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Why It (Also) Matters What Infectious Disease Epidemiologists Call "Disease"

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Abstract

Infectious diseases figure prominently as (counter)examples in debates on how to conceptualize "disease." But crucial epidemiological distinctions are often not heeded in the debate, and pathological and clinical perspectives focusing on individual patients are favored at the expense of perspectives from epidemiology focusing on populations. In clarifying epidemiological concepts, this paper highlights the distinct contributions infectious disease epidemiology can make to the conception of "disease," and the fact that this is at least tacitly recognized by medical personnel and philosophers. Crucially, infectious disease epidemiology can help elucidate how carrying and transmitting infectious, communicable entities is a disease, even if the carriers themselves are not directly affected by symptoms detrimental to them.

1. Introduction

Polio is an infectious *disease,* right? But is one diseased merely because one carries usually innocuous *Escherichia coli*? How about dangerous variants, such as EHEC? How about *Streptococcus mutans* causing all our tooth decay? Are asymptomatic carriers of HIV or SARS-CoV-2 diseased, even though they do not suffer clinical symptoms? What if they potentially transmit the virus? Would one still be "diseased" if one carries HIV but takes retroviral drugs, which inhibit symptoms and transmission? Can we answer these questions in a value-free way? If not, is there just one normative account that fits all? In this paper I want to examine these questions and the philosophical debates on the concept of "disease" from an epidemiological perspective.[1]

In this paper, I argue three main points: First, when utilizing infectious diseases as examples, philosophical debates—at times—get crucial epidemiological details wrong. Second, the two prominent camps rely heavily on clinical medicine and/or pathology, at the expense of epidemiological considerations. And finally, this leads both camps to deem asymptomatic transmission as *not a disease,* while epidemiological considerations—also

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tacitly recognized by clinical and pathological theory and practice—give us reason to postulate that it could count as disease.

In section 2 I clarify important preliminaries and make explicit how the epidemiological perspective differs from pathological or clinical perspectives. I also clarify crucial terminology from infectious disease epidemiology for the subsequent discussion.

In the third section I introduce the prominent naturalist approach to conceptualizing "disease": the biostatistical theory (BST), prominently defended by Christopher Boorse, which offers an account of disease in terms of pathological conditions taken as below normal functional ability, exhibited by an individual in comparison to their reference class—that is, "an age group of a sex of a species" (Boorse 2014, 684). The BST aims to offer a "value-neutral" or "value-free" account of disease (Boorse 1997, 61; 2014, 684).

In section 4 I discuss several counterexamples to the BST, which involve infectious diseases. These counterexamples are offered by normativists, who dispute that concepts of disease and health can be made value-neutral or value-free. They offer accounts that capture various sources of value-ladenness. For the sake of clarity, I mostly focus on those normative accounts for which infectious diseases are introduced explicitly as (counter)examples, such as Lennart Nordenfelt (1995), Scott DeVito (2000), Peter H. Schwartz (2007a, 2007b), and Jerome Wakefield (2014).[2]

Section 4 has five parts, one for each kind of counterexample. First, I discuss "universal" or "common" diseases, which the frequentist core of the BST risks deeming "normal." I argue that carrying an infectious entity (carrier state) is not addressed in these debates. Second, looking at the role of immune responses, I reject Boorse's claim that, for example, fever is generally "non-pathological." Third, this connects to the question of whether Boorse's take on "pathological condition" is sufficient to conceptualize disease, and to the question of whether his view of pathology aligns with pathological theory and practice. I side with normativists on denying both. The final two groups of examples of "asymptomatic transmission" and "persons on antiretroviral treatment," however, show that both the BST and the normativist positions rely on the individual-affecting focus of pathological and clinical perspectives. This comes at the expense of an epidemiological perspective, which views asymptomatic transmission as the continuous failure of a host to contain an infection and prevent transmission, which poses a risk to others. Thus, it ought to count as a disease. On the other hand, persons on antiretroviral treatment do not count as diseased.

Section 5 clarifies that while epidemiology relies heavily on identifying "risk" and "risk factors," an epidemiological view need not equate them with "disease." Finally, I offer an outlook on how the addition of an epidemiological perspective to established pathological and clinical views may shape how we think about the concept of "disease."

2. Preliminary Clarifications

Since this paper aims to provide an epidemiologist's view on the concept of "disease," let me begin by explicating the contrast between an "epidemiological" perspective and "pathological" and "clinical" perspectives. Pathology is the study of states of disease of

[2] Note that there are other accounts: Eliminativist accounts, such as by Germund Hesslow (1993), argue that we may not need the concept of disease in the first place; I do not consider this account here. Pragmatic and pluralist accounts, such as by Quill R. Kukla (2022) argue that no single conception can be formed to unite the purposes for which the term can be deployed. I return to the latter briefly at the end of this paper.

individuals and their structural and functional causes (etiology) and mechanisms (pathogenesis) within an individual (Carton 2012, 2). The pathological view is thus one in which the individual is the focus as both the locus of potential disease and its causes. Clinical medicine studies states of disease and health found in individuals by directly observing the patient (in a clinical setting) (Fishman 2010, 18). Both the pathological and the clinical view thus take the individual as both the locus of potential disease and its causes. Epidemiology, on the other hand, studies states of disease and health found within populations and examines the distributions and determinants of disease by comparing groups (Broadbent 2013, 1; Gieseke 2017, 1). An epidemiological view, therefore, goes beyond a focus on individual patients.

Note here that while epidemiology also examines the etiology and mechanisms of diseases in terms of the prevalence or spread in populations, it may do so by studying risk factors; that is, "factors to which populations are exposed" that may make them "vulnerable" to disease (Krämer, Akmatov, and Kretzschmar 2010, 85). It is crucial not to equate "being at risk" with "being diseased," as we shall see below. Note also that epidemiology can be further divided into epidemiology focusing on "infectious diseases" (infectious disease epidemiology),[3] and epidemiology focusing on noninfectious diseases (Gieseke 2017, 2). While my focus is on infectious disease epidemiology, I also demonstrate how difficult this separation can be.

Infectious disease epidemiology has as its object of study "infectious diseases," a term that already subsumes several partially overlapping but also principally distinguishable aspects. Roughly, "infectious diseases" are diseases brought about by an infection of a host upon exposure to an infectious entity.[4] But there is more to it. First, "infectious disease" is applied to both the entity that upon exposure may infect a host and the symptoms it causes in that host.[5] While the distinction between the two is deemed important in epidemiology (Krämer, Akmatov, and Kretzschmar 2010, 90) and pathology (Kradin and Iafrate 2010, 3), the term "infectious disease" and specific names for them may not—without context—specify which one is referred to.

"Polio," for example, may refer to either the viral entity *Poliovirus,* or it may refer to poliomyelitis—one severe symptom, among others, it can cause in humans. We find this, for example, in an article by Elselijn Kingma, where polio is "an infection" that "can be environmentally caused" and elicit immune responses (Kingma 2010, 259). It is not always clear whether Kingma wants to refer to the viral entity, the infection, carrying it, the invoked symptoms, or the immune response in a host upon infection, which may produce its own set of effects (for example, fever induced by cytokines).[6] As we will see, it may be challenging for a single concept of disease to encompass all these aspects simultaneously. Granted, in other cases, such as for HIV and AIDS, the distinction between the entity (human

[3] Note, there are also subfields of, for example, pathology, with a focus on infectious diseases; that is, pathology of infectious diseases (Kradin and Iafrate 2010, 5).
[4] Hosts come in a variety of shapes and sizes—from animals to plants but also fungi and bacteria themselves. In this paper I focus on human hosts because the existing debate around the conception of "disease" is already mainly restricted in this sense. But my arguments would also very much apply to other types of hosts as well.
[5] Infectious entities are sometimes also called "pathogens" but this already constrains our view to those that are pathogenic; that is, disease causing. It will become clear why I avoid this term.
[6] Kingma (2010) is certainly not helped by the fact that, while figuring prominently in the title, "polio," as an entity and its symptoms, is hardly addressed in the paper.

immunodeficiency virus) and a specific set of caused symptoms (acquired immunodeficiency syndrome) is more widely recognized.

