230–34.

Murphy, D. [2006]: *Psychiatry in the Scientific Image*, Cambridge, MA: MIT Press.

Nelson, R. M., Pettersson, M. E. and Carlborg, O. [2013]: 'A Century after Fisher: Time for a New Paradigm in Quantitative Genetics', *Trends in Genetics*, **29**, pp. 669–76.

Olthof, M., Hasselman, F., Maatman, F. O., Bosman, A. and Lichtwarck-Aschoff, A. [unpublished]: 'Complexity Theory of Psychopathology', available at <https://doi.org/10.31234/osf.io/f68ej>.

Onishi, Y. and Serpico, D. [2022]: 'Homeostatic Property Cluster Theory without Homeostatic Mechanisms: Two Recent Attempts and Their Costs', *Journal for General Philosophy of Science*, **53**, pp. 61–82.

Ostrowski, M. F., Jarne, P. and David, P. [2000]: 'Quantitative Genetics of Sexual Plasticity: The Environmental Threshold Model and Genotype-by-Environment Interaction for Phallus Development in the Snail *Bulinus Truncatus*', *Evolution*, **54**, pp. 1614–25.

Owen, M. J., Craddock, N. and Jablensky, A. [2007]: 'The Genetic Deconstruction of Psychosis', *Schizophrenia Bulletin*, **33**, pp. 905–11.

Parnas, J. and Kendler, K. S. [2012]: *Philosophical Issues in Psychiatry, II: Nosology*, Oxford: Oxford University Press.

Petrolini, V. [2021]: 'On the Brink of Disaster: Vulnerability to Mental Disorders', *Philosophy of Medicine*, **2**, available at <https://philmed.pitt.edu/philmed/article/view/10>.

Petrolini, V. and Vicente, A. [2022]: 'The Challenges Raised by Comorbidity in Psychiatric Research: The Case of Autism', *Philosophical Psychology*, **35**, pp. 1234–63.

Phillips, J. [2020]: 'Rethinking Categories and Dimensions in the DSM', *The Journal of Medicine and Philosophy*, **45**, pp. 663–82.

Pierce, B. A. [2017]: *Genetics: A Conceptual Approach*, New York: Freeman.

Plomin, R., Haworth, C. M. A. and Davis, O. S. P. [2009]: 'Common Disorders Are Quantitative Traits', *Nature Reviews Genetics,* **10**, pp. 872–78.

Pua, E. P. K., Bowden, S. C. and Seal, M. L. [2017]: 'Autism Spectrum Disorders: Neuroimaging Findings from Systematic Reviews', *Research in Autism Spectrum Disorders*, **34**, pp. 28–33.

Regier, D. A., Narrow, W. E., Kuhl, E. A., Kupfer, D. J. and American Psychopathological Association. [2010]: *The Conceptual Evolution of DSM-5*, Washington DC: American Psychiatric Association Publishing.

Riglin, L., Collishaw, S., Thapar, A. K., et al. [2016]: 'Association of Genetic Risk Variants with Attention-Deficit/Hyperactivity Disorder Trajectories in the General Population', *JAMA psychiatry*, **73**, pp. 1285–92.

Robinaugh, D. J., Hoekstra, R. H., Toner, E. R. and Borsboom, D. [2020]: 'The Network Approach to Psychopathology: A Review of the Literature 2008–2018 and an Agenda for Future Research', *Psychological Medicine*, **50**, pp. 353–66.

Robinson, E. B., St Pourcain, B., Anttila, V., et al. [2016]: 'Genetic Risk for Autism Spectrum Disorders and Neuropsychiatric Variation in the General Population', *Nature Genetics*, **48**, pp. 552–55.

Roff, D. A., Stirling, G. and Fairbairn, D. J. [1997]: 'The Evolution of Threshold Traits: A Quantitative Genetic Analysis of the Physiological and Life-History Correlates of Wing Dimorphism in the Sand Cricket', *Evolution*, **51**, pp. 1910–19.

Ruzich, E., Allison, C., Smith, P., Watson, P., Auyeung, B., Ring, H. and Baron-Cohen, S. [2015]: 'Measuring Autistic Traits in the General Population: A Systematic Review of the Autism-Spectrum Quotient (AQ) in a Nonclinical Population Sample of 6,900 Typical Adult Males and Females', *Molecular Autism*, **6**, pp. 1–12.

