

# Proximal and Distal Causes in Medicine

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**1 Introduction.** In modern medicine, it is common to find claims that diseases are multicausal. According to these views, diseases are produced by many interacting causes as opposed to single, main causal factors. While earlier disease frameworks accommodated monocausal diseases—such as germ theory (tuberculosis), vitamin deficiencies (scurvy), and genetic conditions (Tay sachs)—modern perspectives view such frameworks as a limited oversimplification (Kendler 2019; Ross 2018b). Motivation for these multicausal views comes in part from a growing appreciation for social causes, and efforts to capture how social and biological causes interact to produce disease outcomes. Social causes include stressful life events, socioeconomic status, and social structures (such as material resources, education, public policies, and so on). Biological causes, on the other hand, include genetic, immunologic, hormonal, and other factors. While biomedicine overemphasizes the role of biological causes, public health and epidemiology fare better in appreciating social factors that influence health and disease (Engel 1980; Braveman and Gottlieb 2014). Attention to social factors has increased across each of these perspectives, but challenges remain for understanding their influence, importance, and interaction with other causes. In particular, it has proven difficult to clarify how macro-scale social factors “get under the skin” to cause disease and how they integrate with lower-level biological mechanisms in producing these outcomes (Caspi and Moffitt 2006; Gehlert et al. 2008).

One conceptual framework that has emerged to address these challenges, is the proximal-distal model of disease causation (Graham 2004; WHO 2010; Gehlert et al. 2008; Krieger 2011). This model is commonly found in public health and epidemiology contexts, particularly in discussions of the role of social causes—often called “social determinants of health”—on human health and disease. This model organizes causes into linear chains, in which upstream (distal) social factors influence downstream (proximal) biological factors, which directly cause disease. This model provides an account of how social and biological causes interact, it specifies the role that social causes play on health outcomes, and it captures how social causes may be prioritized in serving as the “root” causes that initiate a sequence of domino effects.

While the proximal-distal framework is common in these fields, it is not without drawbacks. In influential work, Krieger criticizes this “problematic” framework for failing to capture the complexities of disease and health causation (Krieger 2008). She claims that this model fails to capture the causal impact of social factors on disease and health, that “proximal-distal” language confuses multifactorial thinking, and that work in this area conflates notions of causal “space,” “time,” and, “strength” (Krieger 2008). Due to these issues, she recommends that we “abandon the deeply confused language of the terms proximal and distal” by omitting them from medical discussions (Krieger 2008). This is not the first time that causal language has come under fire. Her suggestion resembles Russell’s famous call for the “complete extrusion” of the word “cause” from our language as he said it was used in incompatible, confused, and misleading ways (Russell 1912). Even closer to home, consider the strict guidelines for publishing in the *Journal of the American Medical Association* (JAMA) which advises that “causal language (including use of terms such as effect and

efficacy) should be used only for randomized clinical trials” (JAMA 2023). When other methods are used, the results “should be described in terms of association or correlation and should avoid cause-and-effect wording” (JAMA 2023). According to Krieger, after omitting these causal terms, she recommends that we shift to the language of “levels, pathways, and power,” which she claims offer a solution to the noted issues (Krieger 2008).

This paper provides an analysis of the proximal-distal model, which is motivated by Krieger’s (2008) insights. We agree with many of Krieger’s criticisms, but we examine different weaknesses of this model and argue that it has important strengths. In the first part of this work, we clarify key features and assumptions of the proximal-distal model. These include the model’s emphasis on the position of causes along linear pathways and the assumption that proximal causes are often more explanatory, causally relevant, and “interveneable” than distal ones. After clarifying these aspects of the model, we argue that the proximal-distal model well-captures some causal scenarios, but that it does not apply universally. We examine three causal scenarios to show how social and biological causes interrelate in many different ways, which are only partly captured by this model. In particular, we show how social factors can play three types of causal roles: they can be *distal* causes, *parallel* causes, and *proximal* causes. We clarify these three causal scenarios, their implications for the explanatory status of social causes, and how they relate to the traditional proximal-distal framework.

This work shows that social factors can play various causal roles in producing disease and that different justifications exist for privileging them in explanations. Instead of following Krieger’s suggestion of eliminating “proximal” and “distal” causal terminology, we argue that accurate use of these terms is not only possible, but that it is instrumental in capturing the diverse ways that social causes influence health and disease. Instead of omitting causal language (and reference to proximal and distal causes) we call for more clarity and precision in the communication of causality and important causal distinctions in medical science.

