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Invited Perspective: The Mysterious Case of Social Determinants of Health

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Epidemiology is rooted in the social sciences. For example, Mervyn Susser's influential writings[1] on causality refer to Robert Merton's sociology. Complexity and networks are inherent in causal reasoning. However, beginning around the 1980s, epidemiologists increasingly aimed to identify single causes of disease. Randomized controlled trial methodology allowed a more robust identification of single cause–effect relationships. Where randomization was not feasible, efforts were put into isolating and adjusting for confounders. This shift toward so-called risk factor epidemiology enabled researchers to identify many causes of common diseases and estimate attributable proportions, that is, the share of a disease that can be attributed to single risk factors. But these advances came with a cost: Social determinants of health were largely relegated to the realm of "residual confounding." Fortunately, epidemiologists are now rediscovering the importance of these factors.

The review by Neufcourt et al.[2] in this issue of *Environmental Health Perspectives* addresses social determinants of health in the context of exposome research. The exposome framework acknowledges the limitations of risk factor epidemiology by considering multiple exposures (in principle, all of them) over the life course perspective, and mentions the "social exposome" within the "general external" exposome, one of three main components of the overall exposome. The other two components are the "specific external" exposome (encompassing, e.g., classical behavioral risk factors and chemical exposures) and the "internal" exposome (usually based on untargeted measurements of molecules in body fluids or cells).[3] In particular, the authors call for social factors to "be considered in a more systematic way considering their role in structuring both the specific external and the internal exposome."[3]

The inclusion of a social exposome within the overall exposome framework is a huge step forward because it acknowledges that social determinants can play an autonomous role in disease causation through, for example, psychosocial stress. By including the temporal dimension, the exposome framework also implicitly introduces a hierarchy between overarching determinants (which may have a long-term impact) and more circumstantial and variable determinants. A clear example is adverse childhood events (ACEs)—such as violence, neglect, and abuse—and their associated traumas. There is much literature on the association between ACEs and later health effects, such as cardiovascular disease, diabetes, obesity, and mental health problems.[4] The sometimes-lengthy latency of these effects implies a chain of intermediate mechanistic events.

I always found the approach of risk factor epidemiology to social inequalities to be weak. When socioeconomic status (SES) was controlled for, it seemed that something was artificially distorted in the causal framework. When SES was considered as such, it still remained something residual and somehow "metaphysical." In classical noncommunicable disease epidemiology, for example, a proportion of a disease is attributed to smoking, another proportion to alcohol consumption, another to obesity, and so on. These estimations are often adjusted for SES, which implies that the effect of SES is a residual variable of minor interest; if an effect of SES persists after adjustment, we do not know what it is. In addition, isolating single risk factors, mainly behavioral, has led to a conception of prevention largely focused on individual choices rather than considering the structure of society and the long-term effects of deprivation.

Although social inequalities can definitely act via behaviors, such as smoking, diet, and alcohol consumption, the picture that emerges from recent research[5] is more complex than the traditional one cause–one effect paradigm, where "extraneous" variables—such as SES—were dealt with as confounders. Michael Marmot has written that only 50% of social inequalities in health can be explained by classical risk factors, whereas the rest can be due to "status syndrome"—or social standing—in its manifold manifestations and via multiple mechanisms.[6,7] This thesis has been partially supported by empirical evidence showing associations between social inequalities and mechanistic pathways investigated with omic markers.[5] In fact, research has shown that social inequalities can act across multiple biological layers, including physiological changes (such as body weight and blood pressure) and molecular changes (reflected by epigenetic, transcriptomic, proteomic, and metabolomic markers), down to disease onset.[5,8] It is unlikely that associations between all these biological layers and social inequalities are explained away by behavioral variables, such as smoking.[9] Therefore, the best approach seems to be to consider social inequalities as overarching determinants; from these, other intermediate events follow, including ACEs, individual behaviors, yet-unidentified exposures, and more elusive factors, such as psychosocial stress.

In summary, there are many gaps in the epidemiological research on social inequalities in health, which Neufcourt et al.[2] started to identify in their review—in particular, conceptual and practical gaps on how inequalities are defined and measured in exposome research. For example, the same surface variable (e.g., education) can mean something different in a different historical time or cultural context. Much research is still needed, for example, on the best way of treating data. One promising approach is mediation analysis. This approach acknowledges the hierarchical nature of causal models and treats social inequalities and ACEs as upstream, overarching complex variables while also considering intermediate events, such as behaviors and mechanisms, including biomarkers and omic measurements.[10] It is a far cry from the simplistic inclusion of SES as a confounder.

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References

1. Susser M. 1973. *Causal Thinking in the Health Sciences: Concepts and Strategies of Epidemiology*. Oxford, UK: Oxford University Press.

2. Neufcourt L, Castagné R, Mabile L, Khalatbari-Soltani S, Delpierre C, Kelly-Irving M. 2022. Assessing how social exposures are integrated in exposome research: a scoping review. Environ Health Perspect 130(11):116001, https://doi.org/10.1289/EHP11015.
3. Wild CP. 2012. The exposome: from concept to utility. Int J Epidemiol 41(1):24–32, PMID: 22296988, https://doi.org/10.1093/ije/dyr236.
4. Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, et al. 2017. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health 2(10):e356–e366, PMID: 29253477, https://doi.org/10.1016/S2468-2667(17)30118-4.
5. Vineis P, Avendano-Pabon M, Barros H, Bartley M, Carmeli C, Carra L, et al. 2020. Special report: the biology of inequalities in health: the LIFEPATH Consortium. Front Public Health 8:118, PMID: 32478023, https://doi.org/10.3389/fpubh.2020.00118.
6. Marmot M. 2004. *The Status Syndrome: How Social Standing Affects Our Health and Longevity*. London, UK: Bloomsbury.
7. Stringhini S, Carmeli C, Jokela M, Avendaño M, Muennig P, Guida F, et al. 2017. Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1·7 million men and women. Lancet 389(10075):1229–1237, PMID: 28159391, https://doi.org/10.1016/S0140-6736(16)32380-7.
8. Carmeli C, Kutalik Z, Mishra PP, Porcu E, Delpierre C, Delaneau O, Kelly-Irving M, et al. 2021. Gene regulation contributes to explain the impact of early life socioeconomic disadvantage on adult inflammatory levels in two cohort studies. Sci Rep 11(1):3100, PMID: 33542415, https://doi.org/10.1038/s41598-021-82714-2.
9. Vineis P, Delpierre C, Castagné R, Fiorito G, McCrory C, Kivimaki M, et al. 2020. Health inequalities: embodied evidence across biological layers. Soc Sci Med 246:112781, PMID: 31986347, https://doi.org/10.1016/j.socscimed.2019.112781.
10. Laine JE, Baltar VT, Stringhini S, Gandini M, Chadeau-Hyam M, Kivimaki M, et al. 2020. Reducing socio-economic inequalities in all-cause mortality: a counterfactual mediation approach. Int J Epidemiol 49(2):497–510, PMID: 31855265, https://doi.org/10.1093/ije/dyz248.