2.1 The Wide Range of "Infection"

"*Infectious* disease" refers to interactions between a biological entity and a host in a given environment.[7] "Infection" is usually understood as the process by which a biological entity invasively enters a host by overcoming anatomical barriers, such as skin or tissue. "Infection" is also taken as distinct from mere colonization. In case of the latter, an entity does not overcome specific anatomical barriers and only attaches itself to body or tissue surfaces. Such colonized hosts do not show symptoms (Krämer, Akmatov, and Kretzschmar 2010, 92).

The fact that the distinction between mere colonization and invasive infection can be blurry and hard to distinguish in (pathological) practice (Kradin and Iafrate 2010, 3) may play a role in the following example from the debate around disease concepts. DeVito introduces *Helicobacter pylori* as an entity capable of infecting humans and potentially causing gastric ulcers (2000, 539). Note here that the terminology of "infection" by *H. pylori* is also found in scientific papers, even though it merely *attaches* to gastric epithelial cells by "adhesion" and "rarely, if ever, *invades* the gastric mucosa" (Suerbaum and Michetti 2002, 1176; emphasis added). DeVito points out that *E. coli,* on the other hand, as a common colonizer is "generally not taken to be cause for alarm" (2000, 539). So how, he asks, do we distinguish the colonization by *H. pylori* of humans as a disease and the colonization by *E. coli* as not a disease? DeVito's answer is that since "the presence and activity of each bacterium is the same," no distinction can be made without also "taking the health and diseased person's interests into account" (2000, 540). I return to this below.

I want to point out here already that while one could be tempted to address the problem posed by DeVito by assuming a distinction between *H. pylori* as an "infectious disease entity" and *E. coli* as just not such an entity, this resolution fails. Granted, "commensal *E. coli* strains rarely cause disease except in immunocompromised hosts or when the normal gastrointestinal barriers are breached" (Rolhion and Darfeuille-Michaud 2007, 1277). But *E. coli* also does overcome a chemical barrier to get into the human gut—the acidity of the stomach—as they "colonize the gastrointestinal tract of human infants within a few hours after birth" and outcompete other bacteria. Furthermore, their "adhesion enables the bacteria to colonize the mucosa and to resist mechanical removal from the intestine" (2007, 1279).

E. coli is also a good example of a species of entities, some of which are readily associated with benefits, others with harms. Commensal *E. coli* play a mutually beneficial role in the human gut but some *E. coli* strains may also "acquire specific virulence attributes, which … allows them to cause a broad spectrum of disease" (Kaper, Nataro, and Mobley 2004, 123). These variants, sometimes called "pathotypes," may cause severe symptoms. While the symptoms (such as Crohn's disease) caused by such *E. coli* strains may be linked with a

[7] Viruses and prions have no self-sustaining metabolism on their own and lack a certain degree of autonomy, and thus may not be considered "living" biological entities. Alternatively, they may be understood as "intracellular obligate parasites, with a strong emphasis on their *dependency* on a host" (Pradeu, Kostyrka, and Dupré 2016, 58).

"Entity," "host," and "environment" are the three interconnected parts of the epidemiological triad.

higher share of adherent *E. coli,* adhesion is still, even if to a lower degree, found in commensal controls (Rolhion and Darfeuille-Michaud 2007, 1277–1279).

Two things are thus noteworthy: First, the designation of an entity as an "infectious disease" may be used to distinguish disease-causing from commensal strains within a single species. Second, and more importantly, "infection" may already subsume a range of processes from adhesion to invasion and replication within a host's cells. However, whether an "infection" occurs may not only depend on the level of penetration but may already incorporate a take on whether a given activity is beneficial or detrimental, which echoes DeVito's claim. Colonization by *H. pylori* is usually detrimental and called infectious. Colonization by *E. coli* is usually benign and deemed not an infection. Still, we cannot settle what counts as a "disease" simply by limiting our view to invasive infection and dismissing colonization.

Additionally, even in cases of invasive infection, the occurrence of some beneficial effects may occur. Schwartz discusses, in reference to Boorse, the potentially beneficial effects of "an infection with cowpox [as] conferring resistance during a smallpox epidemic" (Schwartz 2007a, 52; Boorse 1977, 545). Another example may be how previous infections with influenza A (H1N1) may have conferred additional degrees of immunity to those again exposed in the 2009 influenza pandemic (Knipe and Howley 2013, 326; 1193). So, are even invasive infections not necessarily diseases, after all? Ought "infectious disease" rather to be applied to the peptic ulcer and not the mere presence of *H. pylori*? Is it Crohn's disease, and not the mere presence of a specific strain of *E. coli,* that ought to be assessed? I will have to postpone further discussion of these specific questions for now, as there is more clarificatory work needed.

2.2 Communicable Diseases

If we merely focus on caused symptoms, we may miss another element of infectious diseases: the difference between "infection" and "transmission." Granted, "infectious diseases" are often (but not always) "communicable diseases." But these terms pick out quite different dimensions. In contrast to the ability to (invasively) infect, which I have introduced above, calling a disease "communicable" is to specifically emphasize an infectious entity's relative ease of transmission from one susceptible host to another (Gieseke 2017, 8).[8] Each term, thus, puts the focus on quite distinct aspects. An "infectious disease" refers to an entity or a set of symptoms caused by (invasive) infection, while a "communicable disease" is an entity or set of symptoms that can arise in other hosts due to the causing entity being (readily) transmitted to these susceptible hosts.[9]

Communicability may even come in several degrees. While communicable entities, such as SARS-CoV-2 and HIV-1, share that they can be directly transmitted from human to human, the respective mechanism of transmission may vary significantly. While SARS-CoV-2 can be easily transmitted via droplets and aerosols (Tang et al. 2021), HIV-1 is primarily transmitted sexually, by blood transfusion, or between mother and infant (Knipe

[8] Note that "contagious disease" is a rather outdated term for "highly infectious" qua easily transmissible via direct person-to-person transmission, while "transmissible disease" refers to transmission not encountered in "natural" environments (Giseke 2017, 8).

[9] Both terms are often used somewhat interchangeably (even within epidemiology) because infectious entities a susceptible host gets infected with have at some point originated in another infected host and thus are *principally* communicable.

and Howley 2013, 1563). There may also be transmission from an animal species to humans,[10] leading to zoonotic events, which play a critical role in the emergence of many infectious diseases (Giseke 2017, 12).

Humans may also recurringly be involved in complex life cycles. We are intermediate hosts in the life cycle of hydatid disease, caused by *Echinococcus granulosus,* transmitted via tapeworms. Humans get infected by consuming water or food contaminated by feces of other mammals (Khanfar 2004, 174). Malaria, which is caused by protozoan parasite species of *Plasmodium,* is primarily transmitted to humans by *Anopheles* mosquito bites, which have previously fed on infected hosts (Tuteja 2007, 4671).

A vivid example of a disease caused by an entity that is readily infectious, but rather noncommunicable, is tetanus. It is deemed a "non-communicable disease caused by *Clostridium tetani,*" as the bacterium is ubiquitously found in soil and remains viable in sporulation, making it "highly resistant to heat and common disinfectants" (Finkelstein et al. 2016, 339; Gieseke 2017, 8). While direct human-to-human transmission does not play a significant role in human *C. tetani* infections, chances are the entities (or rather their ancestors) have been excreted by another infected host at some point. Unsurprisingly, given the physical resistance of *Clostridium* spores, such indirect potential transmission is still deemed a "challenge" in transfusion safety (Strömer et al. 2008).

