Biosocial health geography: New ‘exposomic’ geographies of health and place

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Abstract
Investigating biologically plausible mechanisms for the embodiment of context is a key thoroughfare for progressing health geographies of place. Expanding knowledge of bio-processes such as epigenetics is providing a platform for appreciating the dynamic embedding of social relations in bodies over the lifecourse, and so to tracing the development of health inequalities. By providing a geographic lens on the biosocial, health geographers have key contributions to make regarding the theorisation of place. We put forward the exposome as a holistic framework in which to situate a biosocial health geography, placing ideas of dynamic exposure, plasticity and temporality as central.

Keywords
biosocial, exposome, health geography, health inequalities, lifecourse, place

I Introduction
A theme of exposure and exposures underlies work aiming to reveal the complexities of geographies of health. There is a substantial literature investigating relationships between health and place (Brown et al., 2010, 2017; Gatrell and Elliott, 2009) and a variety of place-based exposures have been linked with a range of health outcomes, including for example, cardiovascular disease incidence, risky health behaviours and depression (Diez Roux et al., 2016; Diez Roux and Mair, 2010; Malambo et al., 2016; Richardson et al., 2015). Research is often focused on specific – in temporal and spatial senses – risk factors, toxins or social features, the emphasis being on this or that place, green space, community networks or distribution of services. We argue in this paper that a perspective of continual accumulating exposure, foregrounded by a Hägersträndian time geography of lifepaths, can be achieved through a biosocial...
By interrogating the imprint of entangled biological and social exposures new insight may be uncovered into the fluid nature of health and place relations, helping to address key lacunae in our current knowledge.

Gaps currently exist in our understanding of the means through which places transmit to individuals and the action of these processes over time. The increasing use of longitudinal data as well as developments in lifecourse modelling provide a means to address this problem (Lekkas et al., 2017; Mishra et al., 2009; Ruijsbroek et al., 2016; Sabel et al., 2009). However, much of the work through which we comprehend health and place remains based upon cross-sectional analyses or short-run temporal windows. For example, over 70% of the US-based studies reviewed by Arcaya et al. (2016) were cross-sectional. The implied assumption of simultaneity of effect not only lacks plausibility in many cases, but also hinders insight into the long-term, accumulated imprints of exposure.

The biological mechanisms for the embodiment of place represent a second void in the health and place literature. There is an established epidemiological literature that has taken up the ‘bio’ in the form of biomarker assessments, recognising the usefulness of bioprocesses such as epigenetics and feedbacks of the stress system to accessing the temporality of health relationships (Ben-shlomo and Kuh, 2002; Gustafsson et al., 2010; Ploubidis et al., 2014; Tehranifar et al., 2018). However, to date there have been relatively few attempts to integrate biosocial ideas with insights from the health and place literature, meaning geographers have important insights to add. More specifically, although biosocial ideas speak to the plasticity of biological development and the permeability of bodies, an integration with developments in the theorization of place – notably work on relational geographies – is lacking.

The paper that follows briefly explores the current linkages proposed in the health and place literature and highlights the current state of the art work. We revisit the developments in the theorization of place, the influence of local context, and health relationships that have emerged in the geographic and epidemiological literatures over the past 30 or so years, highlighting the potential of relational geographies and biosocial theory in combination as an avenue for fruitful inquiry. This integration is exploited to think about extensions to exposomic geographies and the use of the exposome as a holistic framework through which the complex how and when of health and place relationships may be addressed.

II Geographies of health and place

Geography, the context in which people live and become, has long been understood as important to health (Jones and Moon, 1992). A concern with place has dominated geographies of health in recent times. Health and place studies theorise and debate the role of local context in influencing health and wellbeing, privileging more-than-individual perspectives that appreciate the multi-scalar and social construction of life (Jones and Moon, 1993).

