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A retrospective on fundamental cause theory: State of the literature, and goals for the future

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Abstract

Fundamental Cause Theory (FCT) was originally proposed to explain how socioeconomic inequalities in health emerged and persisted over time. The concept was that higher socioeconomic status helped some people to avoid risks and adopt protective strategies using flexible resources – knowledge, money, power, prestige and beneficial social connections. As a sociological theory, FCT addressed this issue by calling on social stratification, stigma, and racism as they affected medical treatments and health outcomes. The last comprehensive review was completed a decade ago. Since then, FCT has been tested, and new applications have extended central features. The current review consolidates key *foci* in the literature in order to guide future research in the field. Notable themes emerged around types of resources and their usage, approaches used to test the theory, and novel extensions. We conclude that after 25 years of use, there remain crucial questions to be addressed.

Keywords

Fundamental causes; socioeconomic status; racism; stigma; medical sociology

Introduction

A stark fact is regularly revealed when rates of morbidity and mortality are arrayed by socioeconomic status (SES) and race/ethnicity in the United States (U.S.). All too often, these facts show that society's poorer members and those disadvantaged by racial hierarchies live in worse health and die younger than their counterparts. Nor is the revelation of facts like these something new – similar patterns have been reported historically in the U.S. (Antonovsky 1967), recently in England (Lewer et al 2020), and across European nations (Mackenbach 2012). With the publication of the Black (1980) report and U.S. data posing the "challenge of the gradient" in SES (Adler et al 1994), national priorities set

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forward in the "U.S. Healthy People" documents challenged the populace to reduce or eliminate health inequalities by race and SES. Despite these goals, and efforts implemented to address them, we have seen growing health inequalities over the past few decades (Meara et al 2008).

The repeated emergence of health inequalities across places and times signifies that the associations in question emerge *even though the types of diseases and their attendant risk and protective factors change from place to place and from time to time*. Fundamental cause theory (FCT) was proposed to help understand the persistence of associations between SES and morbidity and mortality even though the diseases afflicting humans, and the risk and protective factors influencing those diseases, changed substantially across time and place. Associations between SES and disease persist, claimed FCT, because risk and protective factors linking SES to health in one context were replaced by new mechanisms at a different place and time.

Why might mechanisms be replaced, as the theory claims? To answer this question FCT proposed that new mechanisms arise because people of higher SES use flexible resources – knowledge, money, power, prestige, and beneficial social connections – to garner health advantages irrespective of which diseases are prevalent or which modifiable risk and protective factors have been identified at a particular place and time. Put another way, *FCT sought to examine the actions of the powerful in securing health and avoiding illness as a core driver of inequalities*. The idea is that as new knowledge about effective risk or protective factors grows, people of higher SES act both individually and collectively, using flexible resources available to them, to harness the benefits of that new knowledge. As a sociological theory, FCT addresses this issue by linking the medical subspecialty of the discipline to core subareas such as stratification, stigma, and racism. Since the last comprehensive review of FCT was completed a decade ago (Phelan et al 2010), FCT has been tested, applied, extended, and elaborated and new applications have been examined extending central features of the theory. In light of these developments, the goal of the current review was to consolidate key *foci* in the literature to provide guidance on possible future directions for research about FCT over the next decade.

Literature Review

The original Link and Phelan (1995) paper has been cited >5,000 times so, rather than attend to each citation from 2010–2020 identified by our literature review (N=1,456), we developed a review plan (see Supplemental Appendix for additional methodological information) that identified and coded papers developing and extending FCT that allowed us to focus on papers that tested or expanded FCT (n=232) rather than those that simply referred to or applied FCT. Interestingly, this review revealed that the conditions most commonly researched in FCT were behavioral factors (38.9% of citations), gastrointestinal diseases (19.8%), and cancer (18.3%), while osteological (0.0%), nephritic (4.0%), and genomic (4.8%) outcomes were least common. Studies applied key features of the FCT approach when trying to understand inequalities in novel situations and contexts; for example, analyses examined social gradients in the United States (33.2% of all studies), some studies examined outcomes in the world's poorest countries (Clouston et al 2015b, Dagadu 2019)

while others sought to determine the extent to which inequalities were consistently observed between nations within similar regions (Mackenbach et al 2017, Rydland et al 2020). The following sections describe what we learned from the past decade of research in the FCT, starting with describing fundamental causality.

Considering causality

FCT includes the term "cause" in its name. But what kind of "cause" is "fundamental" and how can the theory's claims about causality be effectively evaluated? First, it is possible to ignore what is potentially informative about FCT by demanding rapid and complete translation to the counter-factual potential outcomes approach, which has proved useful in epidemiology and the social sciences (Morgan & Winship 2015). The counterfactual approach seeks to evaluate whether a specific variable (X) predicts a specific outcome (Y). FCT, in contrast, is focused on understanding how a system of relationships is dynamically reproduced in different places and times. In light of this difference, we appreciate a proposal developed by Freese and Kevern (2013) that asks that different types of "causes" be considered. Importantly, in addition to common causal frameworks like necessary/sufficient, proximal/distal they include a category they called "causes of causal relationships" and use FCT as a prominent example (Freese & Kevern 2013). FCT fits this type of cause because SES-related flexible resources cause relationships to emerge between risks/protections and diseases. It is this capacity to cause causal relationships and thereby to reliably reproduce relationships over time that supports the naming of such causes "fundamental." Of course, not all agree that there is value in conceptualizing multiple types of causes and push instead to envelop all causal considerations into a narrower framework with a singular conceptualization of cause. For example, when considering FCT Morgan & Winship (2015) suggest that the potential outcomes approach allows a "more ambitious goal: the careful delineation of the causal states that lie within any purported fundamental causes and then the estimation of the specific effects generated by contrasts between them." We think this is misguided because it steers researchers away from causal considerations of theoretical frameworks that cannot be reduced to a simple input/output framework. In opposition to what Morgan and Winship propose, we concur with Freese & Kevern (2013) who state that: "there are many puzzles to social life that cannot be reduced to analogies of program evaluation" (pg. 40).

We consider FCT to be one of the "puzzles" to which Freese and Kevern (2013) refer. To begin, the strength of FCT is not its capability to determine whether a single risk factor influences a particular disease outcome, but instead whether multiple preventable diseases are influenced through multiple mechanisms. FCT highlights that SES, stigma, and racism influence a range of inputs (X_i) across a range of outputs (Y_i) and that knowing whether or not the theory is useful demands consideration of the range of associations together and not just one at a time. FCT further predicts that extant risk factor mechanisms *change* when new knowledge and technology arises that is relevant to the prevention or cure of disease. According to the theory, flexible SES-related resources shape the distribution of such risk and protective factors to create new mechanisms. Thus, one central feature of FCT involves the substitution of a particular "X_1" with a new "X_2" thereby allowing for multiple risk and protective factors to alight in different places and at different times. If

the theory is valuable then mechanism replacement must occur, something that is not well tested by proceeding one input-output relationship at a time. Finally, FCT is not dependent on a particular disease but rather predicts that a fundamental cause will express itself as new diseases arise (e.g., COVID −19) and new risk and protective factors come to be known. It matters whether the theory can accurately predict what is likely to transpire when the "output" changes to another disease. If it can, the theory could be of considerable value, but this is not something that is well tested by proceeding with thinking that burrows into singular input/output relationships that are only considered one at a time. To summarize, FCT generates predictions about systems of relationships and about the replacement of mechanisms and outcomes that cannot be tested by pursuing outcomes one at a time. The careful delineation of the cause-effect relationships that Morgan & Winship call for is certainly to be desired, but our point is that doing that alone cannot provide a robust test of FCT. We need something more to address the causal inference issue that FCT presents.