In contrast, commensal strains of *E. coli* may fall on the other side of the divide. While mere or commensal colonization and occasional adhesion may not count as invasive infection, *E. coli* may still be readily communicated. As part of the gut microbiota, they may be transmissible among close social contacts. This transmission may be a risk factor of diseases widely deemed noninfectious and noncommunicable, such as obesity (Finlay and Fellows of CIFAR 2020, 250). This may be a case in which the occurrence of diseases traditionally thought of as noninfectious and noncommunicable may be influenced by noninfectious but communicable entities.

Several viruses have been "shown to be associated with the etiology of human cancer" (Knipe and Howley 2013, 14). While it often remains unclear whether these associations are causal, in some cases, such as for some "human papilloviruses [(HPV), there is] mechanistic understanding how these viruses transform cells" (2013, 1681). In this case, it may still be far-fetched to call the associated types of cancer infectious or even communicable diseases but the entities so labeled may still play a crucial role.

2.3 Transmission while Being Asymptomatic

The overlap but also conceptual distinction between "infectious disease" qua symptoms due to infection and "communicable disease" qua transmissible entity comes to the fore in the final clarification. There are instances in which a biological entity is transmitted to other hosts before (clinical) symptoms are displayed or perceived by the transmitting host. A prominent historical case is Mary Mallon (Typhoid Mary) who, in the early twentieth century, was identified as having spread typhus to others while being "widely recognized [as a] symptomless carrier" (Wakefield 2014, 663). A more recent, prominent example is SARS-CoV-2, which has been identified as being potentially transmitted before or even without

[10] The reverse is also possible but further discussion of this issue is beyond the remit of this article.

symptoms being displayed by carrying individuals (Rothe et al. 2020, 970; Qiu et al. 2021, 512; 517).

While the prominent term here is "asymptomatic," referring roughly to the absence of symptoms, there is often more to it. An infection may be "subclinical"—an infected host may show some reactions but they are so mild that they are not deemed clinically relevant and do not warrant medical attention (Gieseke 2017, 9). For hosts that show few, mild symptoms the term "pauci-symptomatic" may also be used. In "pre-symptomatic" infections a host may show symptoms only with significant delay after infection occurs (Oleckno 2008, 41). This period is also known as a "prodromal phase" (Kretzschmar and Wallinga 2010, 212).[11] But even after a host's recovery (from displaying symptoms), transmission can principally occur.[12] For example, infectious Ebola virus may still be found in some hosts during convalescence, such as in breast milk, semen, vaginal fluid, or tears. However, "sexual transmission from survivors seem rare and only anecdotally reported" (Vetter et al. 2016, S179–180). In contrast, in an asymptomatic infection, the host does not at any point show any clinically relevant or identifiable symptoms (Gieseke 2017, 9).

Let me state explicitly that noninfectious, noncommunicable diseases may also involve subclinical, asymptomatic, or significant pre- or post-symptomatic phases.[13] Whether these are or ought to count as "diseases" is not the focus of this paper. Critically important, however, is that for infectious, communicable diseases the (temporal) absence or mildness of symptoms may fall together with the occurrence of a "carrier state" (Gieseke 2017, 9), which occurs if an entity persists in a host for a considerable time. Two types are distinguished: carrier states due to colonization and carrier states due to invasive infection (2017, 10), reflecting the range of "infection" in a broader sense than mere colonization and adhesion to specifically invasive infection.[14]

Clearly distinguishing the above is critical for two reasons. First, even if clinically relevant symptoms are delayed, mild, or even absent, there may be other reactions. That an infection may remain asymptomatic may be due to an effective immune response against a specific infectious entity, which may be mild, even imperceptible, but nonetheless existent. But similarly, some hosts endure significant symptoms precisely because their immune system responds to an infection. I return to this below, as the role of the immune system can be crucial in debates of the concept of "disease."

Second, being asymptomatic may be especially relevant in the case of infectious, communicable diseases, as transmission of the infectious entity itself may occur. While symptoms of infections, such as sneezing, coughing, or scratching, are often associated with transmission, transmission merely piggybacks on such symptoms of infection but, crucially, may also rely on other mechanisms. Transmission may be facilitated, for example, by sneezing or coughing not caused by the entity itself. Transmission may also occur simply by breathing or shaking hands but this does not imply that the latter are symptoms of an infection. This is crucial for two reasons: symptoms caused by infection may facilitate transmission and thus are often associated with transmission events but may not

[11] This is the phase between the incubation phase, in which after initial exposure the entity persists and replicates, and the symptomatic phase, in which clinical symptoms are displayed.
[12] There may also be reoccurring symptoms, remission, or relapse. I do not discuss this here.
[13] Thanks to an anonymous reviewer for pointing this out.
[14] *Staphylococcus aureus,* for example, may colonize human beings without eliciting symptoms. It not only persists (for example, in the throat) but may also replicate and be transmitted by touch and through the air (Wertheim et al. 2005, 751; 755).

necessarily be present in all cases in which transmission occurs. Second, therefore, we may want to grasp transmission of an entity as a process distinct from other symptoms. We see why this is important once we acknowledge that something akin to transmission may also occur elsewhere. Imagine a person with severe depression. These symptoms may elicit depression in others.[15] Or pathological arsonists may elicit copycat effects. Note, however, that if there is no underlying communicable entity, *some* symptoms must be present for transmission-like effects to occur.[16] Granted, such symptoms need not be deemed clinically relevant, or correctly identified by the affected, but they must be apparent enough to be imitated, absorbed, or otherwise taken up by others.

It is here that some instances of infectious entity transmission differ—such as in the aforementioned case of Mary, who carried typhus-causing bacteria but showed neither clinically relevant symptoms nor seemingly any other perceivable symptoms whatsoever. But Mary did transmit the disease and others became symptomatically infected. If we consider Mary alone, she displayed no visible, clinical symptoms. But as the above epidemiological terminology may indicate, Mary's transmission may very well be relevant to our judgment of whether she has had a disease.

Asymptomatic HIV involving transmission to others may be a similar case, in which epidemiology may see a relevant case of "infectious disease." Quite different may be persons infected with HIV on antiretroviral treatment (ART), who may still carry "undetectable viral loads" (Knipe and Howley 2013, 1576). These loads may not suffice to be transmissible, as "viral load is the greatest risk factor for all modes of transmission [and] ART lowers viral load" (De Cock et al. 2009, 488). Here, epidemiologists may agree that transmission is addressed. But I am getting ahead of myself.

3. Boorse's Biostatistical Theory

I have clarified potential difficulties for the discussion of the concept "disease," if infectious diseases are to be captured, too. Let me, now, briefly introduce Boorse's influential BST to see how this naturalist account can handle counterexamples of infectious diseases. Since the BST has gone through some changes over the years since its inception (Boorse 1975), I use the most recent and, as Boorse calls it, "slightly corrected summary" (2014, 684):

1. The reference class is a natural class of organisms of uniform functional design; specifically, an age group of a sex of a species.
2. A normal function of a part or process within members of the reference class is a statistically typical contribution by it to their individual survival (or) reproduction.
3. Health in a member of the reference class is normal functional ability: the readiness of each internal part to perform all its normal functions on typical occasions with at least typical efficiency.
4. A disease (later, pathological condition) is a type of internal state which impairs health, i.e., reduces one or more functional abilities below typical efficiency. (Boorse 2014, 684; on the basis of Boorse 1977, 562)

[15] Thanks to an anonymous reviewer for pressing me to acknowledge potential processes akin to transmission in noninfectious cases.