Place experienced a notable resurgence of interest in health studies starting from the early 1990s. This debate was stimulated by a need for a ‘new’ geography of health that would offer more socially informed discussions of health (Kearns, 1993). This ‘health geography’ was formulated as a progression from medical geographies utilising biomedical models focused on curative medicine and proximate causal interests (see also Philo, 2016). Medical geography was critiqued for its detached perspective, where context tended to be reduced to a spatial sense of location and uncritically employed as ‘container’ (Jones and Moon, 1993; Kearns, 1993). Furthermore, health geography brought an increasing connection to critical geographies.
through knowledge of the social production of health inequalities (Kearns and Moon, 2002). An increased awareness of place, and the structural systems in which place is embedded, reflected an enhanced sensitivity to difference (Hayes, 1999; Jones and Moon, 1993; Kearns, 1995; Kearns and Moon, 2002). Therefore, a concern with place was a central unifying theme to a reformed health geography that reflected growing socio-ecological models, the active role of local context and the importance of lived experience (Kearns, 1993; Kearns and Moon, 2002; Rosenberg, 1998).

Driven by these debates, there was a marked increase in health and place studies. From a quantitative research standpoint, there was an explosion of investigations that sought to demonstrate contextual effects on individual life chances (Kawachi and Berkman, 2003; Van Ham et al., 2012). The context versus composition debate was a recurring theme in these studies, the question being whether found associations were the result of ‘true’ contextual effects or whether they were a function of the characteristics of the individuals residing in that place. The concurrent propagation of multi-level techniques helped to inform this discussion by providing a means to simultaneously model at multiple scales of analysis.

From the plethora of multi-level studies feeding into the debate, studies identified significant associations of areal or neighbourhood socio-economic disadvantage with worse health outcomes. Contextual relationships were demonstrated for a broad spectrum of health measures and behaviours, for example: mortality (Bosma et al., 2001), self-rated health (Cummins et al., 2005), physical health (Voigtlaender et al., 2010), limiting and long-term illness (Gould and Jones, 1996; Malmstrom et al., 2001), cardiovascular diseases and risk factors (Sundquist et al., 2004), mental health (Mair et al., 2008; Skapinakis et al., 2005), as well as smoking and alcohol use (Duncan et al., 1999; Matheson et al., 2012). Review studies reveal the consistency in associations of disadvantage with poor health over time and across study designs and contexts (Arcaya et al., 2016; Diez Roux and Mair, 2010; Pickett and Pearl, 2001; Riva et al., 2007; Schüle and Bolte, 2015). Whilst many of these studies take up the use of ‘neighbourhood’ as terminology to refer to local context, the relationships identified are active across a range of scales and are not restricted to the urban setting ‘neighbourhood’ traditionally connotes.

Whilst the existence of an association between areal disadvantage and poorer health is widely acknowledged, inconsistencies exist with some studies not identifying statistically significant contextual variations, whilst the size and nature of effects can vary considerably by the health outcome measured and the contextual measures utilised (Riva et al., 2007; Schüle and Bolte, 2015). Additionally, selection effects and the historical sorting of ‘healthy’ and ‘unhealthy’ populations remains largely unaccounted for due to a lack of longitudinal studies, a point repeatedly highlighted in commentaries on the neighbourhood literature (see Diez Roux and Mair 2010; Hedman and Van Ham 2012). There remains ongoing uncertainty in the search for a definitive answer to the context versus composition debate and the substantive importance of place.

The context versus composition debate is one avenue through which researchers have tried to explain identified contextual associations. However, the dualistic divide imposed by the context versus composition dichotomy has been criticised for hindering knowledge of the dynamic entanglements of people and places (Cummins et al., 2007; Macintyre et al., 2002). The debate in part encouraged a predilection for identifying direct and independent areal associations (Riva et al., 2007). In response, researchers were urged to embrace the heterogeneity and multiscale nature of health relations (Cummins et al., 2007; Small and Feldman, 2012). Rather than searching for
elusive, overall effects ad infinitum, research addressing how different social and physical environments across the lifecourse may variously impact the health of populations was called for (Macintyre and Ellaway, 2003). In other words, research was in part refocused on the question of process, with theorising and testing plausible pathways linking places and health a central aim (Riva et al., 2007; Van Ham and Manley, 2012).