Schumann, G., Binder, E. B., Holte, A., et al. [2014]: 'Stratified Medicine for Mental Disorders', *European Neuropsychopharmacology*, **24**, pp. 5–50.

Serpico, D. [2018]: 'What Kind of Kind Is Intelligence?', *Philosophical Psychology*, **31**, pp. 232–52.

Serpico, D. [2020]: 'Beyond Quantitative and Qualitative Traits: Three Telling Cases in the Life Sciences', *Biology and Philosophy*, **35**, available at <https://doi.org/10.1007/s10539-020-09750-6>.

Serpico, D. and Borghini, A. [2021]: 'From Obesity to Energy Metabolism: Ontological Perspectives on the Metrics of Human Bodies', *Topoi*, **40**, pp. 577–86.

Serpico, D., Lynch, K. E. and Porter, T. M. [2023]: 'New Historical and Philosophical Perspectives on Quantitative Genetics', *Studies in History and Philosophy of Science*, **97**, pp. 29–33.

Slater, M. H. [2015]: 'Natural Kindness', *British Journal for the Philosophy of Science,* **66**, pp. 375–411.

Solomon, M. [2017]: '"A Messy Business": Balancing Considerations in Revising the Psychiatric Nosology', in K. S. Kendler and J. Parnas (*eds*), *Philosophical Issues in Psychiatry IV: Psychiatric Nosology*, Oxford: Oxford University Press, pp. 70–74.

Sucksmith, E., Roth, I. and Hoekstra, R. A. [2011]: 'Autistic Traits below the Clinical Threshold: Re-examining the Broader Autism Phenotype in the 21st Century', *Neuropsychology Review*, **21**, pp. 360–89.

Uher, J. [2021]: 'Psychometrics Is Not Measurement: Unraveling a Fundamental Misconception in Quantitative Psychology and the Complex Network of Its Underlying Fallacies', *Journal of Theoretical and Philosophical Psychology*, **41**, 58–84.

van de Leemput, I. A., Wichers, M., Cramer, A. O., et al. [2014]: 'Critical Slowing Down as Early Warning for the Onset and Termination of Depression', *Proceedings of the National Academy of Sciences USA*, **111**, pp. 87–92.

Van Der Maas, H. L., Dolan, C. V., Grasman, R. P., Wicherts, J. M., Huizenga, H. M. and Raijmakers, M. E. [2006]: 'A Dynamical Model of General Intelligence: The Positive Manifold of Intelligence by Mutualism', *Psychological Review*, **113**, pp. 842–61.

Van Rooij, D., Anagnostou, E., Arango, C., et al. [2018]: 'Cortical and Subcortical Brain Morphometry Differences between Patients with Autism Spectrum Disorder and Healthy Individuals across the Lifespan: Results from the ENIGMA ASD Working Group', *American Journal of Psychiatry*, **175**, pp. 359–69.

Vessonen, E. [2019]: 'Operationalism and Realism in Psychometrics', *Philosophy Compass*, **14**, available at <https://doi.org/10.1111/phc3.12624>.

Waddington, C. H. [1941]: 'Evolution of Developmental Systems', *Nature*, **147**, pp. 108–10.

Waddington, C. H. [2008]: 'The Basic Ideas of Biology', *Biological Theory*, **3**, pp. 238–53.

Ward, T. and Fischer, R. [2019]: 'Families of Network Structures: We Need Both Phenomenal and Explanatory Models', *Behavioral and Brain Sciences*, **42**, pp. 42–44.

Wichers, M., Wigman, J. T., Bringmann, L. F. and de Jonge, P. [2017]: 'Mental Disorders as Networks: Some Cautionary Reflections on a Promising Approach', *Social Psychiatry and Psychiatric Epidemiology*, **52**, pp. 143–45.

Wijsen, L. D., Borsboom, D. and Alexandrova, A. [2022]: 'Values in Psychometrics', *Perspectives on Psychological Science*, **17**, pp. 788–804.

Zachar, P. [2000]: 'Psychiatric Disorders Are Not Natural Kinds', *Philosophy, Psychiatry, and Psychology,* **7**, pp. 167–82.

Zachar, P. [2015]: 'Psychiatric Disorders: Natural Kinds Made by the World or Practical Kinds Made by Us?', *World Psychiatry,* **14**, pp. 288–90.