[16] Cases of heredity may offer a case in which a noninfectious and otherwise noncommunicable entity is transmitted, such as an oncogene, which is associated with disease. I do not discuss this further here.

Let me note a few crucial things here. Boorse offers necessary and jointly sufficient criteria, and claims that these criteria involve no normative value judgments, are purely theoretical, and not guided by practical concerns (for example, of clinicians or pathologists). "Value-neutral" or "value-free" merely demands that his account does not introduce additional normative values, beyond the values that we find elsewhere in science; importantly in pathology, which the BST relies on (Boorse 1997, 56; 2014, 713).

The distinction between naturalist and normativist positions may be more complex than simple disagreement about whether evaluative components can be part of the conception of "disease." Alex Broadbent suggests that the disagreement runs along two independent dimensions—one concerning objectivity and one concerning normativity. The first discerns that the concepts pick out something objective; that is, not "determined by our *subjective* evaluation of a state" (Broadbent 2019, 609). The other, whether what is to fall under the concept of "disease" can be judged without referring to value assumptions, is a question of normativity. The BST is to provide a concept of "disease" that is indeed objective and normatively neutral, in that it does not require any incorporation of how we subjectively think about the states that affect us, and no value judgments are needed to decide whether a given case falls under the label "disease."

Between Boorse's earlier and later papers there is an important shift in which "disease" is replaced with "pathological condition." Boorse acknowledges that "disease" in a narrower sense is prominently not being applied to "injuries … static abnormalities … functional impairments … poisonings … environmental effects … and other phenomena" (Boorse 1997, 41). "Pathological condition" is a term used to pick out a broad notion of "disease," including the above. Boorse thus leaves the term "disease" behind, which is at times also applied more narrowly.

In this paper, however, I stick with the term "disease" in the broad sense. My reasons are twofold. First, my clarificatory remarks indicate that the epidemiological utilization of the term "disease" may also not always fall neatly into the narrow notion. The narrow notion's exclusion of poisoning, for example, could disregard cases in which infectious entities are involved, such as food poisoning. These are often associated with foodborne, infectious diseases. Second, the shift puts pathology, at least as Boorse claims to define "pathological condition," essentially in charge of the notion of "disease." This has been criticized by some authors, such as Wakefield, as overly restricting the scope to the purview of pathologists at the expense of clinicians. The BST thus hinges on the claim that pathological judgments are necessary and sufficient to describe "disease" in a broad sense, or "medical disorders" as Wakefield calls them (2014, 655). Following Wakefield, the BST's claim of the sufficiency of pathology is criticized below.

Let me briefly introduce some of Boorse's guiding ideas in setting up the BST. It aims to be a "medical concept of health" (Boorse 1997, 42). Still, "disease" is neither to be defined by medical practice nor does it suffice to call "disease" whatever is simply not desired. While health is "certainly desirable," not everything that is bad is a disease, nor is every disease necessarily bad. For example, being of a short body height may be more debilitating than a "minor allergy or viral infection" (1977, 545). Medical personnel regularly treat conditions that are not diseases. Thus, "disease" is not simply what medicine treats. Rather, it matters whether a condition is pathological or not (1977, 545). Note here that Boorse already presupposes the BST's framing of a "pathological condition" as a statistically abnormal dysfunction. Pathologists may be less restrictive and merely pose that "pathological" is an

abnormal deviation from expected structure and function. Statistics is not explicitly invoked there (Lakhani et al. 2016, 7; McConnell 2007, 5).

This is where the biostatistical addition of the theory is located: "In clinical language, diseases or pathological conditions are also called abnormal, and healthy conditions normal" (Boorse 1977, 546). But Boorse is also clear that mere "statistical normality fails as a necessary or sufficient condition of health" (1977, 546). Since rare hair colors or blood types may be healthy, statistical normality cannot alone be necessary. Since some infections are exceedingly common, even ubiquitous, it cannot alone be sufficient (1977, 546). Furthermore, "disease" cannot simply be what causes pain or discomfort either, as there is something pathological medicine is able to identify in "asymptomatic disease of many kinds—tuberculosis, diabetes … heart diseases, syphilis, and so on" (1977, 547).[17] Nor need any condition that is in some form disabling necessarily be a disease, since the inability to walk may be perfectly healthy for infants; our inability to fly without mechanical assistance perfectly healthy for all humans (1977, 547).

Here, we see that normal functioning is tied to certain "reference classes" (Boorse 1977, 556). These reference classes restrict the scope of normal function to a "*species design,* i.e., the typical hierarchy of interlocking functional systems that supports the life of organisms of that type" (1977, 557). Importantly, this is not to conflict with evolutionary variation. Given evolutionary timescales, species design is taken to remain relatively constant and "maintained by normalizing selection" (1977, 557).[18] However, there may be differences in species design even within a species—that is, between sex and age, and maybe even "race as well" (1977, 558).[19]

It does not suffice for a condition to directly inhibit survival or reproduction either. As Boorse states: "It is quite possible for diseases like cowpox or myopia to be advantageous in special environments. They do not thereby cease to be diseases, for the judgment that they are is a judgment about types of condition and mentions no particular environment" (1977, 549). Similarly, being exceedingly good at playing the violin may be beneficial to one's survival or reproduction but to lack such abilities would not count as pathological despite their absence potentially bearing on survival or reproduction (1977, 549).[20] Finally, the idea that a certain equilibrium state or a "homeostasis" must be maintained (1977, 550),[21] cannot be necessary, since many bodily processes do not maintain but rather upset previous states. Such changes, however, ultimately serve "individual survival and reproduction" (1977, 556).[22]

Thus, Boorse proposes normal functioning relative to a reference class (species, age, sex) as the yardstick for health; the failures of it as disease. Still, as seen, infectious diseases already feature prominently. Boorse even stated that "fatal or debilitating illnesses such as malaria, smallpox, cholera, tuberculosis, cancer and so on … [are] what one might call

[17] Note how asymptomatic diseases, both in terms of infectious and communicable and noninfectious and noncommunicable, are lumped together.
[18] Potential problems of this view of the evolutionary time frame have been offered (see, for example Cooper 2002, 269). I do not address this further here.
[19] While species, sex, and age feature prominently in later defenses, Boorse states that while race may need to be a factor in medicine, its relevance in setting reference classes is "disputable" (2014, 4; 22ff).
[20] Such positive effects are sometimes posed as "positive health." I am not concerned with this here.
[21] Some pathology textbooks such as *Basic Pathology: An Introduction to the Mechanisms of Disease* (Lakhani et al. 2016, 3) still rely on such definitions.
[22] Boorse later clarified that some reproductive functions may be detrimental to survival. Thus, the 2014 version states "survival *or* reproduction" (Boorse 2014, 4; emphasis added).

paradigm object of medical concern" (1977, 544).[23] So how does the BST fare, given that infectious diseases are also taken by critics to pose difficulties to the account?

4. Infectious Diseases as Potential (Counter)examples

I start with a potential problem for the BST already alluded to by Boorse: some infectious diseases may affect the majority of individuals (if not almost all) in a reference class. Such "universal diseases" (Boorse 1977, 566), but also "common diseases" (Schwartz 2007b, 375), could pose a threat to the BST, if merely their ubiquitous or prominent occurrence in a population is what saves them from being diseases.

4.1 Universal and Common Diseases

One example Boorse mentions is dental caries (Boorse 1977, 566), which affects the whole human population to a varying extent. This is interesting since one biological culprit (among other factors like sugary drinks and poor oral hygiene), the acid-tolerant *Streptococcus mutans,* has been identified. It is not only communicable but can also potentially cause more serious conditions. Besides the damage to the enamel of teeth due to produced acid, it may in some cases cause endocarditis, a rare but potentially serious inflammation of the tissue of the inner heart chamber. In addition, it is a shared characteristic of many *Streptococcus* variants to lie dormant in a carrier state once they have attached to suitable surfaces and are able to replicate. Then, other factors, such as the "acquisition of a virulent strain," an immune-suppressed state, or the absence of antibodies against the entity, can allow for the strains to invade and give rise to various detrimental health outcomes beyond tooth decay (Mitchell 2003, 219).

