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Introduction: The Boundaries of Disease

Abstract: While health and disease occupy opposite ends of a spectrum, distinguishing between them can be difficult. This is the 'line-drawing' problem. The papers in this special issue engage with this challenge of delineating the boundaries of disease. The authors explore different views as to where the boundary between disease and non-disease lies, and related questions, such as how we can identify, or decide, what counts as a disease and what does not; the nature of the boundary between the two categories; and what sorts of considerations could justify the location of that boundary. In exploring these questions, the papers draw on detailed clinical examples, provide theoretical critiques of existing approaches to disease definition, and offer new ways to conceptualize key features in debates about disease including harm and biological dysfunction.

Keywords: disease definition, boundaries, diagnostic criteria, harm, dysfunction

The papers in this issue originated in a workshop on the boundaries of disease held at Macquarie University. One trigger for the workshop was the increasing medical concern about overdiagnosis, which may be characterized as the identification (and often treatment) of instances of harmless disease through practices such as screening (Welch et al 2011). The phenomenon of overdiagnosis raises ontological and epistemological questions about the nature and identification of disease (Rogers and Mintzker 2016), and in particular, where the boundary lies between disease and health. The aim of the workshop was to bring together a diverse group of scholars from philosophy of medicine, philosophy of biology, bioethics and clinical practice to interrogate challenges such as overdiagnosis and canvas potential solutions in clarifying the boundary between disease states and health. We hoped to explore not only different ideas as to where the boundary between disease and non-disease lies, and why, but also to focus on how we should think about those boundaries: whether they reflect 'real' (physical, social or evaluative) differences in the world or are stipulative; whether they should be regarded as clear and precise; and whether they are static across different contexts.

Several recent trends have complicated philosophical debate about the concept of disease. National and international bodies have sought to establish standard diagnostic criteria for a

number of common diseases. This has led to redefinitions that have tended to expand patient populations to include increasing numbers of apparently well individuals (Moynihan et al 2013). Public health approaches to screening aim to reduce the burden of advanced disease, but the success of screening programs has been mixed, not least because of their capacity to identify apparent pathology of unknown significance in asymptomatic individuals (some of which is overdiagnosis). Increasingly sophisticated diagnostic technologies can detect abnormalities which may or may not have any clinical significance. These developments put pressure on our concepts of disease and health, raising questions about such matters as the distinctions between normal variations, diseases and risk factors; the role of pragmatic considerations in justifying a definition of disease; and the uncertainties involved in predicting whether diagnosis and treatment will provide overall benefit, or cause harms. These trends also raise the possibility that our concept of disease may be changing, or should be revised, in ways that reflect current knowledge and practices, such as to avoid the harm of overdiagnosis.

In response to these challenges, the papers collected here call into question a number of the assumptions often made in philosophical examinations of disease. The papers draw on detailed contemporary clinical examples, provide theoretical critiques of existing approaches to disease definition, and offer new ways to conceptualize key features in debates about disease including harm and biological dysfunction. They aim to answer questions relating to how we can identify, or decide, what counts as a disease and what does not, the nature of the boundary between the two categories, and what sorts of considerations might justify the location of that boundary.

BOUNDARY SETTING IN PRACTICE

Jenny Doust, Mary Jean Walker and Wendy Rogers' paper examines several recent problems in setting disease boundaries. They argue that disease boundaries cannot be determined by appeal to dysfunction alone (as Boorse claims in his biostatistical theory [BST] (e.g., Boorse 1977, 1997, 2014). Instead, professional bodies and health authorities play an authoritative role in setting disease boundaries through stipulating relevant dysfunctions and setting reference classes. While the latter value-laden processes risk leading to overdiagnosis and medicalization, the BST also permits widening the boundaries of disease in problematic ways. Their discussion of polycystic ovary syndrome (PCOS) demonstrates that there is no specific dysfunction common to all cases of PCOS, so that clinical signs which are indicative

of disease in some individuals are taken to be consistent with health in others. The example of chronic kidney disease shows how an individual might be classed as diseased or non-diseased depending on the reference class to which they are assigned. And the authors' discussion of new diagnostic methods for identifying myocardial infarction reveals how the BST is out of step with medical processes of identifying dysfunction that counts as disease. Although proponents of the BST could potentially respond to these sorts of issues by appealing to the distinction between theoretical and practical concepts, Doust and colleagues argue that, given that the BST itself has a practical motivation in resisting certain forms of medicalization, it is problematic if its account of dysfunction instead supports new kinds of medicalization. The authors suggest the need to recognize the role of values in identifying the boundaries of disease, in order to counter at least some forms of overdiagnosis.

