COMMENTARY

Social-to-biological transitions research: review of progress and development

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The present text builds on an earlier publication* which had the same aim: namely, to encourage clarity and coherence in the interdisciplinary area we called social-to-biological transitions. This burgeoning area of research involves a complex workforce with differing career levels and disciplinary traditions, reflecting which the present authors comment from different perspectives (one author from each of early career research, epidemiology, biology and public health) and invite debate. (* Blane, D., Kelly-Irving, M., d'Errico, A., Bartley, M. and Montgomery, S. (2013) Social-biological transitions: how does the social become biological?, *Longitudinal and Life Course Studies*, 4(2): 136–46.)

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Key messages

- The authors of this commentary conclude a number of ways to further mature social-to-biological research:
- learning to integrate the big picture (social structure, history, economics) with meticulous statistical analysis;
- thinking more clearly about the balance between conceptual validity and pragmatism in our measures and concepts; and
- developing the integration of omics technologies, together with the exposomics of lived existence in a social world.

Introduction

Social-to-biological transitions research offers a way of answering questions about how the social becomes biological: how social circumstances get into the molecules, cells, tissues and systems of the body to produce socially patterned differences in health, life expectancy and cause of death (*how life gets under your skin*[1]).

One way of answering such questions involves the statistical analysis of information collected by large, longitudinal, population-representative surveys that measure with equal care and precision both the social and biological characteristics of individuals. Such data are hard to collect, and expensive, so it is important to make best use of them, in terms of scientific productivity and accuracy of findings, by competent documentation and open availability, once anonymised, from a data archive.

Globally, among the studies that meet some or all of these criteria are the Nordic linked registers, France's CONSTANCES, UK Household Longitudinal Study, Work History Italian Panel-Health Study, USA National Institute for Aging's international portfolio of studies of ageing and the 1958, 1970 and Millennium British birth cohorts. As these resources demonstrate, the area is clearly of great interest to research scientists, supported by large amounts of taxpayers' money via major national and international funders of scientific research. In this sense it can be described as potentially a progressive research programme although, to mature, it might benefit from greater coherence and evidence of cumulative and replicable knowledge, to which process the present comment and debate hopes to contribute.

Method

We pursued this initiative via the Inter-disciplinary Health Research group of the Society for Longitudinal and Life Course Studies (SLLS), which, for some years at each of its annual conferences, has hosted a symposium titled Social-to-Biological Transitions Research: Recent Findings from Europe. The Society's Officer extracted from her archive the relevant symposium abstracts for 2017–21, which were reviewed independently by the four authors, including the initiative's student volunteer early career researcher. The four sets of comments were presented to a Panel Discussion at SLLS Annual Conference 2022, from which comes the present text. We are conscious of its Eurocentrism and look forward to having our thoughts broadened by the reaction of our SLLS colleagues in other continents.

Before going to our individual contributions, we make two general observations. First, such research is only possible because some of us collect, document and archive the data; work which deserves high professional respect and commensurate career promotion. Second, we might pay more attention to the relationship between the *longitudinal* and the *life course* parts of our remit: sometimes, longitudinal data are used from only one part of the normal life course; to complete the life course picture and widen our readership, perhaps we need to think about how our findings fit into the life course models we are

trying to explore and explain, by considering as a matter of routine both early precursors and late life consequences. To paraphrase Claude Bernard, we should remember that we take things apart in order to measure them more precisely, but we must not forget to reassemble the parts in order to see what we have learnt about the whole.

Individual takes

Author 1

In reviewing recent symposia abstracts, I found the breadth and diversity of the presented literature striking, lending me a greater appreciation of the interdisciplinary context provided by the SLLS Inter-disciplinary Health Research group (SLLS-IHRg). It also became increasingly apparent that prevalent concepts like the *life course* and *health* hold a variety of meanings to different academic disciplines and other social groups. Without consensual conceptual clarity, the validity of a measure cannot be addressed, however hard one works on its reliability. I also began to suspect that concepts taken as concrete, like the hypothalamic-pituitary-adrenal (HPA) axis, might more accurately be described as hypotheses, drawing an arbitrary line around one part of the body's interconnected biological systems, presenting only part of a complex whole.