**2 The proximal-distal model: What is it?** Medical communities use a rich, colorful, and varied causal terminology to capture the causal nature of human disease. Hippocratic medicine distinguished environmental causes from constitutional causes, eighteenth and nineteenth century medicine separated predisposing from exciting causes, and many communities have appealed to remote versus proximate causes of disease (Kendler 2020; Ross and Woodward 2016; Ross 2018b). A large number of other causal distinctions exist in modern medicine—these include causal mechanisms, pathways, and cascades producing disease, the genetic drivers of a phenotype versus mere passenger genes, multicausal disease models in contrast to monocausal frameworks, and various causal topologies (bowtie, feedforward loop, feedback loop, and so on) in network models of systems medicine (Haber and Settleman 2007; Ross 2021, 2020, 2018a). Additionally, an interest in proximal and distal causes is found in many other fields. This is evident in evolutionary biology with Mayr’s ultimate-proximate cause distinction (Mayr 1961) and in legal settings, which place importance on the “proximate causes” of outcomes (Hart and Honore 1985).

The proximal-distal model of disease in the twenty-first century is a conceptual framework originating in public health and epidemiology. A main goal of this model is to capture the impact of social causes on human health and disease (Graham 2004; WHO 2010; Gehlert et al. 2008; Krieger 2011). Social causes are macro-level factors that are part of an individual’s environment and, in some cases, the social structures around them. Material resources are a type of social factor that influences health outcomes—for example, limited access to clean water and “healthy” foods

influence rates of infectious disease, diabetes, and obesity. Stressful life events are another social factor that impacts health—these are environmental-stresses that can influence major depression, generalized anxiety, and substance use disorders (Kendler et al. 2003, 1995, 2012, 2011). As noted above, the influence of these factors on the health of individuals had led many to refer to them as “social determinants of health” (Braveman and Gottlieb 2014; Marmot and Bell 2019).

While evidence suggests that these social and environmental factors causally contribute to health outcomes, various puzzles have been raised for these claims. One main challenge is that it is not clear how higher-scale, macro-social factors causally impact disease phenotypes at the lower-scales of biology and neuroscience. Caspi and Moffitt refer to this as the “biggest mystery of human psychopathology,” namely “how does an environmental factor, external to the person, get inside the nervous system and alter its elements to generate the symptoms of a disordered mind?” (Caspi and Moffitt 2006). This worry is driven by expectations that causation involves physically connected “mechanisms,” which are not always obvious from the social to the biological (Ross 2018b). These debates are further complicated by the fact that social structure is often viewed as a vague and mysterious factor, with explanatory influence that is unclear (Little 1991).

The proximal-distal model aims to address these issues by providing a conceptual framework for disease causation. This model relies on a linear causal chain or pathway to represent the causal order of factors that lead to disease, as shown in Figure 1 (WHO 2010; Krieger 2008). In this model, social factors are located in the distal or upstream position of the causal pathway, while biological factors are downstream, proximal causes of disease. In this manner, social factors represent the “root causes,” “starting points,” and “beginnings” of disease outcomes (WHO 2010; Graham 2004). The causal impact of these factors is “mediated through” biological mechanisms, which are the “direct,” “proximal” causes of disease. Consider a description of this from the World Health Organization (WHO):

The social determinants of health inequities are causally antecedent to...intermediary determinants, which are linked, on the other side, to a set of individual-level influences, including health-related behaviors and physiological factors...At the most proximal point in the models, genetic and biological processes are emphasized, mediating the health effects of social determinants. (WHO 2010)

As this description and others suggest (see Table 1. (NIH 2020; NIM 2021; Graham 2004; Gehlert et al. 2008)), the causal order inherent to this model implies that upstream causes regulate downstream causes, which lead to disease.<sup>1</sup>