The call to investigate the mechanisms of place has produced an extensive literature, both quantitative and qualitative, revealing various features of health and place relations. Important factors have emerged along major topical themes which we will touch on here. Access to services, particularly health services, are of long-standing interest to health geographers, covering a range of facilities from primary health care, screening and prevention to services related to specific conditions such as mental health (Bissonnette et al., 2012; Ngamini Ngui et al., 2012; Rosenberg, 2014). The role of green space and features of the physical environment is a prominent theme. There has been extensive research emerging under a nexus between food, activity and the built environment (Rosenberg, 2016, 2017), where studies have examined the phenomenon of food deserts, access to recreational facilities and green spaces, physical activity and walkability (Bridle-Fitzpatrick, 2015; Ivory et al., 2015; Kurka et al., 2015; Schüle et al., 2017; Weimann et al., 2015). The concept of therapeutic landscapes is important in revealing the well-being that can be drawn from places, emphasising the role of lived experience and the embodied nature of landscape relationships (Bell et al., 2017; Finlay et al., 2015; Gesler, 1992; Hordyk et al., 2015). Social mechanisms have received attention from health geographers, with research evidencing the benefit of social capital (Bourdieu, 1986; Putnam, 2000) across a range of health outcomes (Aminzadeh et al., 2013; Kim et al., 2008; Murayama et al., 2015). Others have highlighted the complex dynamic operating between place, social capital and disorder, individual experience and health over time (Cattell, 2001; Hooper et al., 2015; Kuipers et al., 2012; Ross and Mirowsky, 2001; Steenbeek and Hipp, 2011).

This diversity of studies has provided insight into potential mechanisms of place and health relationships; deprivation and disadvantage in the form of poorer quality and access to resources, disordered environments, low social capital and discrimination are routinely identified as associated with poor health. However, there are still avenues to further our knowledge and unpack the black box of place and health. Key criticisms of place-focused health geography are the continuing lack of attention to the theoretical frameworks underpinning research, particularly regarding: the processes by which individuals become exposed to networks of disadvantage; the varying spatial-temporal shape of relations; and the mechanisms that operate at the porous interchange of people and places (Diez Roux and Mair, 2010; Rosenberg, 2017). We argue that to address these concerns and progress the discipline, health geographers should engage with biosocial theories and new understandings of bio-processes. The next section exposes how accessing the processes of biological embodiment can align health geography with theoretical developments in understandings of place and can further existing models of health and health inequalities.

III Process and plasticity

1 Relational geography and biosocial theory

To progress the health geography literature, we look towards an engagement with theoretical developments from across the social sciences. This is particularly relevant to quantitative health geographers, who have tended to rely on static notions of exposure, and uncritical assumptions of the causal power of space (Guthman and Mansfield, 2012; Kwan, 2013;
Rosenberg, 2017). Relational geographies are a pertinent thoroughfare to advancing health geography as they align with a focus on exposure and embodiment, on place and health.

A ‘relational turn’ has gained traction across geography disciplines since the early 2000s. The movement reflects a desire to move away from structuralist understandings, towards more mobile, open-ended and networked conceptualisations of space and place (Amin, 2004; Boggs and Rantisi, 2003; Jones, 2009; Murdoch, 2006). Relational thinking provides a processual understanding of space and place. It takes up post-structuralist thought on the interpretation of meaning and action in the interactions between heterogeneous actors, human and non-human (Jones, 2009; Murdoch, 2006). Under a relational lens, space and place are no longer formulated as containers of process, existing absolute, rather as Massey (1994) advocated space is formed of social relations. Within this relational understanding, place becomes understood not as a bounded, static entity with a fixed identity defined by what is within, but rather as a moment’s constellation of social relations (Massey, 1994; Murdoch, 2006).