A useful way to conceptualize this causal inference issue was introduced by Shadish et al. (2002), who differentiate "causal description," which they define as "describing the consequences of deliberately varying a treatment," and "causal explanation," which they state is concerned with "clarifying the mechanisms through which and the conditions under which" a causal relationship holds. Shadish et al. (2002) go on to note the "priority and prestige" that causal explanation enjoys in the sciences because this type of explanation helps in generalizing beyond the singular cause-effect relationships that are the undertaking of causal description. Knowing the conditions of causal relationships matters as such "explanations," if true, provide a broader knowledge base for guiding action.

FCT represents an effort to advance a causal explanation to understand ***how*** **and** ***why*** associations between SES and risk and protective factors emerge, and ***when and under what conditions*** particular risk factors are prominent in the SES disease relationship. A notable strength of FCT, therefore, is that it does not limit researchers to studying a single mechanism or a single outcome. It follows that no matter how beautifully causal inference is executed for any particular exposure-outcome test, it would not represent strong evidence supporting a fundamental cause explanation. Given this, how can the explanatory framework proposed by FCT be tested?

FCT can be supported or refuted to some extent by multiple observations of associations between potential fundamental causes and disease, or potential fundamental causes and risk factors known to influence disease. If expected patterns did not generally emerge, the theory would lose credibility. But even if the patterns are generally evident the case for the theory would not be especially strong because many other reasons for such explanations, that do not involve FCT processes, could be developed. The strongest tests of FCT make novel predictions – *ones that other theories would not make*. To the extent that predictions like these are supported by evidence, FCT gains credence and to the extent that such predictions fail, the theory loses credibility.

Tests and approaches to tests

In keeping with the strategy of testing novel predictions made by FCT we describe three generic approaches and provide examples of how researchers have enacted each one. The

key feature of each involves identifying circumstances in which flexible resources can be more or less effective in garnering a health advantage.

The **disease preventability** approach examines the association between SES and mortality across multiple disease outcomes that vary in the preventability of death (Phelan et al 2004). Since FCT claims that SES associations emerge because people use flexible resources to garner a health advantage it follows that if people are less able to use such resources to protect themselves (low preventability diseases) SES associations with mortality should be smaller than for diseases in which resources can be effectively deployed (high preventability disease). Results showing that preventability is a key concept in FCT have identified disparities among stigmatized sexual minorities (Bränström et al 2016), between area deprivation and all-cause and mortality from preventable diseases in France (Ghosn et al 2017), between domains of social inequalities and mortality from preventable diseases in the U.S. (Masters et al 2015), for preventable cancers in Belgium (Vanthomme et al 2016), and in childhood and adolescent cancers in the U.S. (Delavar et al 2020). Indeed, three independent efforts to determine this effect in Europe have identified large inequalities in prevalence of preventable conditions (Rydland et al 2020) and, in northern Europe with preventable causes of death (Mackenbach et al 2017), though welfare state regimes may attenuate these effects through effective social policies (Craveiro 2017).

The **preventability shifts** approach focuses on particular diseases over time, before and after changes in our capacity to address mortality from that particular disease occurred. FCT predicts that when new knowledge or technology becomes available people of higher SES are more propitiously situated to benefit from that new information or technology and SES associations with the disease will emerge or grow stronger. SES associations with lung cancer mortality emerged and grew slowly following identifying a link between cigarette smoking and lung cancer (Rubin et al 2014). Similarly, SES gradients in suicide mortality rates emerged after selective serotonin reuptake inhibitors became available (Clouston et al 2014b). Finally, the unequal distribution of effective cancer screening that occurred after their development led to emergent SES gradients in cancer mortality (Zapata-Moya et al 2019).

The **manipulated preventability** approach examines whether inequalities by SES and/or race/ethnicity emerge during controlled trials where the interventions are randomly assigned. In this instance, the FCT prediction is that when effective interventions are randomly assigned and require resources to be most effectively adopted, inequalities will emerge because higher SES individuals use flexible resources to extract maximum benefit from the intervention whereas lower SES individuals are impeded in their capacity to do so. Higher SES individuals are more able to consistently adhere to the protocol and thus more likely to see benefits from the intervention. In a placebo group or no treatment control where the beneficial treatment is not available the same flexible resources have little utility because the active treatment is not available to this group. A strong example of this is available in Yang et al (2014) in which the provision of a breastfeeding promotion intervention increased social inequalities in outcomes including preventing early discontinuation of breastfeeding while also showing a trend in childhood cognitive outcomes.

There are two reasons these approaches are effective in testing FCT. First, the predictions are directly derived from the idea of flexible resources and therefore seek instances in which such resources can or cannot be deployed to achieve a health advantage. When such circumstances can be identified a very specific prediction about when SES-disease associations should be stronger or weaker is possible. Second, the predictions are novel in the sense that other theories or explanations for SES-disease associations would not make these predictions. Stress theory, reverse causation (disability leading to lower SES), or an explanation involving a common cause for SES and health (genetic factors) would have no reason to predict stronger SES-disease associations when diseases are more preventable.

Table 1 briefly describes the characteristics and findings of studies published since 2010 (12 labeled disease preventability, 5 preventability shifts, and 4 manipulated preventability) that test the preventability component of FCT. In general, the studies supported predictions of FCT and in no case did a study claim to resoundingly disconfirm the theory. Though publication bias could have selected for supportive findings, we also note that unlike the first preventability test (Phelan et al 2004), the majority of the authors represented in Table 1 were not associated with the development of the theory or its elaborations. Additionally, studies by Mackenbach et al (2015, 2017) and Rydland et al (2020) include multiple tests from a pre-specified universe of countries, thereby providing data highly unlikely to be influenced by positive publication bias. In addition to this general support the represented studies also find instances in which there are anomalies (albeit in a minority of instances) (e.g. Mackenbach et al. 2017, Ryland 2020) or instances in which elaborations were needed to fully account for the pattern of results (e.g. Zapata-Moya et al. 2019). In sum, the evidence signals substantial support for FCT but also, as Mackenbach et al. note, “other mechanisms than the theory implies also play a role” (2017, p. 1117). In keeping with this latter observation, we take up some potential elaborations of the theory that might broaden explanatory power and also present FCT as a “theory of the middle range” that needs to join other theories to achieve a more comprehensive explanation.

Extensions

Since resources are the central mechanism through which many health inequalities are theorized to arise, studies have sought to improve and/or expand upon 1) definitions of flexible and fungible resources that may be used to secure increased survival, and 2) the nature, incentives, and role of the actors who are expected to identify, amass, and direct those resources. Link and Phelan (1995) listed five flexible resources: knowledge, money, power, prestige, and beneficial social connections. These resources were identified because they helped describe how risk factor mechanisms are *replaced in different places and times*. The following, therefore, describes how researchers have discussed these resources and extended a consideration of them.

Social History

FCT did not originally discuss what happened when diseases receded in favor of other disease outcomes in generating SES-disease associations over different historical periods. This is a critically important issue because we know that the diseases afflicting

humans changed dramatically from the 19th to the 20th century during what is called the epidemiological transition Clouston and colleagues (2016) discussed the implications of these historical changes by highlighting the central role of effective knowledge as a mechanism for disparities. Specifically, Clouston et al. identified four ideal-type theoretical stages – natural variation, increasing inequalities, decreasing or stable inequalities, and reducing inequalities – that specific diseases might follow. This conceptualization helps clarify when inequalities would not be expected, and also provides guidelines as to how and when inequalities might emerge, grow in size, recede, and even disappear.