Rachel Ankeny's paper examines conflations of disease and variation in relation to geneticization, via an exploration of the history of the diagnostic catalogue *Mendelian Inheritance in Man* (MIM, later the *Online Mendelian Inheritance in Man* or OMIM). She shows how, as the MIM/OMIM came to play an increasingly important role not only in diagnostics but in research into genetic disorders, its focus switched from disease to genomic variation. The resource came to include detectable genetic variations that were not known to be associated with phenotypically-visible disorders and had no clinical significance, as well as recording phenotypic characteristics whose genetic basis was merely suspected. Although this expansion occurred for pragmatic reasons – as a way of aiding identification of correlations between phenotypically-visible disorders, clinical symptoms, and variations – it also functions as a driver of geneticization, a tendency to understand particular diseases or behaviours as genetically explainable or determined. Geneticization, as a species of medicalization, can encourage individualization of responsibility for health, and the ignoring of non-genetic factors in the causes and progression of disorders. The study of the MIM/OMIM shows how a range of drivers may contribute to conflating variation with disease, and to defining genetic 'norms' which medicalize variation.

PROBLEMS OF DEFINITION

The papers by Lynette Reid, Rogers and Walker, and Leen de Vreese critique several common assumptions made in the existing debate about the conceptual analysis of disease. Reid and Rogers and Walker raise questions, in particular, for analyses of disease that focus on physiological dysfunction. In her paper, Reid uses examples from cancer screening to

challenge the primacy accorded to pathophysiology in some approaches to defining disease. Reid argues that clinicians, in diagnosing patients, engage in inferential reasoning using multiple forms of evidence including patient symptoms, signs, aetiology, pathology, prognosis, and treatment. This probabilistic process is (largely) reliable, but can be seen as messy and subjective. In contrast, a pathophysiological approach seems to promise objectivity by relying upon observable features of biological states. This is evident in cancer screening, which assumes that cancer can be identified on the basis of pathological findings alone, in the absence of contextual features such as patient presentation and clinical reasoning. Yet cancer screening is highly unreliable, because there are both epistemological and ontological limits to the significance of isolated pathophysiological findings (demonstrated by the existence of false positives and identification of lesions of unknown significance). According to Reid, appeal to objectivity via biological sciences, especially evolutionary theory, is likewise mistaken because we must choose whether our concept of disease applies in terms of population fitness or individual well-being, which is a question biological theory cannot answer. Using a pathophysiological paradigm in disease definition also involves pitfalls as this may lead us to ignore critical features in diagnosis such as background probabilities or phenotypic variations. Finally Reid argues that the process of looking for essentialist features of disease limits the range and scope of relevant considerations that will help to determine the boundaries of disease, leaving us vulnerable to more rather than less medicalization.

Rogers and Walker's paper focuses on the assumption, in some of the philosophical literature, that 'disease' and 'health' are clearly distinct, mutually exclusive states—that 'disease' is all-or-nothing. They argue that this assumption is in tension with the claim that disease is analyzable in terms of dysfunction, because biological dysfunction occurs by degree. They show, drawing on several detailed medical examples, that dysfunctions are often matters of degree, not only in 'spectral' diseases like hypertension, but in cancers and some infections. Rogers and Walker then provide a conceptual map of options for responding to this tension, by either dropping one of the claims that generate it (i.e., 'disease is all or nothing'; and 'disease is analyzable in terms of dysfunction'), or understanding the claims in such a way that they can be made consistent. They argue that two of these options are plausible: retaining dysfunction in the analysis of disease but considering disease to be a matter of degree rather than all-or-nothing; or retaining both claims by understanding the boundary between disease and health to be vague, so that borderline cases are not clearly

either disease or non-disease. They suggest that these two options might be appropriate for different kinds of diseases.