I found great value in the fact that the SLLS brings together researchers from different generational and geographical contexts, adding depth of knowledge to contemporary scientific innovation. Reviewing symposia abstracts has worked to highlight a number of conceptual and methodological points to take forward into future social-biological life course research: when using directed acyclic graphs (DAGs) to address causality in population research, it is worth equally considering that plausibility, whether social, biological or both, is one of Bradford Hill's criteria for inferring causality in non-experimental science. Similarly, in harmonising data from international or cohort studies, an emphasis might be placed on replication, which has long been considered the difference between a study finding and an actionable scientific fact.

The intergenerational nature of the SLLS-IHRg can also add a critical edge to contemporary developments. In using area deprivation as a stand-in for social class, it might be useful to consider how to address the ecological fallacy – how can we use data more effectively to avoid inference errors? When using routine medical records as a substitute for population-representative social surveys (and similarly, health diagnoses data within social surveys) issues like the clinical iceberg should be considered: is there a social pattern to those who do not meet our cut-points? When deriving a longitudinal analytical sample, it is useful to consider how far selective attrition might bias the final sample; how far might longitudinal studies lead us to misestimate the size of social and health inequalities in the whole population? And, when advocating for the usage of biomarker data, it is beneficial to remember that, as yet, there has been a lack of reliable evidence for biomarkers that causally predict one of the most prevalent types of morbidity (mental illness) and, short of biopsy or autopsy, for the most prevalent cause of death (cancer).

Author 2

We dedicated much attention to the conceptual and methodological questions arising from composite biomarker measures like allostatic load, or the metabolic syndrome

in the early years of the research group. This work was important in establishing why these measures were/are of interest when working on social-to-biological questions, such as examining their social pattern. It also allowed us to highlight important methodological issues arising from their use, namely, their ability to capture internal physiological processes. This work also points to our interest, as a scientific community, in getting to grips with overall meaningful 'adaptive' internal biological processes, rather than markers of much more specific biological phenomena. Such measures that endeavour to capture overall processes are related to a number of others used to measure ageing or fragility, but with the advantage of being relevant at earlier stages of the life course.

This brings me to my second remark, which is that fewer works examined biomarkers in childhood and adolescence. Therefore, we still lack visibility about how social-to-biological processes operate within a life course perspective. When do the social differences across allostatic load, or individual biomarkers become marked? Does this vary by biomarker? An important question that remains to be examined stemming from this is: can social differences in biomarkers change over the life course? In other words, can people 'reverse' the effects of social determinants on biological processes?

Finally, the role of education as a consistent mediating variable between a given social exposure, such as social class, and one or several biomarkers, has been noted repeatedly. However, the hypothesised mechanisms of this mediating role remain underexplored. Sociological theories such as the transmission of cultural capital, or psychological theories around the locus of control, or indeed many other theories, deserve to be examined as part of the social-to-biological processes operating via education from early life.

Author 3

Much of the work included in this review takes a social epidemiological perspective – that the social environment determines health rather than vice versa. However, it appears in the work presented that we have a limited set of social exposures. Europe and especially the UK is blessed with a range of representative social surveys that have had biology added to their protocols. The content is designed to enable researchers to investigate social determinants of health, with rich and detailed measures of the social environment, rich and detailed biology coupled with measures of health across the entire adult age range.

As a biologist I am pleased to see the work on the biological pathways by which the environment might be associated with health through investigations of both specific pathways, for example inflammation, to broader concepts such as allostatic load or biological age. In addition to the pathways driven approaches already noted, recent technological advances in so-called '-omics' mean that there is potential to pinpoint pathways using systems or total approaches to analyses. A number of population studies now include genomic, proteomic and metabolomic data to enable this whole systems research.