The recognition that SES inequalities for particular diseases fluctuate historically and are contextual in nature extends the FCT hypothesis. Specifically, FCT is based on the observation that overall SES inequalities in health and mortality are persistent. Clouston et al.'s social history concept clarifies that this persistence is maintained in part due to, and in part despite of, the waxing and waning of underlying diseases and specific causes of death. Recognizing these stages supported a secondary question, which was about the extent to which social inequalities emerge from delayed access to new knowledge and methods for improving health and delaying the disease. In a social history approach, inequalities are a sign of inefficiency whereby individuals who might otherwise use new technologies are unable to access them in a timely fashion and, therefore, do not benefit from their existence. Clouston et al also point out that these newly developed health interventions are often not immediately efficacious or readily adopted and posited that there would therefore be a transition between the ideal-type stages as effective usage transitioned from low to high levels and diffused throughout the population. To that end, Clouston et al (2016) built on work from others such as Miech et al (2011) who clarified the impact of rising causes of death to propose that the historical context in which uptake of novel preventions operates is crucial when trying to understand the patterns of change in social inequality.

An important benefit of thinking in terms of ideal-type disease stages is that the field is encouraged to consider where a particular disease is situated in terms of such stages, and how its current location might affect future inequalities in that disease. For example, Saldana-Ruiz et al. (2013) noted that well before an inverse association between SES and colorectal cancer arose in a specific year, SES trajectories had been building momentum over the course of 30 years, with rates in lower SES areas increasing at the same time as rates in higher SES began to decline. By the time that inequalities disadvantaging people in low SES area were evident in a given year, decades of accumulated disadvantage had already occurred, making efforts to remediate those disadvantages all the more difficult. Understanding the social history of disease is crucial because it helps to interpret the specific context in which inequalities are arising, and therefore to identify when inequalities began to form. Ideally such knowledge could hasten transitions between stages so as to more efficiently reach a stage in which inequalities begin to diminish.

Methodological Innovation – the inflection point approach

In the **preventability shifts** approach where SES-disease associations are examined before and after new knowledge or technology becomes available, Clouston et al (2017b) introduced a novel approach to explicitly map shifts in the underlying rate of change in

diseases under the assumption that the shift itself is unequally distributed. The authors exemplify the approach in a study of the initial diffusion of endoscopic methods to remove adenomatous polyps, an intervention that can result in an abrupt change in the underlying risk of mortality from colorectal cancer. If access to the technology is diffused unequally through communities in ways that are impacted by the distribution of resources, SES-gradients in mortality are predicted to change over time. The method of inflection point analysis relies on joint modeling of both predictors of the underlying mortality rates and of *the point at which a trend changes when a prevention becomes available*. Inflection point modeling, therefore, seeks to determine predictors of the time at which a disease switches from a less to a more preventable stage. The results from Clouston et al. (2017b) helped clarify that one way in which communities influence health is through the commencement of interventions. Specifically, they tested the role of the timing of shifts in mortality trends, thereby allowing the researchers to examine how variations in such shifts coincide with variations in the uptake of interventions. Building on these ideas, Clouston et al (2020) sought to better understand which interventions may have been most relevant to contextual factors identified in prior studies and showed that colonoscopy acted as a strong mediator, in conjunction with changes to health behaviors, of the relationship between SES and colorectal cancer mortality. Future work with inflection points should develop a theory about how best to interrogate the changing course of disease outcomes.

Metamechanisms

Lutfey and Freese (2005) introduced the concept of "*metamechanism"* to indicate that a fundamental cause is "responsible for how specific and varied mechanisms are continuously generated over historical time in such a way that the direction of the enduring association is preserved…" (1327–1328). In a subsequent elaboration of the concept Freese and Lutfey (2011) propose three new metamechanisms – ***spillovers***, ***habitus***, and ***institutional processing*** – as complements to individually-based resources. The major goal of their proposal was to account for situations in which higher SES people benefit *without directly identifying a health-enhancing action or choice to use resources*.

Spillovers refer to the fact that "individuals are embedded in social relations in which other people also value their health, and the actions of other people have consequences that accrue differently to people of different social positions" (Freese and Lutfey 2011, p. 72). It follows that people can derive a health benefit from the actions of others if those others keep noise and pollution away from where one lives or negotiate a strong preventive health care health package in one's place of work. Freese & Lutfey (2011) also draw on Bourdieu (1984) to define ***habitus*** as "basic dispositions of interpretation and action that reflect an actor's social position." The idea that *habitus* shapes health decisions outside of conscious, directed use of resources is supported by Cockerham's (2005) health lifestyle theory where Cockerham describes *habitus* as a map that routinely guides action so that actions can be carried out nearly automatically – "They are simply habitual ways of acting when performing routine tasks" (Cockerham 2005). ***Institutional processing*** was proposed as a third metamechanism to integrate "the agentic, dynamic action" of institutions that facilitate or block actions of individuals seeking to enhance health. This concept coheres with Bird and Reiker's (2008) more general concept of "constrained choices" which we subsequently consider with FCT.

While from very early on FCT emphasized the role of contextual factors operating in addition to and outside of individual action (Phelan et al 2004), spillovers, *habitus*, and institutional processing are extremely useful for their precision in specifying some of the processes through which this occurs. However, it would be unfortunate if these concepts detracted from the importance of resources by indicating that resources are just one component. People are not accidentally situated in neighborhoods or networks where spillovers occur, in social contexts where healthy dispositions (habitus) can be developed, or in institutions that can be expected to differentially process them. They may not nestle themselves into circumstances like these because of health concerns but they do regularly use resources to enhance their location in these respects. For these reasons, we argue that resources should retain a primary position in FCT.

Collective Health Agency

Whereas Freese and Lutfey (2011) usefully pointed out that high SES people might benefit from processes that do not involve the active use of resources, we thought it important to also expand and clarify the importance of resource-use at the collective level. We call this "collective health agency." The idea is that collections of people propitiously situated in societal hierarchies will share interests in good schools, safe parks, crime-free neighborhoods, excellent medical facilities, and many more. Simply put, *powerful* people *protect members of their communities by securing and sharing flexible resources within their communities*. Because of these health-relevant interests, they are likely to join together, pooling resources of knowledge, money, power, prestige, and beneficial social connections to achieve desired ends. They collectively and agentically insist on better health conditions in their schools, neighborhoods, cities or nation-states. As they push for these benefits, they set themselves apart thereby creating sharp inequalities concerning the social determinants of health that reliably yield inequalities in prominent health outcomes.

As an example consider that in many instances researchers have relied on individual-level factors such as educational attainment as indicators of SES (Masters et al 2015) while others have relied on county-level indicators of SES (Saldana-Ruiz et al 2013). While these are related, we need to ask the extent to which the risk of mortality at the individual level is driven by individuals seeking out protective factors and avoiding risky ones, or by "**collective agency**" – the communal pooling of resources from public or other private financial efforts that are unequally distributed across communities. For example, as the COVID-19 pandemic spread in the United States an enormous demand for testing kits, personal protective equipment and ventilators emerged, and with that a communal competition at multiple levels – countries, states, counties, and hospital systems – emerged. Beyond what the COVID-19 pandemic reveals, this kind of communal action occurs regularly as people try to build capacity and effectiveness for people in their domain. This communal wrangling for the best is an FCT process that needs more attention in future research. An existing empirical example is developed by Wang et al (2012) who note that an individual's ability to utilize a health beneficial cancer screen depends on *whether community actors have marshaled communal resources to make the beneficial screen available and accessible to individuals*. Specifically, Wang et al (2012) reported that communities that were slow adopters of technologies were also more likely to have

been slow to uptake life-saving technologies. This is crucial because each state has individuals with unequal resources, *but each state also has its own context and capacity for technological diffusion*.