A health geography inspired by relational thinking necessitates bringing forward the temporal dimension through longitudinal research. The dominant format of cross-sectional analysis implicitly relies upon assumptions of the power of static space and its bounded features to determine outcomes. In contrast, relational theorisations treat space and time as inextricably entangled; social relations are played out across and themselves construct space-time. The spatial cannot be understood when divorced from the temporal. The inherent dynamism implicated in such a theorisation is important for articulating an open-ended plasticity to space and place. As Harvey (1996) described, the creation of spaces is in the temporary stabilisation of relations, of ‘permanences’ that are not permanent but rather open to change and ‘perpetual perishing’. Places viewed through the lens of relational thought necessarily become porous to ‘outside’ influences; the ‘global’ is always entwined with the production of the ‘local’ (Massey, 1994). Employing this formulation of space and place, therefore, also helps to shift health and place researchers from dualistic perspectives of individual health determined by factors within place, reinforcing the interconnectedness of relations across interfolding scales over time. For instance, relational work on poverty has expanded inquiry of the production of disadvantage beyond the boundaries of specific nations, territories or spaces (Elwood et al., 2017).

By comprehending the plasticity and open-ended becoming of people and places, relational geography aids the study of health inequalities. Social relations are imbued with meaning and power; through repetitive processes of interactions networks are continually remade which can strengthen or weaken the capabilities of people within those networks (Massey, 1991). By tracing relations of place over time, geographers can help to distil circuits of power that serve to marginalise certain populations (Murdoch, 2006). For example, feminist geographers have used relational approaches to gender to understand its construction in embodied social relations and stratifications that serve to reproduce oppressive relations (Connell, 2012; Massey, 1994).

Health inequalities are a major motivation for health researchers. Health (the ability to achieve a state of physical, mental and social wellbeing) is recognised as a fundamental human right (Braveman and Gruskin, 2003; Marmot, 2007). Health inequalities which reflect social hierarchies and societal structures, as revealed by the WHO’s Commission on the Social Determinants of Health (World Health Organisation, 2008), are viewed as avoidable and unjust. The Dahlgren and Whitehead (1991) model of the social determinants of health is an influential framework for those aiming to assess health inequalities across academic and policy spheres
The model conceptualises a layered picture of the factors important to health, expanding from constitutional factors such as age and sex, to individual lifestyle factors, social and community networks, living and working conditions and the general socio-economic, cultural and environmental climate. This multi-scale model emphasises the interdependence between the social determinants as they act in process, with the separate layers viewed as levels for policy interventions (Dahlgren and Whitehead, 1991). The viewpoint advocated by the social determinants of health, therefore, aligns with a relational viewpoint on the interconnections of social and health processes from the global to the local.

Under the social determinants model the most proximate factors of age, sex and genetic makeup are viewed as given and are not considered as contributors to social inequities in health. They are, therefore, placed outside the control of policy. To a degree this may be true. However, it is important to retain an appreciation for the entanglements of these factors with the broader social determinants. This is particularly clear in relation to sex and gender. Sex is not purely a biological mechanism but always intermingled with gendered social relations (Springer et al., 2012). This melange of biological and social processes serves to place this constitutional factor under the purview of health policy and the potential for change. It is such ‘biosocial’ conceptualisations which are missing from Dahlgren and Whitehead’s (1991) model, reflected in a wider lack of attention to the biological in the place and health literatures.

Calls for theoretical models which reflect the entanglement of social and biological phenomena have been made in other health literatures. From social epidemiology, work by Nancy Krieger has made the case for an ‘ecosocial’ theory of health (Krieger, 1994, 1999). Krieger (1994) critically evaluated the long-standing and widely accepted web of causation model, revealing the biomedical individualisation and the consequent focus on the proximate causes of ill health promulgated in epidemiological studies. The argument was for the integration of social perspectives into epidemiological work. The social offers an understanding of population health as more than the sum of individual health and is an integral way of understanding health inequalities. The benefit of an ecosocial or biosocial framework is in bringing forward the conceptualisation of health differentials as socially produced through and within dynamic biological processes; the biological is not rejected but understood in process with social relations (Krieger, 1999).