Much of the work presented is descriptive; perhaps this is feature of social epidemiology, given that this field is less amenable to experimental studies such as interventions that make long-term change. However, the availability of data sets such as the birth cohorts and household panel studies, with their repeated collection of

biological data, should enable a range of activity that take a more causal or policy relevant approach than simple description. This includes the use of DAGs, 'natural experiments', Mendelian randomisation and machine learning, each with their own limitations that need exploring.

Perhaps a feature of the need for high quality and expensive data collection is that the studies presented are largely limited to the Global North, which obviously represents a gap, given that the interest is social differences in health.

Author 4

I was struck by how many of the presentations reported undesirable health outcomes preceded by social disadvantage (see later for details). The reported health outcomes are many and varied but their association with some form of prior social disadvantage is constant, replicable and, in principle, preventable. Also noticeable is that in most cases the reported effect sizes are quite small. Taken together, these aspects of the presentations are consistent with a socially and biologically plausible explanation of social class differences in both all-cause mortality and positive health (by which I mean optimum growth and development during childhood and adolescence; maintenance of maximal functioning into midlife; and resilience to the adversities of older age): namely, that they result from a constellation of misfortunes or benefits, each perhaps quite minor on its own, which cumulate and interact across the life course. In other words, social class could be the causal factor because it drives the process of cross-sectional clustering and longitudinal accumulation of advantage and disadvantage. One way of developing social-to-biological transitions research might be to develop ways of testing such hypotheses.

List of symposium abstracts

- For those employed in the most disadvantaged occupations, working longer at older ages increases their risk of hospitalisation with heart attack or stroke (Ardito et al, 2019).
- LIFETRAIL results for a variety of health outcomes mostly fit with the generalised Strachan-Sheikh model, where childhood socio-economic circumstances affect the biological phase of growth and development and adult socio-economic circumstances affect the phase of biological decline (Cullati and Blane, 2019).
- Adversity at older ages (living alone; urinary incontinence; clinical depression) increases the risk of hospitalisation after a fall (Abell et al, 2019).
- Concussion, which is more common among those employed in hazardous occupations, is followed by an increased long-term risk of irritable bowel syndrome (Montgomery et al, 2019).
- Painful respiratory tract infections during the first two years of life, which are more common in crowded residences, are more likely to be followed by low stress resilience in late adolescence (Montgomery et al, 2018).
- Adults whose parents were employed in disadvantaged occupations are epigenetically older, by one Hannum year, than those who had more advantaged parents (Hughes et al, 2018).

- Disadvantaged socio-economic circumstances in early life are associated with poor lung function at older ages (Cheval et al, 2018).
- Those employed in disadvantaged occupations for the past 20 years had poor objective metabolic, cardiovascular and immune health (Hoven et al, 2021).
- Children whose family culture is at odds with that of their school teachers have higher allostatic load scores in midlife (Joannès et al, 2021).
- Divorce and death of spouse at older ages are associated with increased mortality risk (Abell, 2021)
- The children of those employed in disadvantaged occupations were physically shorter during 1946–2001 and lighter during 1946–70; and more likely to have a higher body mass index in adulthood (Hardy et al, 2018).
- Children raised in deprived socio-economic circumstances had lower physical capability in early old age (Caleyachetty et al, 2017).
- Childhood socio-economic disadvantage during 1958–70 was associated with poor mental wellbeing in adulthood (Wood et al, 2017).
- Parental economic adversity during childhood was associated with hearing impairment in early old age (Lassale and Zaninotto, 2018).
- Those who completed fewer years of schooling were at higher risk of experiencing adversity in early old age (Vanhoutte, 2018).
- Perinatal stress is mitigated by paid maternity leave and family allowances (Avendano et al, 2018).
- Those employed in occupations with reduced-hours flexible working arrangements have lower levels of allostatic load (Chandola, 2019).
- Maternal depression and poor child physical health reduce formal school performance (Sullivan et al, 2019).
- Midlife mental health is associated 13 years later with income, quality of life, social participation, economic activity and partnership status (Ploubidis et al, 2019).
- Disadvantaged socio-economic circumstances in childhood predict weak muscle strength in early old age, partly as a pathway to adult social class (Cheval, 2017).
- Socio-economic deprivation during the first year of life is associated with Epstein-Barr virus infection at age 3 years (Garès, 2017).
- The number of older siblings predicts low stress resilience in late adolescence (Montgomery, 2017).
- Adverse childhood experiences (not living with biological parents; death of parent; periods of hunger; property taken away; adolescent parenthood; stillborn child in adolescence) are linked to frailty at older ages (van der Linden et al, 2018).