Individual Traits

Seeking to expand on the range of resources used in FCT, researchers have explicitly proposed adding individual cognitive capabilities (Gottfredson 2004) or non-cognitive skills (Tam & Wu 2013) as fundamental causes. Others, without explicitly mentioning FCT, have similarly proposed that health literacy (Nutbeam 2000), and patient activation (Greene & Hibbard 2012) may be critical resources explaining health differences achieved *via* self-empowerment. While these are important concepts, there are some potential problems with integrating these new resources into the FCT framework. First, it is not clear that they are independent of a person's characteristics as promoted into further usage *via* personal *habitus*. For example, studies have noted that childhood SES and early life traits and experiences can be central predictors of old-age health outcomes, thereby highlighting the potential importance of *habitus* as individuals age (Clouston et al 2017a, Deary 2012, Hayward & Gorman 2004). If integrated into *habitus*, then these factors should be considered *indicators* of lifelong disparities emerging from educational or intergenerational processes, rather than *mechanisms* through which social factors cause inequalities to emerge. Second, analyses examining the utility of these as trait resources have tended to support the idea when socioeconomic status has been inadequately measured, but to not usefully increase capacity to predict outcomes within the health sphere when SES is measured adequately (Clouston et al 2015a, Link et al 2008). Trait explanations remain prominent in the literature and need further consideration as to whether they might operate as fundamental causes. At the same time, while the accumulated evidence shows that such traits can sometimes be important for health, they do not appear to be prime reasons for disparities by SES and race/ethnicity.

Racism as a Fundamental Cause of Health Inequalities

Health inequalities by race exist across multiple disease outcomes and are plausibly influenced by multiple risk factor mechanisms. It, therefore, makes sense to wonder whether White racism might be considered a fundamental cause of health inequalities. But beyond these descriptive facts is there evidence to suggest that other characteristic features of a fundamental cause such as replaceable mechanisms are also present? And how do we think about race and racism in relation to SES?

Phelan and Link (2015) presented a two-step process in seeking to address these questions. In the first step, racism is a fundamental cause of SES-related resources, which in turn is a fundamental cause of health outcomes. In the second step, racism is a fundamental cause independent of SES-related influences. If we allow that SES can be considered a fundamental cause of health inequalities, the two points requiring further consideration are first whether racism is a fundamental cause of SES-related resources and second whether racism is a fundamental cause of health inequalities independent of those SES-related resources. Concerning the first issue, Phelan and Link (2015) provide evidence that racism is associated with multiple SES-related outcomes (educational attainment, housing, jobs)

through multiple mechanisms (redlining, incarceration, interpersonal discrimination, etc.). One clear example is evident when we take a broad historical perspective and see that mechanisms of White racism have changed from the institution of slavery to Jim Crow laws and community-based intimidation (e.g., Klu Klux Klan) to current-day incarceration policies and policing. Finally, in keeping with FCT, inequalities have persisted while mechanisms have changed. Educational attainment, income, and wealth have increased over time for both Black and White Americans but racial gaps in median income (since 1948), wealth (since 1983), and percent with at least four years of college (since 1940) have remained relatively steady or grown (U.S. Census Bureau 2020). The FCT idea that multiple replaceable mechanisms result in similar outcomes across time appears to be consistent with a substantial body of evidence.

As for the second issue concerning whether racism can be considered a fundamental cause of health inequalities independent of SES, Phelan and Link (2015) considered whether Blacks are disadvantaged relative to Whites in access to flexible resources that can be separated from SES. They conclude that with respect to prestige (honor/deference), as evidenced by, for example, Whites' negative explicit and implicit attitudes (Simmons & Bobo 2018), power as reflected in influence in interracial groups (Webster Jr & Driskell Jr 1978), and beneficial social connections as influenced by racial segregation and collective disadvantage, Blacks experience decrements in flexible resources separate from SES.

Consistent with the idea that racism affects the distribution of flexible resources over and above its influence on SES-related resources, most research shows that Blacks experience worse health outcomes with SES controlled than Whites (Williams & Sternthal 2010). For example, the children of Black caregivers reporting racism in New Zealand had poorer mental health, self-esteem, and behavioral scores than children of caregivers not reporting racial discrimination (Paine et al 2019). Similarly, when adjusting for individual factors and community-level poverty, Blacks in states with higher rates of structural racism reported more myocardial infarction (Lukachko et al 2014). However, as noted in the constrained choices section racism also acts by modifying resource utility by, for example, changing how privilege and discrimination are perceived in healthcare (Stepanikova & Oates 2017). Phelan and Link (2015) conclude that the connection between race and health outcomes endures largely because racism is a fundamental cause of racial differences in SES and because SES is a fundamental cause of health inequalities, but that racism also has a fundamental association with health outcomes independent of SES.

Stigma as a Fundamental Cause: Motives, Power and Flexible Mechanisms

Critical to forming a fundamental cause relationship, as we saw with respect to SES and racism, is a social process that invigorates the creation of new mechanisms should any existing mechanisms be blocked. In light of this, a critical question in considering stigma as a fundamental cause is what such a social process might be.

Phelan et al (2008) identified three prominent motives people have in stigmatizing others. First, stigma can be used to "keep people down" so that they can be exploited or dominated. Stigma assists by creating, legitimating, and perpetuating the identification of the stigmatized group as being inferior in terms of intelligence, character, competence, or the

basic human qualities of worthiness and value (Phelan et al 2008). Classic examples are the racial stigmatization of Blacks beginning in the era of slavery, the Europeans' colonization of countries around the globe, and U.S. Whites' expropriation of the lands of American Indians (Feagin 2014). Second, stigma can be used to "keep people in" normative bounds so that they can be effectively controlled. Stigma assists by punishing people who step out of normative bounds and by warning others of the punishment they might receive if they do so. A classic example of an effort to keep people in is the banning of gay marriage that occurred in US states from 1995–2010. Third, stigma can be used to "keep people away," effectively excluding them from social, cultural, political, and economic relationships often *via* the use of structural means to accomplish exclusion such as the incarceration of stigmatized individuals (Ramaswamy & Freudenberg 2012). Stigma operates by justifying and then enacting the exclusion of people who are deemed to be dangerous, undesirable, or costly.

Power to Stigmatize.—To effectively act on stigmatizing motives, people need to have the requisite power to do so. They need the power to make the designation/labels they deem to be important salient, affix stereotypes to such labels and propagate them broadly in the population, and construct "us" *versus* "them" distinctions that place the stigmatized in a separate group. Finally, stigmatizers must have the power to control access to the goods and services of society to deny stigmatized people access to them (Link & Phelan 2001).

Flexible Mechanisms.—In the domain of stigma, there is a massive and very flexible repertoire of possibilities to keep people down, in or away. These can occur at the macro-level through structural stigma (Hatzenbuehler & Link 2014) and/or at the interpersonal level in the form of person-to-person discrimination and other individual processes (Link & Phelan 2001). At each level, there are multiple ways to put people down, slight them, exclude them, avoid them, reject and discriminate against them that when motivation and power are in place, stigma processes are effective at achieving these ends (Hatzenbuehler et al 2013, Link & Phelan 2014).

Evidence.—While the case can be made that stigma is a fundamental cause of health inequalities because it is related to multiple disease outcomes through multiple replaceable mechanisms, explicit tests of the possibility are somewhat rare. One exception is a study by Bränström, et al. (2016) that relies on the preventability of disease approach to testing FCT. They predict that health disparities for sexual minorities should be greater in diseases that are more preventable compared to ones that are less so. Using morbidity data for the years 2001– 2011 from a representative general population- based study in Stockholm, Sweden they found no sexual orientation differences in morbidity due to low-preventable diseases. In contrast, both gay/ bisexual men and lesbian/ bisexual women showed higher prevalence of illness compared to heterosexuals for high- preventable morbidity. But clearly many more tests using this and other strategies are needed, representing an important gap to be filled in the literature on FCT.