Initially, Boorse seems ready to accept that "medicine is prepared to view the entire reference class [that is, *Homo sapiens* of every sex and age] as functioning abnormally" (Boorse 1977, 566), adding specifically an additional clause to include "limitation on functional ability caused by environmental agents" to be a disease (1977, 567). Later on, however, Boorse offered to drop the clause (1997, 86), and subsequently abandoned it completely by commenting that "it may not be worth the criticism it evoked" (2014, 684). This additional criterion is identified by Schwartz as "meant to handle cases of universal diseases, where a virus or toxin becomes common" (Schwartz 2007b, 376).

The critical point for Schwartz is that Boorse's BST, given its frequentist core, struggles not only if everyone (or a majority) but even a significant portion of a given reference class incurs a decrease in function (Schwartz 2007b, 375). As age increases, below-normal functioning of the enamel of teeth may become common in reference classes. The problem is that, since Boorse's account relies on what counts as normal function within a reference class, some reduced functions may be so common as to count as normal (within some standard deviations) and would therefore not count as diseases. Thus, argues Schwartz, the normative dimension of "negative consequences" must be incorporated (2007b, 376).

Granted, Schwartz voices doubts about whether there really are diseases that are universal. There are, however, common ones (Schwartz 2007b, 375). I would point out that carrying *S. mutans* and being affected by tooth decay in some shape or form may be

[23] I doubt the inclusion of cancer in this list can be taken to imply that Boorse takes it to be caused by infectious, communicable diseases, as some cancers may potentially be.

universal in humans, not merely common. Second, and here I follow Schwartz, I am not convinced that even common diseases are truly a nonissue. Common diseases may not be as unique, rare, or easy to avoid as Boorse claims (Boorse 2014, 714).

Take, as another example, a common disease carrier state—the single-cellular eucaryotic parasite *Toxoplasma gondii,* which, once it has infected humans, stays there for life. Mostly without causing issues, it may reproduce and be potentially transmitted. However, it may also cause—if undiagnosed and untreated—congenital defects during pregnancy. Most surprisingly, a population-based representative seropositivity study in Germany found 55 per cent of participants to be seropositive, indicating previous infection. Estimates for individuals older than 60 in East Germany to be as high as 80 per cent (Wilking et al. 2016). Thus, the occurrence of this infectious entity is—at least in Germany and at the time of the study—a statistically "normal" phenomenon in some reference classes.

It is also crucial to remember the distinction between the presence of an infectious entity and the range of symptoms they may cause. Thanks to the successes of polio vaccination campaigns,[24] poliovirus exposures are, in most regions of the world, an extraordinary circumstance. But even when the entity Poliovirus (PV) was much more common in some regions, the symptoms of polio need not have been. While paralytic poliomyelitis is probably the symptom most associated with polio as a symptomatic infection with PV, it is not the most common—that would be "abortive poliomyelitis," a mild fever with possibly "gastrointestinal signs" occurring in merely "4% to 8% of individuals" (Knipe and Howley 2013, 510). Paralytic poliomyelitis is even more rare. Like Enterovirus infections generally, Poliovirus infections are mostly asymptomatic (2013, 508). Since in both the cases of toxoplasmosis and polio, disease qua substantial, clinical symptoms are rather rare, one could suggest that as a disease they are not universal or even common.

I want to extract two points here, for now. First, the BST does require—at least to account for common or universal symptoms—an additional clause like the one Boorse subsequently abandoned. As Schwartz points out, however, this may not alleviate issues for common diseases not involving an external, infectious entity. I cannot discuss this specific claim here. Second, such an additional clause would also not address cases in which the presence of the infectious entity itself is present. Since such carrier states may be common, I address them, especially in connection with transmission, further below.

4.2 Immune Responses to Infection

Common may not only be the presence of some infectious entities and severe symptoms but also immune responses. Where do our immune responses fall, given that they can detrimentally affect us (like a very high fever)? In question here is the role of our immune responses as species-typical functioning. Fittingly, Nordenfelt asks whether our immune response to entities infecting and destroying cells, and our immune system inducing inflammation and fever, producing antibodies against toxins and entities, are "species-typical contributions to the ultimate goals" of survival or reproduction (Nordenfelt 1995,

[24] The ongoing usage of live-attenuated oral poliovirus vaccines in low-income countries, despite safer alternatives, given their associated low but existent risk of "vaccine-derived poliovirus," infection, transmission, and "vaccine-associated paralytic poliomyelitis" is a critical issue (Martín 2006, 117).

30). Thus, a "typical disease can be seen, on the BST, as a species-typical reaction".[25] So, are our immune responses species-typical reactions? But what if these very reactions constitute detrimental effects?

Boorse first admits that "inflammation and fever are often called pathological in medical books" (2014, 712). But he then goes on to call this an error on the pathologists' part and due to a lack of distinction between "indicating disease" and "pathological." While an immune-system-induced fever is indicating disease, it is "normal" and thus "non-pathological." Boorse makes a good point here but I take both sides' claims to be somewhat misleading in glossing over vital details.

Our immune system, unless one is fully immunocompromised, is continuously active. It is the self/foreign distinction that keeps even the ubiquitous, beneficial *E. coli* strains and other gut and skin bacteria from invading us further; our immune system tolerates them as far as they usually get. Critically, infectious entities are ubiquitous in *all* environments.[26] But when combating foreign biological entities, our immune system may increasingly escalate defense mechanisms. The innate immune system's macrophages, for example, excrete cytokines, such as TNF–α (tumor necrosis factor), which elicits inflammation and blood clotting to decrease the entities' mobility (Murphy 2012, 108)—surely, a species-typical function supportive of survival or reproduction. The same factor may also, once it spreads throughout the body, cause sepsis and septic shock. Here, while species-typical, this reaction is dysfunctional in hampering survival or reproduction. Cytokines also elicit an increase in body temperature to inhibit the entities' reproduction, hence a fever. But excessive fever becomes increasingly lethal (Murphy 2012, 109; Knipe and Howley 2013, 197).

So, generally, immune responses are species-typical functioning, and have evolved because they are (within limits) conducive to survival or reproduction. Whether a given response is actually conducive to survival and reproduction cannot be deduced from this general statement. Our immune responses can also devolve into an "aberrant immune response directed both at [a] virus, and to self-cellular constituents, resulting in auto immune disease" (Knipe and Howley 2013, 215). Some inflammations and fevers may be pathological; some may not. Immune reactions may indicate an infection is ongoing but they need not always indicate disease.[27]

Boorse's and Schwartz's example of cowpox infections as conveying beneficial effects against smallpox (Boorse 1977, 545; Schwartz 2007a, 52) may provide a good illustration of the difficulty of generally calling one kind of immune response non-pathological. On the one hand, the "low-dose" infection and elicited immune response by a comparatively harmless live strain of cowpox virus did convey significant protection against smallpox, which may cause severe and life-threatening symptoms in humans. It was deliberate cowpox infections qua vaccination that brought about the only eradication of an infectious entity, which only has humans as hosts. On the other hand, the infection with cowpox does commonly cause "localized lesions" (Knipe and Howley 2013, 387; 2171).