Summary and conclusion

Our focus on the social as the driver of health does not imply that we deny biology's ability to impact the social: the Black Death, which depopulated Europe in the 14th century, is a well-known example that helped to end feudalism by increasing the value of the workers who survived. Rather, we focus on the social as the driver of health because it has been documented as a statistical association or pattern for at least the past two centuries, a fact which the combination of increasing life expectancy,

an unchanged social class structure and the life course natural history of chronic degenerative disease may help to explain.

Among the points made in the four 'Takes' are a number of ways such social-to-biological transitions research could be further pursued. First, is the challenge of integrating the big picture (social structure, history, economics) with meticulous statistical analysis. Early career training and experience in the analysis of large and complex data sets teaches a skill that is in high demand, but it is the big picture that asks the important research questions. Here intergenerational discussions of, for example, the clinical iceberg, Bradford Hill criteria and shifting distributional cut-points can be useful. The importance of pursuing research on social-to-biological processes across the range of human populations and habitats was raised. The lack of research on non-White populations has been partly due to the paucity of appropriate data, however these are increasingly being collected worldwide. As we develop our research in different populations, we will be able to sketch a landscape of the broader context of situated human biologies.

Second, it might help to think more clearly about the balance between conceptual validity and pragmatism in the social and biological concepts we commonly use. For example, many studies use education (dictionary definition: the process of acquiring knowledge and understanding; see Collins Dictionaries, 1995) as a social measure, which is often operationalised as length of formal schooling. While this approach has the benefit of being easily harmonisable across data sets, it also has the double disadvantage of ignoring the university of life and being significantly determined by parental affluence; using the number of languages a person speaks might be closer to the concept. Similarly, many studies use allostatic load, body mass index or metabolic syndrome as ready-made biological measures without thinking about their suitability for the hypothesised social-to-biological pathway being investigated, nor their endocrine and neurological links to other parts of the body's homeostatic mechanisms.

Third, recent technical advances in the efficient analysis of many analytes in smaller and smaller samples have created interest in the -omics technologies of genomics, transcriptomics, proteomics and metabolomics, together with the exposomics of lived existence in a social world. Collaboration with both biologists and sociologists will be required to pursue this opportunity, which often raises questions about the nature of causality in non-experimental science. Here, we should take heart from astrophysics where the impossibility of manipulating causal variables did not prevent the moon landings. Rather it should remind us that social and biological plausibility in social-to-biological research and the replication of its findings can be a useful alternative to laboratory manipulation.

Finally, we offer an example of how the findings of recent studies can be aggregated to generate hypotheses which are potentially testable.

Note

[1] See Bartley, 2012, about which one UK science journalist said: 'one of the best examples of science communication I've ever seen' (Goldacre, 2012).

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Data availability statement

The authors take responsibility for the integrity of the data and the accuracy of this analysis. The data on which this review is based consists of abstracts from previously archived SLLS symposia, which can be accessed at: https://www.slls.org.uk/pages/conference-archive.

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Conflict of interest

The authors declare that there is no conflict of interest.

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