Paradoxes

Some descriptive epidemiological patterns of mortality run counter to expectations based on FCT and other SES-related theories. One of the most prominent of these has been called the “Latinx paradox” due to the finding that people of Latinx origin tend to live longer than their White counterparts (Ruiz et al 2013) despite being substantially disadvantaged in education, income, wealth and exposure to discrimination. Similarly, women generally live longer than men despite differences that strongly disadvantage women in terms of income and power. These descriptive patterns suggest that something other than resource utilization is at work. Beyond these examples of epidemiological patterns, we identify two sets of processes that are likely to produce “paradoxical results” from an FCT vantage point: giving greater value to ends other than health and exposure to constrained choices. Following Lutfey and Freese (2005) we call these “countervailing processes” as they push away from associations predicted by FCT.

Competitive Valuations

One key assumption in FCT is that when presented with an option to improve survival, individuals and communities will seek to improve health. Studies have suggested that this assumption, while generally valid, does not always apply. Specifically, there are reasons to suggest that concerns regarding long-term survival may be subsumed by competing values that the actor may identify as being more critical to maintaining their identity, their core values, or their income and wealth. One example may be engagement in known risky behaviors that provide individuals with an opportunity to enhance some component of their lives that is critical to them. For example, dangerous or unhealthy behaviors identified with masculinity such as playing pro-football, fighting in wars, or bravely dashing into buildings that are burning bring status and/or monetary reward even though they are likely to be harmful to health (Courtenay 2000). Indeed, interventions seeking to reduce the risk of colorectal cancer often require either that individuals collect and provide for analysis their fecal matter, or undergo endoscopic procedures resulting in the insertion of a thin endoscopic tube into the colon *via* the rectum and anus. Refusal rates for these types of procedures are often highest among men who endorse traditional views of masculinity and who may value their “masculinity” more than the health benefits of procedures that are perceived to diminish their masculinity (Christy et al 2014). Similar processes have been used to explain the common tradeoff younger individuals make when assessing engagement in risky behaviors such as smoking (Denney et al 2010), or engagement in traditionally masculine behaviors such as eating red or fatty meats at higher rates (Rothgerber 2013). Thus, individuals actively ignore future implications of risky behaviors to enjoy their potential social or personal benefits including, for example, inclusion in specific cultural groups, or gaining other benefits attributed to the risky behavior including increased perceived social status or feelings of control among other factors. Nevertheless, while there are exceptions the value of health is generally strong.

Choice Constraint

A second basic assumption in FCT is that individuals are able either individually or collectively to reliably utilize flexible resources to improve health and survival. Bird and

Rieker (2008), however, famously observed that choices are constrained by circumstances operating at multiple levels including, 1) at work and in the family, 2) in community contexts and 3) in social policy regimes. People are either facilitated or blocked from pursuing goals by norms, policies, and practices at each of these levels (Bird and Rieker 2008). For example, consider women who opted to protect themselves via smoking cessation, being placed at risk by individuals such as spouses and extended family members who opted to continue smoking (Bottorff et al 2010). This lack of capacity to change behaviors in an area with low social power results in increased exposure to second-hand smoke among women with spouses who smoke (Bonevski et al 2014), and carries increased risk of downstream events including increased asthma in children (Simons et al 2014).

In the context of institutional racism, racial/ethnic minorities are constrained in their use of resources *via* structural discrimination. For example, Colen et al (2018) examined 20 years of longitudinal data to show that Black people experiencing upward class mobility earn a restricted return in terms of health for such mobility when compared to Whites. Assari (2018b) similarly reports results from a growing body of research showing that Blacks benefit less from access to educational resources when universalist policies are enacted as compared to Whites, suggesting the potential for generalization of constrained choice theory beyond gender to race. For example, researchers find that the protective effects of educational attainment are more pronounced in resourced populations (Assari & Lankarani 2016), and that protective effects attributed to employment status were concentrated among higher educated White men over other populations (Assari 2018a). This restricted return suggests that even when resources are available to Blacks, their choices were constrained by institutional racism.

Constrained choices may sometimes be beneficial, however, as they also make it possible for communities to actively facilitate healthy choices by community members. Indeed, a central tool in the public health portfolio includes the use of policy-based changes that restrict the capacity for individuals to access risky goods or engage in risky behaviors such as, for example, the use of bans on sugary drinks to reduce the burden of diabetes and obesity (Muth et al 2019). One study of the mechanisms linking neighborhood context with health outcomes noted that men who had sex with men and who were living in gay communities were much more likely to use protection when having sex as compared to those living outside of these communities possibly because they were influenced by increased access to targeted sexual-health information provided in such communities (Frye et al 2010).

It is important to note that while these countervailing processes push against the fundamental relationship, they are generally not strong enough to erase it. Health inequalities by race and socioeconomic status are reliably observed. Still, it is critical to recognize them as they can help explain variation in the magnitude of health inequalities across places and times. Additionally, if as Phelan et al. (2010) suggested, they are identified *a priori* and used to develop hypotheses they can help test FCT. The reason is that each one suggests a turning off of the capacity to use flexible resources for health advantage, in one instance because people value something else more than health and in the other because other social conditions block the use of such resources. If the association is weakened when

the use of flexible resources is blocked it helps us believe more firmly that they matter when they can be used.

Theory of the Middle range

Epidemiological paradoxes and countervailing processes also signal that FCT needs to join with other theories in order to account for observed patterns of health inequalities. In this respect, Link and Phelan (2010) use classic distinctions to identify FCT as a "theory of the middle range" (Merton 1949). In explicating his concept of middle-range theory, Merton (1949) proposed the need for theories "intermediate to the minor working hypotheses evolved in abundance during the day-by-day routine of research, and the all-inclusive speculations comprising a master conceptual scheme." Middle range theory synthesizes explanations beyond working hypotheses but remains testable in a way that broad conceptual schemes are not. Middle range theory is also useful because multiple such middle-range theories are required to build explanatory evidence. In light of paradoxes suggested by the descriptive epidemiology of disease and by countervailing processes, FCT cannot, as currently formulated, fully explain health inequalities. It follows that it is most useful to think of FCT as a theory that needs to join with other middle range theories such as social-stress theory, health lifestyle theory, constrained choice theory, and the sociological theory of health selection, among others.

FCT and Current Trends in Social and Medical Research

Deaths of despair

The deaths of despair categorization was created to incorporate a relatively wide array of causes of death including but not limited to suicide (International Classification of Diseases Version 10 [ICD-10]: X60-X84 & Y87.0), alcohol-related (ICD-10: E24.4, F10, G31.2, G62.1, G72.1, I42.6, K29.2, K70, K85.2, K86.0, O35.4, P04.3, Q86.0, R78.0, X45, Y15), and drug-related (ICD-10: F11–16, H40–44, Y10–14) deaths that are thought to arise from a socially induced condition of despair (Stein et al 2017). The evidence suggests that such diseases of despair are increasing in populations in which they were previously rarely seen (Case & Deaton 2015). The focus on the social sources of despair suggests that SES may play a role in influencing the health of individuals via pathways linked to mental health. SES is an established predictor of poorer mental health with studies suggesting alternatively that both relative and absolute differences in educational attainment can predict increased depressive symptoms (Dudal & Bracke 2016) and concomitant suicidal ideation (Nyundo et al 2020). Others have noted that such effects may not be limited to SES when experienced in adulthood, but also affect individuals' mental health as they experience low SES in childhood (Morrissey & Kinderman 2020).