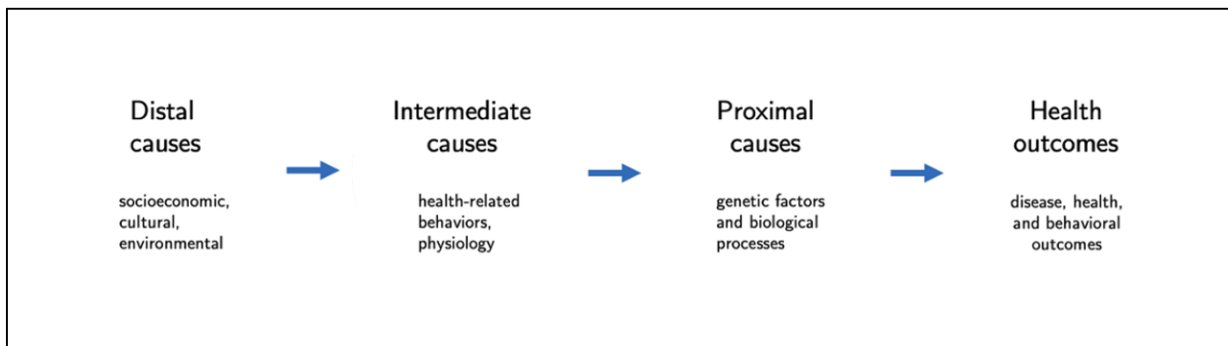
This model supports various assumptions that are important to highlight. First, it presupposes that disease causation is well-understood with a linear “pathway” model of sequentially ordered causes. Second, it maintains that social factors are always distal in this sequence and that biological factors are always proximal. This is used to suggest that upstream social factors causally determine downstream outcomes.

Third, this model is used to justify various claims regarding the priority of social and biological causes. Interestingly, while this model was developed to highlight the “causal priority” of social factors, it can “unwittingly reinforce” a preference for biological causes (Link and Phelan 1995). This is seen in claims that proximal causes are more causally relevant, explanatorily powerful,

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<sup>1</sup>However, as noted below in point three, it also suggests that proximal causes can be targeted to potentially stop the influence of distal causal factors.

Figure 1: Proximal-distal model of disease causation and health outcomes. Causal factors relevant to a final health outcome are organized along a causal pathway. This framework represents the causal location of various factors—in terms of a more distal (upstream) and more proximal (downstream) position—with respect to the final outcome of interest.



and “intervenable” for control. For example, it is claimed that as we move further upstream our inferences are “less secure” and our interventions are “less efficient” and “less effective” (Rothman et al. 1998). Furthermore, this model can seem to imply that, if biological factors are a funnel through which all other upstream causes operate, then biological interventions alone could control and explain whatever health outcome follows.

**3 Krieger on the proximal-distal divide.** Krieger’s analysis of the proximal-distal model highlights some of the already mentioned points, but also provides more historical context. She examines early uses of “proximal” and “distal” in medicine, which often referred to spatial distance in anatomical contexts. When considering the location of anatomical structures—such as the bones, blood vessels, or nerves in the forearm—those structures closer to the center of the body are more proximal (the elbow), while those that are further are more distal (the wrist). In this usage, the center of the body is a point of reference that helps capture differences in spatial location. This language was extended to temporal dimensions in various sciences, such as geology, in which it captured the position of events along a timeline (closer or further to some point of interest).

According to Krieger, the link between causation and these proximal-distal concepts was formed when views in physics (such as the inverse-square law) suggested that closer proximity implies increased causal power. She suggests that the assumption that “‘proximal’ causes remain most potent” continues to this day and is present across the life and physical sciences (Krieger 2008, 223). We see this in cases where biological causes are emphasized over social causes, when bodily causes are privileged over remote environmental causes, and in cases where local physiological causes are prioritized over distant evolutionary causes.

Krieger rightly notes two issues with the above developments, which are that (i) causal order is not the same as spatial or temporal order, and that (ii) proximal causes are not always more powerful, explanatory, or potent than distal causes. With respect to the second, very spatially distant causes can provide powerful explanations, while creeping further along a causal chain to some effect does not always identify stronger or more explanatorily relevant causes. For example,