[25] Kingma also touches upon the question of how to distinguish a "normal immune responses and a pathological or absent immune response to an infection" and whether in reference to "situation-specific functions" the BST can be salvaged (2010, 259; 247). I cannot discuss this approach in satisfying detail here.
[26] Sterilized lab environments may be one exception. But the great effort in keeping them that way may give you an idea how unstable such clean environments are.
[27] Some autoimmune reactions can arise without being indicative of an ongoing infection.

Suffering lesions from cowpox was dwarfed by the substantial risk of morbidity and mortality due to smallpox but we may have no trouble accepting cowpox lesions as "pathological," even if part of the immune response. Today, in the absence of smallpox, pathologists, clinicians, and epidemiologists could certainly call such symptomatic cowpox infection a disease.[28] While this is echoed by Boorse calling cowpox a disease, despite an infection with the entity potentially having advantages in some situations (1977, 549), it remains unclear how to distinguish the lesions as pathological, but the production of antibodies as non-pathological, given that antibodies can play a role in facilitating the progression of infections, too. For example, dengue fever may not only facilitate the production of antibodies but "instead of neutralizing the virus, the antibodies mediate the expansion of the host cell repertoire" (Knipe and Howley 2013, 88). Thus, we simply cannot do without referring to the detrimental and beneficial effects our immune responses may have.

How about DeVito's *H. pylori* and *E. coli* (DeVito 2000)? The mere colonization or adherence to gastric epithelial cells need not pose a theoretical problem to the BST as the toxins excreted by *H. pylori* and some *E. coli* pathotypes disrupt normal functioning or functional ability of the gastrointestinal tract. So, under the BST, such colonization may count as pathological, irrespective of the noninvasiveness of infection. I also take it as unproblematic that such noninvasive infections may fall in the broad notion of "disease" under poisoning.

More interesting may be how noninvasive, commensal *E. coli* strains are to be treated, given that they still elicit a constant immune reaction, which keeps them at bay. On the one hand, we could engage in a "trade-off" argument, as just suggested for cowpox. While commensal strains of *E. coli* may elicit minor pathologies, the associated benefit outweighs the harm they do. But neither could the BST rely on this argument, nor would it, as in the above case, change that even commensal *E. coli* colonization would remain a disease. Rather, we may solve the riddle by acknowledging that while commensal *E. coli* may cause some part-dysfunction, it is crucially part of a higher-level normal functioning of the defensive arsenal and digestive system of humans. As already mentioned, commensal *E. coli* inhibits the growth of other infectious bacteria by outcompeting them, and they support the digestive functions of the gut. Thus, we could argue that we can disregard lower-level pathologies if there is a higher-level normal functioning conducive to survival or reproduction. I take this to be echoed in Boorse's response to natural cell death as not pathological (2014, 706), which I discuss next.

Still, whenever the immune system is involved, it seems that this is exactly the range of functioning of the immune system in relation to survival and reproduction that poses difficulty. If we see an immune reaction, it is not always clear on which side of the divide of normal or abnormal, pathological or non-pathological it falls.[29] On the other hand, if we do not see our immune system working, we may be fine, as it is doing its job of fending off potential infectious entities without much hassle. But it may not be working properly if we are immunocompromised. Thus, it seems, Nordenfelt (1995) may have a valid point to

[28] Such adverse events associated with live-attenuated vaccines is one reason why they are increasingly phased out today.

[29] I want to note here that this may be a factor why some portions of the public may assume that desired immune responses due to vaccinations are indications of disease, while they are rather indications of it working effectively. Cases of rare, severe side effects of vaccination, however, may be accidental poisonings.

question whether the BST can make clear that "inflammation" and "fever" are—as claimed by Boorse—"non-pathological" and merely indicating disease. This also raises questions of whether the BST's reliance on the distinction between pathological and non-pathological is sufficient to capture all cases of disease, and solely throw out what is not; and further, whether the BST definition of "pathological condition" actually aligns with pathological theory and practice.

4.3 The Low Threshold of Pathological

Countering Boorse's claim of sufficiency, Nordenfelt (1995, 28) and later Wakefield (2014, 655), pose the "one-dead-cell argument." According to the BST, even the death of one, single cell is pathological, as it inhibits the statistically normal functioning of that one cell to contribute to survival or reproduction.[30] Boorse can respond—and I noted this above—that lower-level, below-normal function, or dysfunction, may serve higher-level normal functioning, and thus need not be called pathological. Pathology may be taken to reflect this, in differentiating between the "planned cell death [called] apoptosis" and "cell death caused by disease [called] necrosis" (McConnell 2007, 24) due to "sudden changes in the microenvironment abolishing cell function" (Lakhani et al. 2016, 58). One can, however, see that this distinction already depends on the identification of a disease, or is viewed as an effect of it.

But since cells vanish all the time, and this may not always be in service of higher-level functioning, there may be no non-diseased person, whatsoever. And, as Wakefield points out, Boorse is willing to accept this (2014, 656). This is interesting for infectious disease epidemiology, given the sheer variety of infectious entities, their ubiquitous collective prevalence, our constant exposure to them, our continuous immune responses, and our perpetually being colonized, adhered to, and infected. In this light, an infectious disease epidemiologist may have no issue concurring that epidemiologically no ideally healthy person or population exists.

But Wakefield goes on to say that while this move saves the BST from the rather obvious horn of the objection, it may thrust it into conflict with the foundation it is built on: pathology. Granted, pathologists may agree that one cell's death is pathological but merely as a "trivial piece of pathology" (Wakefield 2014, 657). Thus, without disagreeing that the death of one cell is principally pathological, a pathologist may disagree that it therefore constitutes a disease, if there is no further, clinically significant below-normal functioning.[31] Boorse (2014, 688) is rather clear that the BST is not "constructivist," so questions of significance or relevance have no place in it. So, the BST risks seeing disease where the science so heavily relied on may see none.

Interestingly, the above argument plays a critical role in Wakefield's counterexamples of asymptomatic Mary and asymptomatic HIV infections. It serves as motivation to argue for alternatives to the BST—for example, Wakefield's harmful dysfunction analysis (HDA), which specifically appeals to individual harms as a normative condition (Wakefield 2014, 663; 649; 677). But, as I argue in the next section, Wakefield may fall prey to a reverse kind

[30] Which as a part-functioning is covered by the BST.
[31] Instead, it seems pathologists would want to provide the underlying pathology, given that a person is presented (in a clinical setting) as being diseased.

of argument: in overly relying on clinical considerations, he restricts "disease" to what falls into the purview of clinical medicine; more specifically, to individual clinical considerations.

4.4 Asymptomatic Transmission

Before I can embark on the specific implications of asymptomatic transmission, let me first reconstruct Wakefield's introduction of Mary's case. Wakefield states that the initial infection is clearly recognized as a part-dysfunction by Boorse's naturalist BST. The lack of any symptoms displayed by Mary herself, however, seemingly raises a problem as "medicine standardly describes asymptomatic carriers as not diseased" (Wakefield 2014, 663). Thus, it seems, the BST goes too far in this case. Wakefield's references to medical journals, medical professionals, and to the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) support this assessment. But is the BST promiscuously picking out a part-dysfunction that is medically irrelevant?

If we only look at the initial infection that Mary must have suffered at some point in her life by at least one of the infectious entities that can cause typhus, it clearly involves some below-normal functioning. Bacteria invasively overcame anatomical barriers to reach the gall bladder before further infection had been halted. For the carrier state to be sustained, the entity must have replicated, and some cells may have been affected. For the BST it suffices to call the persistence of the bacteria in the gall bladder pathological. Thus, Boorse must call asymptomatic carriers "diseased," while pathologists and medical practitioners (as Wakefield claims), and Wakefield do not.