In this context, we propose that FCT highlights at least three possible pathways linking SES and the increased risk of deaths of despair. First, chronically reduced SES may leave individuals and their family members unable to access the types of resources necessary to treat mental health problems, thereby increasing the risk that poorer mental health results in deaths from deaths of despair such as suicide (Clouston et al 2014b). Second, chronically reduced SES may create individual histories and cultural contexts that integrate

risky behaviors into the *habitus* in a context, resulting in a situation in which individuals in that context see their behaviors as normal (Cherian et al 2018). Correspondingly, higher SES allows community action to promote health by improving the context in which lives are lived thus causing an informational disparity whereby some communities fail to identify or effectively act upon risks because such risks are common and are thus perceived to be "normal" (Quaife et al 2017). Third, individuals with higher SES backgrounds can more actively avoid the conditions that lead to deaths of despair. For example, higher SES individuals tend to be less burdened by conditions characterized by chronic pain at midlife, largely due to better work conditions and engagement in low-strain physical activity. Consistent with the view that higher SES individuals are able to avoid the "risks of risks", these relatively higher SES individuals are therefore less likely to feel a pressing need for substances such as alcohol or opioids that might temporarily reduce pain or relieve stress (Nicholson 2020).

While access to resources helps to describe differences in the levels of poverty evident in deaths of despair, they do not help to explain differences in the treatment of the crack cocaine *versus* opioid epidemics. The language used to describe people (generally Whites) using opioids as compared to those using crack (generally Blacks) revealed different levels of policy empathy. Responses to the crack epidemic of the 1985–94 lead to a massive war on drugs and sharp increases in incarceration (Leigey & Bachman 2007), while responses to the opioid epidemic has resulted in legal backlash for pharmaceutical companies such as Purdue Pharma that facilitated opioid abuse (Dyer 2019) and widespread movements to legalize non-lethal recreational and medical marijuana (Cerdá et al 2020). The result of these efforts clearly has the potential to, on the one hand, provide help to some community members while effectively pushing others down and away. The difference between these policy initiatives can be construed in terms of some of the concepts we have introduced. First, we see what we have called "collective agency" in operation, in the crack epidemic the collective agency of White elites was marshalled to criminalize addiction and in the opioid epidemic to push for treatment and decriminalization. Second, and perhaps lying behind the collective agency exercised in each circumstance were processes consistent with the idea that racism is a fundamental cause of health inequalities.

Precision Medicine

The application of FCT to precision medicine is of increasing importance, as resources spent to develop a highly specific treatment for relatively common diseases are more likely to benefit those with the most resources or diseases with large at-risk populations. At the nexus of social, epidemiologic, and biologic research, there is an increasing interest in *Omics* – a branch of biology that is focused on the in-depth characterization of a single complex system such as the genome in order to allow interventions to precisely target specific subpopulations. Overall, Omics analyses have shown substantial support for the hypothesis that SES affects health. For example, research seeking to control for genetic factors using twin studies has also reported SES inequalities in more preventable diseases even when holding genetics constant (Ericsson et al 2019), while another study using Mendelian randomization to examine causal hypotheses (see e.g., Davey Smith & Ebrahim 2003) report, for example, that higher education was associated with improved body mass

and reduced risk of smoking both *via* a direct effect of education and through changes in the genetic propensity for obesity and smoking (Mann et al 2019). Omics work has even found that deoxyribonucleic acid (DNA) may encode SES information using methylation operations (King et al 2015). Other work highlights the role of epigenetics as a biological mechanism facilitating the intergenerational transfer of inequality in health (Jadotte 2019). This work supports the FCT hypothesis in suggesting that the effects of SES are often broadly distributed across multiple mechanisms including both increased behavioral risk independent of genetics and also increased biological risk as risk factors accumulate over time and between generations. However, while methodological innovations may be useful to better understanding mechanisms of inequality, more work is needed in this area that considers the extent to which the unequal influence of genetics across contexts.

COVID-19

Would a disease that did not exist when FCT was developed be shaped in a manner the theory might predict? The COVID-19 pandemic has caused a global emergency that is particularly interesting to consider through the lens of the previously mentioned stage of disease framework introduced by Clouston et al. (2016) with its four stages of natural variation, increasing inequalities, decreasing or stable inequalities, and reducing inequalities. The first two stages seem relevant to COVID-19 – the first being a stage in which people cannot protect themselves because they have insufficient knowledge and the second a stage when knowledge grows, and intervention becomes possible.

In the early stages of the COVID-19 pandemic, the virus was transported to the U.S. from infected countries *via* prosperous elites during international travel. Cruise ships and ski resorts were sites of early outbreaks. In the early stages of COVID-19 in the U.S., the disease was spreading among these travelers without anyone's awareness. Simply put, there was insufficient knowledge about the reach of the disease thereby diminishing an effective defense. In a second stage, however, as knowledge of the threat grew it was possible to implement tried and true public health measures to combat the disease such as sheltering in place, social distancing, handwashing, and others thereby allowing the same social elites to reduce within-community transmissions and to reduce further infection in their social circles. Concurrently, disadvantaged individuals from predominantly minority populations were much more likely to be classified as essential workers and/or to be living in crowded circumstances with minimal worker protections. These circumstances forced individuals who were at higher risk to remain in the active workforce. This *redirection of exposure* appears particularly concerning since a lifetime of adversity often places individuals in lower SES circumstances at elevated risk of one or more health conditions (Langenberg et al 2006) that may be risk factors for unfavorable COVID-19 outcomes (Zhou et al 2020).

Once infected, inequalities may also arise because higher SES provides improved access to well-resourced and knowledgeable medical staff (Arabi et al 2020), who may encourage patients to receive treatment promptly when the disease is most treatable. The contexts where higher SES individuals are treated may also be better at controlling transmission within the hospital while experiencing an influx of new patients (Meng et al 2020, Singer et al 2020). Concurrently, in a pandemic characterized by lockdowns, patients with

fewer resources and who are managing chronic conditions will have markedly worse care (Khilnani et al 2020). Additionally, if research efforts are fruitful then vaccines will be deployed globally. Vaccine deployment has long been a topic of interest in FCT research with some work showing SES inequalities in vaccine interest and uptake in the U.S. (Polonijo & Carpiano 2013), while others show inequalities in vaccination completion by SES in a global context (Clouston et al 2014a). In this effort, we might anticipate that some individuals will have more ready access to vaccination and that SES disparities will emerge. In sum, FCT and stage of disease concepts have applicability to the COVID-19 pandemic and could be useful guides for reducing inequalities in the future.

Conclusion

What do we think about after 25 years of FCT? FCT remains an important approach because instead of seeking to legitimate the extant hierarchical structure by identifying ways in which those who are disadvantaged fail to be healthy, *FCT seeks to focus attention on understanding how the powerful secure health and avoid illness while sometimes redistributing illness-causing and health-depleting exposures to communities with less power*. FCT has benefited greatly from elaborations and extensions of the theory since its formulation. Among these are: 1) the stage of disease formulation that points out that not only are mechanisms replaced in a fundamental relationship but so are diseases as well; 2) the “metamechanisms” formulation that specifies alternatives to the purposive use of resources in creating a fundamental relationship; and 3) the concept crystallized in the paper of “collective agency” that underscores the importance of resources deployed at a collective level. The theory has also been extended to include racism and stigma as fundamental causes that are related to multiple disease outcomes and plausibly recreate health-harmful mechanisms over time. Finally, following the concept of “countervailing mechanisms,” we introduced “competitive valuations” and also drew on “constrained choices” to indicate circumstances in which FCT processes might operate differently.