Leen de Vreese's paper critiques the assumption that disease is definable as a single, unitary concept with clear boundaries. But she rejects alternative views offered in response to this problem, such as the pluralism of Peter Schwartz (2007) and the eliminativism of Germund Hesslow (1993). Instead, de Vreese builds on the intuition that disease is a practical, rather than a theoretical term. She characterizes philosophical inquiry about disease definition as an iterative process of conceptual construction and change, involving an abstraction from practice to develop a description, which is in turn used to reflect on the notion of 'disease' at work in practice. She proposes that disease as a practical concept is related to two key factors: value-laden considerations about the (un)desirability of certain physical and/or mental states; and the discovery of causes that are explanatorily relevant in determining medical interventions to ameliorate the (un)desired states. Drawing on Nick Haslam's (2002) work on kinds of categories in mental disease, De Vreese offers detailed examples of kinds of physical disease. These may be distinguished on the basis of explanatorily relevant causes, showing how different kinds of disease can involve varied interactions of these two factors. This approach leads to a flexible account of disease that can be modified in response to counter examples, but in which the factors triggering disease designation are clearly recognizable.

HARM AND OBJECTIVITY

The papers by John Matthewson and Paul Griffiths and by Patrick McGivern and Sarah Sorial continue the focus on new approaches to thinking about disease, turning to the role of normativity and harm in setting disease boundaries. Matthewson and Griffiths' paper is partly motivated by the view that an account of disease should be equally applicable to diseases of humans, non-human animals and plants. In developing such an account they reconceptualize the roles of normative and descriptive criteria in disease, developing a notion of 'biological normativity'. Biological normativity refers to criteria that may be found in biology for indicating when something is 'going wrong' for an organism, understood as a failure to flourish. These features can be objectively described, yet are evaluative insofar as they are connected to the notion of flourishing. Their normative status, however, is biological, rather than connected to social values. Matthewson and Griffiths identify four ways that things can go badly for an organism, biologically speaking, underwriting which are two sources of

biological normativity. One source relates to a lowering of fitness, while the other relates to failure to discharge a selected effect. While these two sources share some similarities with naturalistic accounts of disease that rely upon appeals to proper function (such as Wakefield 1992) or contribution to fitness (Boorse), Matthewson and Griffiths do not see these as mutually exclusive alternatives, each of which excludes important ways of going wrong in biology. Rather they argue that drawing on both of these sources of biological normativity leads to a less restrictive account of the role of biology in defining disease, and provides a way of developing an account of human disease that is consistent with disease in non-human animals and plants.

In contrast to this account of sources of biological normativity, McGivern and Sorial investigate the possibility of a harm-based but naturalistic account of disease, challenging the typical view that harm is necessarily a normative criterion for disease. Normativist approaches to defining disease claim that the common feature linking the heterogeneous disorders categorized as disease is their interference with a good life. On the other hand, the most influential naturalistic account of disease focuses on dysfunction, which may or may not be harmful to the affected individual. Thus recognizing the role of harm in the conceptualization of disease has become linked to rejecting descriptive criteria in favour of the normative. Yet, argue McGivern and Sorial, harm can be (and in some contexts, is) regarded as objective in some senses, if not value-free. This raises the possibility of a harm-based but naturalistic account of disease. The authors draw on Feinberg's (1984) analysis of harm as setbacks to interests. On this analysis harm is in one sense relative to where one's interests lie, but, as they show, a non-relative sense of harm can also be identified in relation to vital interests shared between humans, and also with other organisms. They explore how the notion of interests might be fleshed out, drawing on Nordenfelt's (1995) discussion of vital goals, seeking an account that can accommodate the possibility that we might be mistaken about our own interests. They then show how this approach can respond to a number of arguments against including harm in an account of disease, to show that the distinction between harm-based and harm-free accounts does not align with that between normative and naturalistic accounts.

Peter Schwartz's commentary responds to four of these papers that explicitly engage with his recent work on disease. Schwartz provides an overview of his idea of 'philosophical explication', as well as the positions he has developed on dysfunction-requiring accounts, and

on the distinction between diseases and risk factors, and the relationships between them. In his thoughtful responses to each paper, Schwartz finds common threads while posing challenges for the authors. He questions the role of distinctions among kinds of disease concepts in de Vreese's pragmatic account, and the evidence for this distinction in practice; and pushes Matthewson and Griffiths on the relationship between some of their identified biological 'ways of going wrong' and pathology. His critique of Rogers and Walker's paper questions the implications of their use of vagueness to understand the continuous nature of dysfunction for the project of conceptual analysis of 'disease' and the assumptions about meaning that underlie it. And he finds a number of points of agreement between his and Reid's approaches to risk factors and disease.

In summary, the papers in this issue open up new avenues in the debate about disease and are notable for their practical bent in seeking to locate or set the boundary between disease and health.

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