Engaging with biosocial theory is essential to understanding the embodiment of place, how social relations become incorporated in the changing health of bodies. It provides a framework which reflects bodies as porous and mutable, open to processes beyond the individual. Our understanding of health inequalities, marginalisation and resilience can be progressed by using a biosocial framework to track the imprint of disadvantage. Evidently, geographic thought, particularly relational understandings of space and place, are a useful accompaniment to biosocial theory. They direct thought to the emergent nature of geographical relations and thus to the nature of exposures and being ‘exposed’. For instance, Hall and Wilton (2017) highlighted the potential of relational theories to expose the production of dis/abled bodies in the interplay of social structures, objects and spaces with the physical, biological realities of impairment. In the following section, we unpack how new and developing understandings of bio-processes are invigorating discussion for biosocial, relational frameworks of health geographies.

2 Biosocial processes
Biosocial research has been expanding in recent years, through increasingly rich data resources,
innovations in data methodologies, and discoveries linking biological data to health and social lives. Importantly, increasing knowledge of the development of later life health states and the ongoing interactions between exposures and biological responses is offering novel insights into the marginalisation of some populations and the growth of health inequalities.

Research on lifecourse epidemiology and the developmental origins of health and disease has highlighted that exposures in early life, particularly during gestation, can have long-standing impacts in the later life outcomes of individuals. The foetal origins hypothesis (or Barker hypothesis), based on an identified link between being small at birth and adult cardiovascular disease and type II diabetes, was instrumental in the development of these research fields (Barker, 1995; Barker et al., 1989, 1993). The hypothesis posits that foetal undernutrition is associated with adaptive responses that impart a biological ‘memory’ of undernutrition, which in combination with exposures through life can increase an individual’s chances of poor health outcomes (Barker, 1995; Barker et al., 1993, 2002; Hales and Barker, 2001).

Studies of the developmental origins of disease have also indicated that the operation of the stress response system can be differentially programmed by experiences over the gestational period, early life and childhood, implicating tobacco exposure, maternal affect, and social interactions and trauma (Brooker et al., 2016; Clark et al., 2016; Del Giudice et al., 2011; Flinn et al., 2011). The stress system plays a vital role in regulating responses to environmental stressors, including playing a role in behavioural responses. The importance of early life environments is further emphasised by studies which link macroeconomic and social conditions with birth outcomes. Work by Margerison-Zilko et al. (2017) related increases in the unemployment rate of US states to heightened risk of pre-term births, making adjustment for selection into live birth. Additionally, they were able to demonstrate the extra burden on pre-term birth risk associated with the Great Recession (2007–9). The plasticity of development can thus reveal histories of patterned marginalisation and vulnerability that contribute to health inequalities.

Epigenetics, that is, processes which alter gene expression without altering the underlying genetic sequence, are posited to play a role in the embodiment of the environment signposted by developmental studies (Guthman and Mansfield, 2012; Thayer and Kuzawa, 2011). The emerging field of epigenetics highlights the plasticity of phenotypic development, and in doing so proffers a suite of challenges to traditional notions that continue to underlie many approaches to health studies. For example, the nature-nurture divide is blurred: epigenetic processes highlight that genes do not entirely determine phenotype. Rather genes provide a range of possible outcomes that the biological system can manifest in interaction with the environment (Guthman and Mansfield, 2012; Kuzawa and Sweet, 2009). This revelation of epigenetics furthers the need to integrate biosocial theory with the social determinants of health to reveal new sites of policy relevance.

The complex temporality of epigenetic processes also highlights the inadequacies of contemporaneous spatial measures of exposure (Guthman and Mansfield, 2012). Responses to epigenetic triggers can have long lag times, as most clearly demonstrated by gestational exposures being associated with adult outcomes, such as the cases of thalidomide and DES. Research has also revealed some epigenetic processes can be heritable, leading to intergenerational effects (Guthman and Mansfield, 2012; Thayer and Kuzawa, 2011). For example, the impact of psychosocial stress on parents can be transmitted across generations through DNA methylation modifications affecting germ line cells (Franklin et al., 2010). Studies of epigenetic processes invite a relational perspective where the dynamics of time are privileged, and
more so, epigenetic studies necessitate a life-course approach that pays attention to timing as well as social and historical context (Benschlomo and Kuh, 2002; Elder, 1998). Kuzawa and Sweet (2009) reviewed evidence for life-course and developmental pathways of cardiovascular disease, highlighting how social environments and epigenetic bio-processes in combination offer more apt explanations for persistent racial disparities in cardiovascular disease outcomes.  