In this context, FCT has helped to understand the presence, emergence, and depletion of social inequalities in health across decades and over a broad range of outcomes. Additionally, FCT helped to characterize and contextualize changes that have emerged and provided a foundation on which to understand new mechanisms as they arose. In providing this focal element, FCT helps us to predict and understand the risk of new diseases and might also help to understand resurgences or second waves of older diseases. In so doing, FCT reminds us that the potential for SES, racism, and stigma to influence a disease outcome should become a familiar refrain in health research. FCT has helped to advance and has also benefited from, an increasing recognition that social inequalities are indeed powerful drivers of the determinants and distribution of disease. The fact that the theory has been further developed, clarified, and tested over the past ten years suggests the possibility that the next decade will yield more advances. This review concluded that to engage and catalyze the next decade of research in further elaborating and extending FCT, perhaps as suggested above into new approaches to testing and novel topics such as COVID-19. However, while these emerging topics are likely to be of long-term interest, it is worth highlighting many topics have the potential for much more discussion. Even after 25 years

of conceptualization and research, there remain crucial questions to be asked and further topics to be addressed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Tests of Preventability in Fundamental Cause Theory 2010–2020 – Type of Test, Key Results and Author's Conclusion.

Author/Year	Descriptions	Results	Author Quote
Disease Preventability			
Bränström et al (2016)	Morbidity data (2001 to 2011) from a representative population–based study in Sweden. Studied individuals identified as heterosexual homosexual, or bisexual.	There were no sexual orientation differences in morbidity from low-preventable diseases. By contrast, gay or bisexual men and lesbian or bisexual women had a greater risk of high-preventable morbidity than heterosexual men and women.	"Our findings support fundamental cause theory and suggest that unequal distribution of health-protective resources, including knowledge, prestige, power, and supportive social connections, might explain sexual orientation health disparities (p. 1109)."
Delavar et al (2020)	Retrospective cohort study using US Surveillance, Epidemiology, and End Results data. Children and adolescents diagnosed with a first primary malignant cancer were followed up. Race/ethnic differences in in survival for cancers for which death is more versus less preventable.	Compared with non-Hispanic white children and adolescents, a significantly higher risk of death was observed for high- than low-amenability cancers for non-Hispanic black patients.	"We found racial/ethnic disparities in childhood and adolescent cancer survival for non-Hispanic black, non-Hispanic American Indian/Alaskan Native, non-Hispanic Asian or Pacific Islander, and Hispanic (any race) patients. These disparities were larger overall for more survivable cancer types, which are generally more amenable to medical intervention (p. 435)."
Ericsson et al (2019)	Study conducted to investigate socioeconomic differences in mortality by comparing preventable with non-preventable causes of death in participants from the Swedish Twin Registry.	SES gradients by education and occupation were observed and were not explained by family or genetic factors that the twin study allowed the authors to assess. In cohort analysis results the hazard ratio associated with having an occupation of low versus high standing was higher for high-preventability causes of death versus for low-preventability causes.	"There was a social gradient in both preventable mortality and non-preventable mortality, but with an indication of a moderately stronger effect in preventable causes of death (p. 1701)."
Kiadaliri and Englund (2020)	Studied over 92,000 people with osteoarthritis (OA) in Sweden following them for an average of 6.5 years for high preventability versus low preventability causes of death.	There were educational gradients for both more avoidable and less avoidable causes of death. The magnitude of relative educational inequality was greater for more avoidable than less avoidable Causes.	"The Results suggest that educational attainment is a fundamental cause of inequality in OA." (p. S448)
Mackenbach et al (2015)	Harmonized mortality data by educational level on 19 national and regional populations from 16 European countries to assess relative risk of mortality among men and women aged 30–79 for 24 causes of death classified into four groups: amenable to behavior change, amenable to medical intervention, amenable to injury prevention, and non-preventable.	Lower education is associated with elevated risk for regardless of preventability, but the relative risks are generally higher for diseases that are more versus less preventable. The median relative risk for low education for preventable causes is 2.15 for men and 1.90 for women whereas for low preventability causes they are 1.53 for men and 1.43 for women. Across countries/regions low education relative risks for men and women separately were higher for diseases preventable by behavior change than for low preventability diseases in all country wide comparisons (24/24), and 30/35 possible comparisons when regional studies conducted in Spain and Italy were included.	"Our results provide some further support for the theory of "fundamental causes". However, the absence of larger inequalities for preventable causes in Southern Europe and for injury mortality among women indicates that further empirical and theoretical analysis is necessary to understand when and why the additional resources that a higher socioeconomic status provides, do and do not protect against prevailing health risks." (p. 60)
Mackenbach et al (2017)	Harmonized mortality data by educational level for 22 causes of death and 20 In European populations 1980–2010). Educational differences in rate of decline among four categories: amenable to behavior change, amenable to medical intervention, amenable to injury prevention, and low preventability.	Mortality declines more rapidly over time for more highly educated than less highly educated people. The largest differences in mortality decline between low and high educated people are for causes amenable to behavior change. Mortality *increases* by 0.80 per cent per year among the low educated but *declines* by 0.93 per cent per annum among the high educated. Differences between low and high educated are also observed for conditions amenable to injury prevention and are smallest for low preventability conditions.	"While our results provide support for the fundamental causes theory, our results suggest that other mechanisms than the theory implies also play a role." (p. 1117)