An epidemiologist initially may want to side with the BST. The infection is an epidemiologically relevant dysfunction. Not only was there a past failure of some anatomical barriers and failure of the immune response insofar as it has failed to stop the spread to an organ. There was also an ongoing failure of the immune system to remove the causing entities from a site where they do not normally belong. However, an epidemiologist may also easily agree that such an asymptomatic carrier is not diseased or disordered in a clinical sense, if we only consider Mary.

The term "disease" as utilized by many epidemiologists, however, may not only reflect a patient- or individual-centered view: "The objectives of infectious disease epidemiology include [, among other things,] assessing the extent of the disease in a given population in terms of transmission, new 'incident' cases, and existing cases" (Abubakar 2016, 2). The critical difference to medicine is that epidemiology takes a population view and not an individual patient view (Broadbent 2013, 1). This usage of "disease" by epidemiologists accepts that asymptomatic carriers themselves are not diseased or disordered in a individually clinical sense but still points to transmission being epidemiologically relevant.

This cannot be taken up by Wakefield and other normative accounts that restrict the normative criteria to exclusively apply to the individuals in question. Wakefield's added normative condition is specifically restricted in such a way that "the *lack of direct harm to carriers* from the internal dysfunction means that carriers may be judged to be nondisordered" (Wakefield 2014, 663; emphasis added). This is echoed by other normative accounts—for example, by Schwartz's "frequency and negative consequences account" (2007b, 376), in which it is specified that "the relevant negative consequences should be those that impact some standard activity or capacity *of the organism*" (2007b, 379; emphasis added). Rachel Cooper, who while not discussing asymptomatic carriers, states

that a "condition can *only* be a disease if it is a bad thing *for the potential patient*" (2002, 272; emphasis added). Note, however, picking up on another criterion in Cooper's account, an asymptomatic carrier that transmits may have reason to consider their transmission as "unlucky."[32] Then, epidemiology would provide such a reason, and Cooper's account would be going somewhat beyond an individual focus.

If an individual focus is retained, however, this poses a problem. Asymptomatic transmission specifically need not be an individual problem for the carrier, if any lower-level dysfunction does not feed into a higher-level dysfunction directly for them, as in the case of Mary. Still, Wakefield seems to accept that there is a dysfunction and problem: "Mary's dysfunction was in urgent need of treatment to prevent harm to others, so extensive efforts were made to cure Mary of her carrier status … Mary's condition was highly clinically relevant and demanded treatment" (Wakefield 2014, 666).

Initially, it seems simply a case of a problem that falls into the purview of medical practice but is not a medical condition.[33] So, is an asymptomatic carrier state merely treated by medical interventions but not as a medical problem? It is crucial here to emphasize again that medical efforts concerning Mary were not primarily aimed at the carrier state per se but at a carrier state that allowed for transmission to others. Had Mary not transmitted, the carrier state may not have been a problem. Treatment was indirectly aimed at what I would argue is a genuine medical condition generally—the symptomatic infections, morbidity, and mortality that some entities can bring about, and which Mary transmitted to others.

This is what the epidemiologist may pick up on as a pathological condition. There was an ongoing failure of Mary's immune system to remove a foreign entity from an organ and a failure to stop its dispersal to other hosts. While Mary's immune system may have been functioning just well enough to contain the bacteria, so that they did not spread further within her body and impede her, her immune system continuously failed to inhibit transmission. This is arguably a below-normal functioning that impacts survival or reproduction more generally.

By not only treating Mary to disrupt transmission but also recognizing it as a problem, albeit for others and not for Mary, the medical personnel at the time already recognized the relevance for public *health*. But this need not collide with the assessment that her individual health was not under direct threat. The above recognition of medical personnel of a condition that is not individual but one of public health is what distinguishes transmission from, say, cosmetic surgery. In both cases, medical interventions are utilized but only in the case of transmission do even medical experts agree that there is a health-related problem in the patient. This was also the case for Mary, as Wakefield shows. It did not, however, fall into the purview of individualized clinical medicine, as carriage and transmission did not impact Mary directly. But it did directly impact the health of others, and thus did fall into the purview of a science that also utilizes the term "disease": epidemiology.

Interestingly, if one rereads the second condition of the BST, it also explicitly connects function to *individual* survival or reproduction and (part-)dysfunction to their disruption

[32] Thanks to an anonymous reviewer who pointed this out. Cooper is, however, clear that all conditions (a bad thing to have for the individual, an unlucky occurrence, and principally be medically treatable) must be met for something to be a disease (2002, 271).

[33] Wakefield identifies other such conditions to be treated in "'derived' professional tasks," which are delegated to medical professionals, given their "unique technical skills"—for example, "contraception, relief of normal pain, and cosmetic surgery" (2014, 678, note 3). I do not discuss these examples here further, except to say that cosmetic surgery needs to be distinguished from reconstructive or grafting surgery.

(Boorse 2014, 684). So, must the BST also dismiss transmission as non-pathological, since in asymptomatic transmission individual survival or reproduction are not detrimentally affected? Note the specific wording here: "A normal function of a part or process within members of the reference class is a statistically typical contribution by it to their individual survival [or] reproduction" (2014, 684). Transmission clearly does *neither typically contribute* to an individual's survival and reproduction, nor is it even a normal function of part or process of humans in this sense. Responses of the immune system, on the other hand, do contribute, and transmission crucially hinges on the failure of this species-typical normal functioning of self/foreign distinction. While it did not impact Mary in this case directly, her immune system did perform below-normal functioning in comparison to the appropriate reference class.

What becomes clear here, however, is that some (part-)dysfunctions may not disrupt *individual* survival or reproduction directly but that of others. Thus, Boorse's BST may have, in all its overzealous reliance on pathology even of minute parts, uncovered a pathology that is not clinically (qua individual-afflicting) but epidemiologically (qua other-afflicting) medical.

4.5 Asymptomatic HIV and Antiretroviral Treatment

Let us now look briefly at those with asymptomatic HIV and those infected with HIV on ART to check whether the above analysis holds here, too. In the case of HIV-positive but asymptomatic persons, Wakefield again points to the BST identifying a part-dysfunction and thus HIV as "a disease irrespective of manifest symptoms" (2014, 667). He goes on to again disagree, given that asymptomatic cases of HIV are "explicitly excluded from the 'infectious disease' list", and rather are classified in group Z of "non-disordered conditions."

In the ICD-10, this group, however, specifically includes "persons with potential health hazards related to communicable *disease*" (WHO 2019, Z20–Z29; emphasis added), and in ICD-11, under "risk factors associated with infectious or certain other conditions" and "carrier of infectious *disease* agent" (WHO 2023, 24; QC90; QD0Y; QD0Z; emphasis added).[34] Referring to this, Wakefield merely reiterates the insight that carrier states, and specifically asymptomatic ones, are often encountered in the medical sphere, and thus need to be classified somewhere. But the fact that they are classified with other entries under "reasons for contact with health services" (WHO 2019, XXI; 2023, 24) tells us that while encountered by medical practice, they are not an *individually* medical disorders from a clinical perspective. And again, epidemiologists may have no trouble agreeing. But there is part-pathology involved, which the BST does identify, and for an epidemiologist picks out an infectious, communicable disease's epidemiological effect, if transmission does occur.

So, should we stick with the BST? If an asymptomatic carrier does not transmit, the BST may still identify part-pathologies. The BST therefore must still declare it a "pathological condition" or "disease" in a broader sense. But it does not pick out a condition that is *individually* clinical. Again, an epidemiologist need not deny this. Furthermore, if there is also no transmission, there is no pathology that is epidemiologically relevant. Thus, there is no need to invoke an epidemiological take on "disease."

[34] Granted, the latter refers to risk factors and entities. But that the term "disease" shows up here at all may be taken as an indicator that epidemiology is accepted as utilizing the term.