Figure 2: Selected quotations relevant to the proximal-distal framework

Author, Year	Relevant Text
World Health Organization (WHO)	The structural determinants operate through a series of what we will term intermediary social factors or social determinants of health. The social determinants of health inequities are causally antecedent to these intermediary determinants, which are linked, on the other side, to a set of individual-level influences, including health-related behaviors and physiological factors...At the most proximal point in the models, genetic and biological processes are emphasized, mediated the health effects of social determinants. The main categories of intermediary determinants of health are: material circumstances; psychosocial circumstances; behavioral and/or biological factors; and the health system itself as a social determinant (p. 36-37)
Graham, H.	The most distal factor is the social structure of society, variously labeled general socioeconomic, cultural, and environmental conditions, social structure, social context, and social, economic, and cultural characteristics of a society...Radiating out from this societal level, the models contain a set of intermediate social factors: social position and its attendant working and living conditions, and the social networks of family and community. The intermediate social factors are ranged above a set of individual-level influences, including health-related behaviors and physiological factors. At the most proximal point in the models, genetic and biological processes are emphasized, mediating the health effects of social determinants (p. 106)
Gehlert, S. et al.	In these frameworks, upstream determinants are defined as features of the social environment, such as socioeconomic status and discrimination, that influence individual behavior, disease, and health status. Viewing health disparities through a lens that incorporates social/environmental conditions as upstream factors in multilevel models better allows us to design and implement interventions targeted at levels downstream from those conditions (p. 340)
National Institute of Mental Health (NIMH)	What the NIMH lists as social determinants of health `` social determinants of health (e.g., education, economic stability, quality of housing, access to health care, experience of discrimination)...Of particular priority is research that identifies mechanisms contributing to the persistence of mental health disparities
National Institutes of Health (NIH)	The set of factors that impact health beyond individual-level characteristics are often referred to as “upstream factors” or more commonly, social determinants of health. Social determinants of health (SDOH) are sometimes loosely defined as the conditions in the places where people live, learn, work, and play that can affect a wide range of health risks and outcomes. Some examples include access to healthy foods, access to quality health care, reliable transportation, stable housing, and economic stability. Societal or macro-level influences, including structural racism, discrimination, and certain policies can result in inequities observed in these determinants

remote decisions in Washington can be a main explanatory and causal factor for far reaching effects in the country (such as access to healthcare). Additionally, when biological causes such as genes explain disease outcomes, we do not view more proximal causal intermediates (such as damaged proteins) as more potent causes. And concerning the first point, when temporal or spatial order is confused with causal order—that is to say how causal factors and their influence is organized in relation to each other—it seems important to point out this confusion and the different meanings these orderings involve.

These issues with the proximal-distal model lead Krieger to suggest abandoning the language of proximal and distal causation, while replacing these with concepts of levels, pathways, and power. If these terms are to help, this will need to be supported and established in future work, as Krieger does not discuss this replacement process in detail. There are clear formulations of the “pathway” concept, which clarify its meaning, and we rely on this concept in our following analysis (Ross

2021). However, one complication with her suggestion is that many view the notion of “levels” in science as highly ambiguous and imprecise, much more so than the notions of proximal and distal causation (Potochnik 2021). Until “levels” and “power” receive a clear treatment that can advance these discussions, whether they provide clarity in these contexts remains an open question.

What we focus on, instead, are ways of understanding, clarifying, and specifying a principled use of the proximal-distal model. While this model may mistakenly emphasize biological causes in some situations, it is often used to capture the importance of social causes and their explanatory priority over biological causes. This is a main goal of many analyses of social determinants of health. Explicit reference to these distal factors as “root causes” and “the causes of the causes” is intended to capture their critical causal influence. Insofar as these frameworks may capture important principles that follow from causal order and can be used to assess causal relevance, we suggest that it is worth examining their claims and reasoning. Even if proximal and distal causal relationships are confused in the literature, they may still represent a distinction that is principled, ripe for clarification, and important in capturing important explanatory distinctions.<sup>2</sup>

**4 Locating the causes of health and disease.** We provide an analysis that clarifies the notions of proximal and distal causation, primarily their use in medical contexts. We examine three scenarios that clarify distinct ways that social and biological causes relate to each other, in leading to a health outcome of interest. These cases aim to clarify the notions of proximal and distal causes, including assessments of when and why such causes differ in explanatory power.

**4.1 Disease distribution: Social as a distal cause.** We describe a first causal scenario to show that, in some cases, it is perfectly reasonable to view social causes as distal to biological ones, as suggested by the proximal-distal model. However, in these cases other assumptions commonly associated with this model do not always hold.

A main explanatory target in public health and epidemiology is disease distribution in populations (Krieger 2011). In some cases, infectious diseases—such as cholera and Covid-19—are more common in lower socioeconomic groups compared to higher ones (Patel et al. 2020). In these situations, social factors (such as access to clean water, safe employment, etc.) are upstream as they control exposure to downstream biological contagions that produce disease. The difference in exposure explains the population-wide disease pattern, as social factors “shape distribution of main risk factors” (Marmot and Bell 2019). A central concept in these examples are causal pathways or “pathways of action” that connect upstream, social factors to downstream, biological intermediates. In these situations, social factors are considered the “causes of the causes” as they causally influence biological factors that are the proximal causes of disease (Marmot and Bell 2019).