Author/Year	Descriptions	Results	Author Quote
Masters et al (2015)	19 waves (1986–2004) of the National Health Interview Survey are linked to official death records up at the National Death Index (NDI). The resulting file provides annual individual-level cause-specific mortality status for over 900,000 Black and White, males and females in the United States through December 31st, 2006.	Cohort-based reductions in mortality are larger for more preventable causes of death and, consistent with FTC, the greatest reductions in these deaths occurred among the more highly educated populations. But there were inconsistencies in this general conclusion when results are broken down by race and gender.	"Overall, findings are consistent with nearly all features of fundamental cause theory. Results show, first, larger education gradients in mortality risk for causes of death that are under greater human control than for less preventable causes of death, and, second, that these gradients grew more rapidly across successive cohorts than gradients for less preventable causes. Results also show that relative sizes and cohort-based changes in the education gradients vary substantially by race/ethnicity and gender" (p. 19)
Rydland et al (2020)	More versus less preventable morbidities were identified in the 2014 European Social Survey of 12,073 men and 13,488 women aged 25 to 69 from 20 countries.	In both men and women, the proportion of educational gaps were larger for the high-preventable than the low-preventable conditions in most countries. In the pooled conditions and countries analysis, no associations were significant among the low-preventable conditions. For the high-preventable conditions there were significant but modest educational gaps in both men and women.	"In a first explorative comparative European analysis we found support for the FCT hypothesis. Thus, the FCT can be used on morbidity data classified as low- versus high-preventable. We recommend extending this framework with institutional theories to explain within- and between-country health inequalities (from prepublication)"
Tehranifar et al (2016)	51 cancer sites were classified into least amenable, partly amenable, and mostly amenable cancers. Cox regression models, on 516,939 cancer cases diagnosed between 1995–1999 examined whether racial disparities in mortality rates varied according to the amenability associated with a cancer site.	Blacks and Hispanics diagnosed with partly and mostly amenable cancers had higher mortality rates relative to whites with cancers of the same amenability levels; further, these differences decreased in magnitude or reversed in direction with increasing age. In contrast, the racial differences in mortality were smaller and remained fairly constant across age groups for least amenable cancers.	"Cancer survival disadvantage for racial minorities is larger in younger age groups for cancers that are more amenable to medical interventions (p. 553)."
Vanthomme et al (2017)	Data were from a record linkage study between the Belgian censuses of 1991 and 2001 and register data on mortality. The study population comprised all Belgian men aged 50–79 years during follow-up.	Despite an overall downward trend in cancer mortality, educational differences are observed for the majority of cancer sites in the 2000s. Generally, inequalities are largest for mortality from preventable cancers.	"Educational differences in site-specific cancer mortality persist in the 2000s in Belgium, mainly for the more preventable cancer sites" (p.480).
Zapata Moya et al (2015)	Data from three waves of the Spanish National Health Survey (collected between 2003 and 2010), and European Health Survey in Spain examined education gradients in more (depression, diabetes and myocardial infarction) versus less (malignant tumors) preventable diseases.	Education gradients in more-preventable illness are observed, while this is far less the case in our less-preventable disease group.	"However, as expected (Hypothesis 1) based on the Fundamental Cause Theory, educational gradients are only observed for the relatively more-preventable ill-nesses (depression, diabetes, and myocardial infarction), and not for the less preventable (malignant tumors) (p. 148)."
		Preventability Shifts	
(Clouston et al 2014b)	Age, race, sex, specific mortality rates for suicide among U.S. residents 25 years or over (1968–2009) were derived from death certificate and population data from the National Center for Health Statistics. Change in associations between county-level SES and suicide (prevention knowledge developed) mortality are compared.	Suicide mortality rates are initially similar in higher SES counties but shift upon the distribution of antidepressant medications (SSRIs) in lower SES counties are at greater risk and by 2009 the difference in mortality between counties with SES one SD above compared to one SD below grew substantially following the distribution of SSRI medications.	"We found support for the theory that SES based disparities in suicide arose with the widespread dispersal of SSRIs, which were concentrated in areas of higher SES. (p. 7)"
Rubin et al (2014)	Age, race, sex, specific mortality rates for lung and pancreatic cancer for people 45 years or over (1968–2009) were derived from death certificate and population data from the National Center for Health Statistics. Change in associations between	Lung cancer mortality rates are initially higher in higher SES counties but by 1980 persons in lower SES counties are at greater risk and by 2009 the difference in mortality between counties with SES one SD above compared to one SD below average was 33 people per 100,000. In contrast, for pancreatic cancer	"These data support the fundamental cause hypothesis: social conditions influencing access to resources more greatly impact mortality when preventative knowledge exists (p. 54)"

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Author/Year	Descriptions	Results	Author Quote
	county-level SES and lung (prevention knowledge developed) and pancreatic cancer (little prevention knowledge developed) mortality are compared.	where changes in preventability did not occur, people from higher SES counties were slightly more likely die of this cause with the association remaining relatively stable over the period of observation.	
Saldana-Ruiz et al (2013)	Data from the National Center for Health Statistics were used to calculate age-, gender-, and race-specific colorectal cancer mortality rates for counties in the continental United States (1968 to 2005). Change in associations between county level SES and colon cancer morality before and after screening improvements are examined.	Prior to 1980, people living in counties of higher socioeconomic status (SES) were at greater risk than people living in lower SES counties. Beginning in 1980, this gradient began to narrow and then reversed as people living in higher SES counties experienced greater reductions in colorectal cancer mortality than those in lower SES counties.	"Our findings support the fundamental cause hypothesis: once knowledge about prevention and treatment of colorectal cancer became available, social and economic resources became increasingly important in influencing mortality rates" (p. 99).
Wang et al (2012)	Mortality data (1968 to 2008) from the National Center for Health Statistics are used to calculate age-, gender-, and race-specific colorectal cancer mortality rates for counties in the United States. Changes in associations between county level SES and colon cancer mortality and a State-level of diffusion of innovations score and colon cancer mortality were examined before and after screening improvements were developed.	Beginning in the 1980s, the impact of county SES on colorectal cancer mortality developed into an inverse association (high SES lower mortality) and grew over time. States with a propensity for faster diffusion experienced faster reductions in mortality over this period. Finally, the tendency for rapid diffusion had a moderating impact on the influence of SES: the influence of SES was attenuated in states with a higher propensity for faster diffusion	"By examining geographical and contextual factors, we confirm the importance of fundamental cause theory in determining how social disparities in colorectal cancer arise (p. 613)."
Zapata-Moya et al (2019)	50 to 69-year-old participants in the Onco-barometer survey (2010) of the non-institutionalized Spanish adult population in 2010. Assessed socioeconomic differences in access and use of health screens according to the stage their stage in the diffusion cycle.	SES was associated with use of cancer screening tests (PSA tests, Pap smears and mammograms), but not for preventive practices at early diffusion stage, like fecal occult blood tests, and for cardiovascular diseases (blood-pressure checks and cholesterol readings) that are in a late stage of diffusion. SES inequalities varied according to diffusion stage being smaller in the early stage of diffusion, growing in the intermediate stages and declining in the late stages of the diffusion process.	"Taken together, FCT and DOI theory can provide an integrated framework with which to study health inequalities in the adoption of preventive practices from a temporal and comparative perspective (p. 191)."
Manipulated Preventability			
Bann et al (2016)	70–89-year-old participants of a multicenter lifestyle intervention study using individuals randomized to a structured physical activity program. Assessed the incidence of mobility disability among higher and lower SES participants.	The benefits from the intervention seeking to reduce incidence of mobility disability via increased physical activity were concentrated among participants with some postgraduate education. Trends were evident in associations with income alone but were not statistically significant.	"the benefits of a physical activity intervention in preventing mobility disability did not significantly differ by socioeconomic group, yet effect sizes of intervention benefits were largest among those with higher education or income." (p. 931)
Grytten et al (2020)	Studied the staggered implementation of a school reform that increased the length of compulsory education from seven to nine years in Norway. Follow-up for high versus low preventability until maximum age 64.	The estimated effect was of the policy change as it was rolled out over time in Norway and not educational attainment per se. The regression coefficient for being exposed versus unexposed to the reform led to a reduction for preventable deaths. For causes of death that could not be prevented, the estimate was small and not statistically significant.	"Our results supported the fundamental cause theory. This is because education had a stronger effect on mortality for causes of death that are preventable than for causes of death that are not preventable. More education had no effect on the probability of dying of diseases that were amenable to medical intervention only (online prepublication)."
Yang et al (2014)	Patients at 31 Belarusian maternity wards and their affiliates were randomized to receive breastfeeding promotion interventions	The promotion of breastfeeding resulted in graded inequalities in the intervention group by maternal education that were not evident in the control group.	"Our study intervention, which was designed to promote prolonged and exclusive breastfeeding, slightly widened socioeconomic inequalities in discontinuation of exclusive breastfeeding by 3 months and of any breastfeeding by 12 months." (pg. 1291)

Author/Year	Descriptions	Results	Author Quote
Zapata Moya and Navarro Yanez (2017)	Quasi-experimental design examining differences in standardized mortality rates between neighborhoods that were participating in urban regeneration processes versus those without ongoing regeneration projects.	Areas where urban regeneration projects were active experienced increases in SES inequalities in more preventable, but not less preventable, causes of death	“Area-based initiatives improve the opportunity structure by providing different types of flexible resources to residence, which may mediate the well-documented inverse relationship between SES and mortality risk.” (pg. 245)

[1] **Disease Preventability** examines the association between SES and mortality across multiple disease outcomes that vary in the preventability of death; **Preventability Shift** examines particular diseases over time before and after changes in our capacity to address mortality from that particular disease occurred; **Manipulated Preventability** examines inequalities emerging during controlled trials in which exposure to an intervention is randomized.