People with HIV on effective ART may exemplify a similar case, in which the BST points to an ongoing pathology but both individualistic, normativist approaches comparatively dismiss these low-level pathologies. Epidemiology also does not have any other affecting pathology to point to. As said, HIV-positive persons on ART may still carry some viral loads. According to the BST, they arguably suffer a lower-level dysfunctions, such as some cells dying due to rare replication. Given that ART may lower the individual's immune response generally (Knipe and Howley 2013, 1577), the lower-level part-dysfunction of reproduction may even translate into a higher-level, below-normal functioning of a reduced immune response.

Initially, individualistic normativist positions may be taken to argue that HIV-positive persons on ART are afflicted with a harmful dysfunction, a negative consequence, or are even considered being afflicted with a "bad thing to have," as they must submit themselves to treatment and its effects. But compared to the possible individual symptoms that could occur otherwise, the side effects of ART may not be a harmful dysfunction, negative consequence, or a bad thing to have.[35] Here, the epidemiological view may agree, even if sporadic replication or cell death occurs. As long as there is no transmission, the remaining pathologies may not be epidemiologically relevant, and the epidemiologist is happy to agree that this person is as healthy as an HIV-positive person can be. However, there is a chance that this treatment may also fail (Knipe and Howley 2013, 1577), and this is again epidemiologically relevant. So, an epidemiologist may be ready to say that an HIV-positive person is affected by a "disease" if transmission reappears, not waiting for an individual medical condition, as viewed from a clinical perspective, to reappear first.

In summary, as much as the push of normativism to include additional criteria helps us to cast "disease" in the purview of the individually clinical, the insufficiency of the minute pathological may also open the door for other, scientifically productive criteria. This, however, does not mean that we now must accept any other-affecting conditions as "diseases" either. A variety of states, such as poverty, sexual inclinations, war, and so on need not be diseases or cause disease, only because we accept that epidemiology identifies a specific other-affecting condition (tied to entity transmission) that may occur without being an individual-afflicting medical condition as appropriately being called "disease."

5. A Potential Objection and an Outlook

I briefly want to address a critique that could be leveled against the above.[36] Infectious disease epidemiology is a science engaged in identifying risk factors of disease occurrence (Krämer, Akmatov and Kretzschmar 2010, 87), and is not to be engaged in conceptualizing disease. After all, "being at risk" of infection or "bearing a risk factor" of being susceptible to infection does not equal "disease." So, when epidemiologists talk about infectious, communicable *diseases,* both qua entities and conditions, are they encroaching on the

[35] It may be debatable how an HIV-positive person on ART would be captured by Cooper's account. Given the criteria (Cooper 2002, 272), an HIV-infected person may consider carrying even a single HI-viral entity a bad thing to have. But they may also find it not a bad thing to have, given the alternative of developing AIDS. The person could consider themselves "unlucky" to be HIV-positive but rather lucky to be on ART. And while HIV-positive persons on ART would ideally be medically treatable to full sterilizing immunity, ART is also already a treatment for HIV.

[36] Thanks to an anonymous reviewer for pressing me on this point.

purview of pathology and clinical medicine, and should they rather stick with studying and designating risk factors?

Let us examine how "risk factors" figure in debates of the concept of disease, as epidemiology clearly utilizes the concept of risk factors to study determinants of health and disease. Some authors have already introduced an epidemiological take on risk factors into the debate on the concept of "disease" (Schwartz 2008, 321; Giroux 2009, 52; Boorse 2023, 2; 17). However, they focus on noninfectious conditions like hypertension and high cholesterol, while infectious, communicable diseases rarely appear in these analyses.[37]

Boorse, however, does echo the above critique by objecting to "risk factors masquerading as disease" (2023, 17). Élodie Giroux and Schwartz, on the other hand, argue that many risk factors identified by epidemiology should be considered diseases. For Giroux (2009, 58), the incorporation of reference class by the BST is already a concession to a population view, and epidemiology may even be better situated to take this up as an empirically substantiated scientific field. For Schwartz (2008, 332), the importance of reducing risk, both by means of medical and nonmedical interventions, should prompt us to call resulting conditions "diseases."

I want to concur with Giroux and Schwartz, and add how a population view helps us identify carriage and transmission of infectious entities not merely as a risk factor for others but as a concrete dysfunction of individuals that is epidemiologically relevant. To view transmitting asymptomatic carriers as having a condition that is—at the very least—not entirely healthy, we need not equate "risk" or "risk factor" with disease, even if risk does play a role. Rather, while not suffering from an individual medical condition (in terms of clinical symptoms), persons transmitting asymptomatically are displaying transmission as an "other-affecting" condition. In its effects it may even ought to be called its own "symptom" that medicine, including clinical medicine and pathology, should and do care about.

But, crucially, Mary's condition did not only pose a risk of disease to others; her condition was a concrete cause for cases of typhus around her, as she spread the entity. Mary was not merely at risk, herself, but *did carry and disperse* typhus. There was a continuous failure of her immune system to contain an infection and prevent transmission. Only as an "other-affecting" symptom did this pose a risk (of infection) to others. Epidemiology is ready to also call such transmitting carrier states "disease."

So, what might all this mean for the debates on the concept "disease" overall? First, I want to reiterate how critical it is that if infectious diseases are to be included in these debates, we need to get the concepts of infectious disease epidemiology right.[38] Second, I take the BST's prominence in the debate to be not accidental, as it plays the role of a fruitful theoretical foundation to start the debate. It is, however, insufficient in its reliance on statistical frequency, and selective in its view of what pathology is to designate as pathological. The normative positions looked at here offer suitable constraints to capture swathes of other noninfectious cases not looked at here but restrict "disease" to merely individual-affecting conditions. I have argued that infectious epidemiology is, among other things, concerned with the transmission of infectious entities, an effect that risks falling

[37] Boorse does point to *Vibrio cholerae* to make clear that detecting antibodies against it is a "risk marker" and not a "risk factor for having cholera" (2023, 13).
[38] In the case of infectious disease epidemiology, this includes all the fields it relies on, including virology, bacteriology, mycology, microbiology, and immunology.

under the table in such individual-focused normative approaches. Cooper's account (2002) may be read as to allow for effects on others to be a reason to count as "unlucky." However, I think this would require considerable reinterpretation of Cooper's account.

Nonetheless, I am rather confident that if one were to offer an alternative normative account aimed at including transmission as other-affecting at all costs and to pose it as a replacement of either the BST or one of the normative accounts, it would fail in some way or another to account for arguably clear cases of (noninfectious, noncommunicable) disease, or include putative non-diseases. Thus, I will not attempt it.

But I think this also indicates that neither monist definitions (Van der Linden and Schermer 2022, 132) nor eliminativist approaches will do. Rather, I want to take the above insights on transmission—in particular—to be one aspect that a pluralistic (or unified) account may be able to take up. I think Kukla's 2022 paper is on point: we may "wish to identify productive, unified objects of scientific study," "be interested in identifying productive, unified targets of treatment," and "want to know how a condition or set of symptoms spreads and is distributed" (Kukla 2022, 133). The terms "infectious *disease*" and "communicable *disease*" may do just that.

Carrying and spreading an infectious, communicable disease may be a case of disease if the entity transmitted causes significant medical conditions in other people, irrespective of some carriers being asymptomatic. It is also, given the other-affecting nature of transmission, a normative and social task to evaluate the significance of transmission that informs our designation of a disease. SARS-CoV-2 has shown how this may connect to a myriad additional evaluations: from matters of justice—for example, when it comes to contact tracing along carriage and transmission (Klenk and Duijf 2021)—to whether mitigation strategies could be epistemically justified—for example, when it comes to justifying lockdowns (see Winsberg, Brennan, and Surprenant 2020 versus Van Basshuysen and White 2021, to name only two). Alas, this paper is merely a start.

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