Biological factors are, of course, “part” of these explanations—they are intermediates along the causal pathway from exposure to disease. However, for this explanatory target, social factors are more explanatory because they can account for much of the population-wide disease distribution, which is lost at the lower-levels of biology. For this reason, these outcomes are referred to as “socially structured patterns of disease” (Metzl and Hansen 2014).

This causal scenario reveals several important points. First, social causes can be distal to biological causes, consistent with the proximal-distal model. Notice that, while these social factors

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<sup>2</sup>In fact, if confusions exist in the literature, you might think that setting the record straight and clarifying language is fruitful (while outlawing language is less realistic).

are distal to some biological causes (contagion-triggered immune reaction, cellular damage, etc.), they are not distal to others such as genetic profile, which have the potential to moderate disease susceptibility. This indicates that, while some biological causes are intermediates along socially triggered pathways to disease, these intermediates are not always genetic, as suggested by standard representations of the proximal-distal model. We consider this situation further in the next subsection.

A second lesson from this example, is that the elevated status of proximal causes within the proximal-distal framework is not always justified. In contrast with the assumptions of this framework, distal causes are sometimes better targets for explanation, causal relevance, and control. We see this in the ability of social causes to explain disease distribution and in the fact that they can provide better targets for intervention. Policies that change social conditions can be more effective than genetic, cellular-level, and individual treatments. For example, in efforts to reduce alcoholism, higher-level policies (such as restrictions on marketing, availability, and screenings for drunk drivers) remain more effective than individual treatments (Babor et al. 2010). Social factors can also be easier to intervene on for technological and practical reasons—in some cases interventions on genetic and cellular causes are not available, while interventions on social causes are. Additionally, social causes can involve a single main point of intervention, in contrast to targeting the multitude of biological factors they initiate. Public policies that target smoking cessation are fewer in number than interventions fine-tuned to the distinct carcinogens, various mutagenic effects, and heterogeneous cellular pathologies leading to lung cancer. This is not to say that social interventions are not without challenges or that they are always better. The suggestion is that social factors are sometimes better locations for control despite being upstream, distal causes to their effects. Finally, if they address social needs like access to clean water and safe working conditions, they result in many positive effects.

The proximal-distal model well-represents these causal scenarios, but this requires appreciating the unique explanatory target in these cases—namely, disease distribution. The medical sciences contain various types of explanatory targets, while different targets pick out different factors as more or less causally relevant. Insofar, as disease distribution is a central explanatory target for public health and epidemiology, much would be lost in discarding this model and the language of proximal-distal causation.

This suggests that the proximal-distal model has some utility, but does it provide a comprehensive picture of how social factors influence health and disease? We explore two further case studies to identify situations in which this model does not apply but that capture alternative ways that social factors have causal influence.

**4.2 Genes and environment: Social as a parallel cause.** The proximal-distal model applies to some cases, but not others. One set of examples it does not capture are situations in which social and biological factors are “parallel” causes of a disease outcome. In these cases, social and biological causes operate in parallel without either upstream cause operating “through” the other.

Examples of this are found in models of how genetic and environmental factors cause disease. In modern research, many different methods are used to quantify the causal influence of genetic and environmental factors on disease. These include path analysis, heritability studies, multivariate analyses in various populations (including twin and adoption samples), and gene intervention experiments in animal models (Kendler and Eaves 1986; Caspi and Moffitt 2006).

Many of these studies use statistical methods that support causal claims, although these meth-

ods do not reveal fine-grained causal details about the biological process itself (Kendler and Gardner 2010). A number of these methods distinguish two main ways that genes and environment interrelate statistically—their interrelations can be additive or multiplicative (Kendler and Gardner 2010; Kendler et al. 1995). In the additive model, the impact of one factor on the outcome is the same without or without the other. In the multiplicative model, the magnitude of the impact of each factor on the outcome depends on the other.