Explaining health inequalities requires not only understanding the early life origins of health states, but also of understanding the cumulative, interactive processes acting between bodies and environments. Measures of biological age, such as DNA methylation age – a measure of the cumulative effects of epigenetic processes (Horvath, 2013) – can be used to explore accelerated ageing which may reflect increased exposure to negative experiences. Here, the concept of allostatic load provides an avenue for accessing the imprints of heterogeneous exposure over the lifecourse. Allostatic load refers to a weathering or ‘wear and tear’ on the body induced through chronic exposure to various stressors, whether they be from the familial, workplace, neighbourhood or wider environment (McEwen and Seeman, 1999; McEwen and Stellar, 1993). Exposure to stressors incites the protective ‘fight or flight’ response in the body; however, repeated cycles of this response over time result in a cascade of dysregulations across systems of the body (Juster et al., 2010). It is this multisystem biological response to chronic stress which is characterised by allostatic load and which increases the chances of poor health (Juster et al., 2010; McEwen, 2008; McEwen and Seeman, 1999). Allostatic load, therefore, represents a biosocial process to understand the consequences of cumulative and long-term exposure to stressful circumstances that those who are part of vulnerable, exposed and marginalised populations are more likely to experience.  

Identifying common processes linking a multitude of exposures to differentially healthy bodies demonstrates the aptness of biosocial thinking to studies of health. Epigenetic and allostatic mechanisms highlight the porosity of the body to its environment, challenging those geographies of health which have placed bodies as passive subjects. By bringing forward the mutability of biological function, knowledge of bio-processes helps position the environment as an active component in health systems. Echoing the view championed by relational geography, place also becomes more than mere container for human action when biologically plausible pathways are considered (Guthman and Mansfield, 2012). Therefore, biosocial processes provide access to the signature of socially patterned histories of experience, offering insight into mechanisms by which vulnerable populations may be constrained to lifecourses of ill health.

The expanding biodata resource across social surveys, as in, for instance the UK with the Understanding Society study (University of Essex, 2017), the Avon Longitudinal Study of Parents and Children (University of Bristol, 2017) and the UK Biobank (Biobank UK, 2016), is facilitating the assessment of biosocial pathways over the lifecourse. Biomarkers improve our knowledge of health processes by serving as indicators of the state of physiological systems (Crimmins et al., 2010). For example, returning to allostatic load, it is possible to utilise objectively measured biomarkers to construct indices of load for use in quantitative analyses. The theoretical background of the allostatic load concept as both a predictor of physical and mental health outcomes (Hwang et al., 2014; Juster et al., 2010; Kobrosly et al., 2014) and as a biological response to stressful experiences, such as poverty and psychological distress (Kakinami et al., 2013; Szanton et al., 2005; Winning et al., 2015) has been corroborated in this way.
However, biomarker studies have tended towards individual-level perspectives of social exposure, with more limited consideration of geographies of disadvantage. In other words, place has been neglected in comparison to the bio. This is particularly evident among longitudinal or lifecourse studies. Research which has introduced considerations of place in relation to biodata has generally utilised single-point-in-time measures of contemporaneous contextual exposure (Barrington et al., 2014; Bellatorre et al., 2011; Stein Merkin et al., 2009; Theall et al., 2012). Where biodata has been integrated with a lifecourse framework, studies have aimed to model relationships of individual-level socio-economic gradients. For example, a burgeoning literature relating to allostatic load and the stress response has evidenced cumulative impacts of individual disadvantage across life stages (Gruenewald et al., 2012; Kakinami et al., 2013; Ploubidis et al., 2014). There remains a need to explore pathways for the embodied expression of socially structured geographies of inequality. The next section will highlight the concept of the exposome as a potential framework in which to situate a biosocial health geography.