Consider a causal scenario discussed by Kendler and Eaves, which is captured by the additive model (Kendler and Eaves 1986). In this example, the disease outcome is stomach cancer and the candidate causes are genetic risk profile and environment. The genetic risk profile captures three gene variants a patient can have ( $AA$ ,  $Aa$ , and  $aa$ ), which place them at high, intermediate, and low risk of developing this disease. The environmental factor is dietary intake of high or low levels of processed meats (H or L), which increase or decrease likelihood of disease, respectively. This represents a “common sense” model for how environment and genetics influence disease risk, as they are independent factors with additive influence. These factors are independent in the sense that no matter what the patient’s genetic profile, changes to diet influence disease risk. Similarly, no matter what the patient’s dietary status, differences in their genetic profile alter disease risk.

When this statistical model is interpreted causally, each factor acts as a “parallel cause” as they operate concurrently without one being upstream to the other. This is evident by the fact that when one cause is held “fixed,” changes to the other still provide causal control over the outcome. Both factors explain the risk of stomach cancer—both causally impact the outcome, without one being causally upstream of the other.<sup>3</sup>

Appreciating that social-environmental factors can be parallel causes is important for many reasons. First, this shows that social causes are not always distal to biological factors, as they can operate concurrently with them. This reveals a helpful role of targeting social causes—they can alter likelihood of disease without operating through genes. This also shows how both are individually important causes and should be equally prioritized in our explanations.

It should be noted that one of Krieger’s concerns rings true in this context—the worry of conflating causal location with temporal location. In some of this literature, causes that present earlier in time (e.g. genes) are referred to as “distal,” while causes triggered closer in time to the outcome (e.g. environmental stressors) are “proximal” (van Heeringen 2012). These temporal differences relate to the distinction between “predisposing” and “exciting” causes as earlier causes predispose to disease, while later ones trigger or excite it (Kendler 2020). Care should be taken to distinguish these different uses of “proximal” and “distal” terminology. Just because a cause takes place earlier in time than a second does not mean it is upstream on a causal pathway leading to the second. Both causes can still operate in parallel, even if one is set at an earlier point in time. Maintaining the utility, clarity, and meaning of “proximal” and “distal” terminology requires specifying whether it is used to capture a distinction that is causal, temporal, or of some other nature.

This parallel causal framework shows how social and biological causes can interrelate in more complex ways than is captured by the standard proximal-distal model. While this framework captures a basic relationship between these causes, ways in which they interrelate and depend on

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<sup>3</sup>Another example (and way of illustrating) parallel causes, are cases in which two causes act conjunctively to produce an outcome (Lucas et al. 2014). These are cases of interacting causes, in which both causes control the outcome, and the control they each have is dependent on the other (Spirtes et al. 2000; Ross 2018a).



each other can be (and often are) far more complex.

**4.3 Social genomics: Social as a proximal cause.** In a final causal scenario, the location of social and biological causes are switched relative to the standard proximal-distal model. In this case, biological causes are distal, while social causes are proximal.

One example of this scenario is when genetic factors work “through” the environment to influence behavioral outcomes (Rietveld et al. 2013; Bates et al. 2018; Stefansson et al. 2018). As an illustration of this, consider explanations of educational attainment in children. Standard explanations cite combinations of the child’s genetic profile and environment, which are both causal factors present during the child’s lifespan. In recent work, an alternative “intergenerational” explanation is provided, sometimes called “genetic nurture,” which includes gene variants of the parents (Bates et al. 2018). In these studies, evidence suggests that the parent’s gene variants have influence over the “environmental niche” they create for a child (for example, the degree to which they provide intellectual stimulation for their children through challenging dinner table discussions or taking them to museums, etc.), which influences the child’s educational attainment (Bates et al. 2018). (The parental gene variants in these studies are not transmitted to the child, and so rule out their direct influence on educational attainment by being present in children.)

In this manner, the causal pathway of interest runs from genes, to environment, to outcome—namely, from parental genetics, to environmental niche, to educational attainment, respectively (Bates et al. 2018). As genes work through an “environmental route” they have an “indirect” influence on the outcome (Bates et al. 2018; Stefansson et al. 2018). Other studies support a similar causal intermediate role of environment for other health outcomes (Thorgeirsson 2008).

This research is associated with a social genomics perspective, in which genetic factors are included in a social science approach to health outcomes Harden and Koellinger (2020). While studying genetic causes is often viewed as distinct from (if not in conflict with) a social science approach, this perspective brings both together. Instead of competing, advances in genetics are viewed as a helpful “toolbox” for social scientists to use in clarifying the complex role of social and biological factors on health outcomes Harden and Koellinger (2020).

This causal scenario shows, first, that the causal position of social and biological factors can be switched. Social factors can influence health outcomes as proximate causes that biology operates through. This matters because it reveals how the proximate cause can be a better intervention point in overriding the influence of upstream genes. If genes and environment worked in parallel, as discussed in 3.2, this would not be the case. Furthermore, intervening on this social cause can be easier, more effective, and more practical (even possible) than interventions on upstream biology. In contrast to standard assumptions, privileging proximal causes sometimes means privileging social factors.

Second, this case also shows that, in contrast to Krieger’s suggestions, we should not want to remove “proximal” and “distal” terminology from our lexicon. This causal language is crucial for capturing the accurate causal location of these factors, their relation to the outcome, and their difference in causal influence. The problem is not with using these terms, but with using them in a way that is principled, clear, and accurate.

Finally, this case and others can help resolve puzzles regarding the causal influence of macro-level social factors. These puzzles are tied to connected process accounts of causation, which can influence expectations about social causes. Connected process accounts maintain that causes are physically connected to their effects—a view related to identifying detailed “mechanisms” or

intermediates from causes to effects (Woodward 2003; Ross 2023b). This perspective can make social causes seem mysterious, as there are often no clear physical connections from public policies, social resources, and environments to the downstream health outcomes they impact. The problem here is that connected process accounts are misleading and poor guides to successful causal reasoning in scientific contexts. For example, many absences (deleted genes, lack of resources, etc.) are causally relevant to outcomes, despite lacking a physical connection to these outcomes.

A better account of causation is an interventionist one, which more accurately captures causal reasoning in science (Woodward 2003; Kendler and Campbell 2009). On this account causes are factors that provide control over their effects—intervening and changing the cause, leads to a change in the effect (Woodward 2003). While extra detail about intermediates can be useful, it is not necessary for identifying causal relationships and these relationships need not involve physical connection. This is consistent with the methods and reasoning used by social scientists (and scientists in many other fields) used to understand, study, and describe causation (Morgan and Winship 2015).

In the three models discussed in this section, social factors are causal in the sense that if they were intervened upon and changed, this would lead to changes in their downstream effects. These causal dependency relations can span levels and capture external causes that get “under the skin” to produce health outcomes. Proper use of “proximal” and “distal” causal conceptions requires specifying an account of causation and appreciating the many ways that social and biological causes interrelate to produce health outcomes.

**5 Conclusion.** This analysis shows that social factors can influence health outcomes in a manner outlined by the standard proximal-distal model, but in many other ways as well. Social factors can be distal causes, parallel causes, and proximal causes of disease and health. This reveals three unique ways that social factors interrelate with biology and exert causal influence. We have also shown how some assumptions of the proximal-distal model are incorrect, including assumptions about causal relevance, explanatory power, and targetable factors for control. Although this model is sometimes used to support a prioritization of proximal causes, this should be resisted as a universal principle. In some cases, social causes that are distal can have more explanatory power, as was seen in explanations of disease distribution.

Although the proximal-distal model is not a comprehensive conceptual framework for the influence of social causes on disease and health, this does not call for abandoning “proximal” and “distal” terminology. In fact, this language is helpful in capturing important distinctions in causal architecture and how causes interrelate in producing outcomes. Care needs to be taken in deciding when and how this model is applied to causal scenarios (if this is done accurately) and what assumptions are associated with the model’s use (such as viewing proximal causes as always more explanatorily potent). One byproduct of clarifying the rationale behind this model is that this identifies reasons for prioritizing social causes for some explanations. Policies that change social conditions can be more effective than genetic, cellular-level, and individual treatments. In short, there are many situations in which social causes better serve the goals of controlling, preventing, and treating health outcomes.

Examining the concepts of proximal and distal causes relates to other important causal distinctions in medicine. These include distinguishing: causal mechanisms from causal pathways; predisposing from exciting causes, higher from lower-level causes, and structuring from triggering causes (Kendler 2020; Ross 2018a, 2021, 2023a). It is important to clarify what these distinctions

capture in science, how they should be understood, and why they matter. This requires examining the causal concepts we use in scientific settings, how they capture causal differences in the world, and specifying how these differences matter for our goals of explanation and understanding in medicine.

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