**IV Exposomic health geography**

The convergence of relational geographies and biosocial theory produces a nexus ripe for progressing bio-geographies of health. This section exposes technological and methodological developments in health and place research, exploring how a health geography reflecting the plasticity of people and places can be applied through the lens of the exposome. To a large extent the ‘tool-box’ for this undertaking already exists – the challenge is to bring a diverse range of techniques together under the framework of the exposome to implement the research of a lifecourse biosocial geography.

Following the completion of the Human Genome Project, Wild (2005) proposed the exposome as a complement to the genome, recognising the fundamental importance of the environment to the development of health but the deficiencies in capturing environmental exposure. The exposome is devised to encompass every exposure to which an individual is exposed, from conception to death (Wild, 2005, 2012). To facilitate implementation of the exposome, it categorises exposure into: internal exposures (processes and factors within the body); specific external exposures (including chemical toxins and pollutants, diet, lifestyle and infectious agents); and general external exposures (the broader causes of health, such as social and economic forces) (Jacquez et al., 2015; Wild, 2012). However, the exposome is concerned with pathways of exposure, placing the overlap and dynamic interaction between these domains as of vital importance.

The exposome as originally conceived, covering the totality of life, can appear non-operational. It may invite an overly simplistic and deterministic viewpoint whereby health outcomes are considered explained through representing all that can be easily measured and quantified. However, rather than attempting to ‘sequence’ the exposome it its entirety, health geographers can benefit from reconsidering the exposome through a framework for biosocial geographies of health. As this final section explicates, the exposome can be conceptualised within a Hågerströmdian space-time geography and a heterogeneous, multi-scalar, mobile characterisation of exposure which aligns the concept with developments in geographical thought and methods.

The exposome is allied with a drive to understand the plasticity of people and places, where health is appreciated as the sum of interactive and heterogeneous processes across the lifecourse (Wild, 2012). It takes a broad conceptualisation of the environment, reminding researchers of how individuals and places are situated and constituted within a wide range of environmental scales. In this way, applying
studies of health through the lens of the exposome helps avoid strictly dualistic thinking where place is set up in apparent opposition to individual-level explanations (Diez Roux, 2001; Macintyre et al., 2002; Riva et al., 2007). The holistic nature of the exposome is particularly beneficial to the integration of biosocial ideas into geographic health enquiry; processes and exposures in the body are explicitly understood alongside external environmental factors. Three large-scale initiatives in the European Union, EXPOsOMICS (Vineis et al., 2017), Human Early-Life Exposome (HELIX) (Vrijheid et al., 2014) and the Health and Environment-wide Associations based on Large population Surveys (HEALS, 2017), are foregrounding projects in the practical assessment of the exposome and demonstrate the interconnected biosocial viewpoint advocated by the concept. The projects are concerned with gathering, collating and analysing environmental exposure data, social survey data and biological data deriving from ‘-omic’ technologies, in order to understand the interactions of environment and health through biological process.

Employing a biosocial health geography through the lens of the exposome will improve the purview of the exposome concept, particularly in regard to the social dimension. So far, exposome research has targeted more proximal causes of health, aiming to elucidate the minutiae of specific chemical or biological factors. Studies have focused on, for example: processes of DNA damage (Nakamura et al., 2014); carcinogenesis and cancer stage latencies (Jacquez et al., 2015); air pollution (Steinle et al., 2015); and chemical toxins (Rager et al., 2016). These studies do not present the wider complexities of the processes linking people and their environment. Assessment of the broader social forces important to health is at this point underappreciated. For instance, the Genetic GIScience framework for exposome research provided by Jacquez et al. (2015) gives cursory acknowledgement to social exposures. The lack of the social is damaging to exposomic studies; environmental exposures and their biological correlates cannot be separated from the broader social, economic, political and cultural relations in which they are embedded. Recognising the interdisciplinary potential of the exposome, particularly through integration of geographic and epidemiologic ideas, will be important in enabling the exposome to achieve its proposed potential (Stingone et al., 2017).

The multi-environment conceptualisation of the exposome, alongside relational perspectives, highlights the inadequacies of the static, bounded contextual definitions often employed in quantitative health studies, particularly those employing multi-level modelling. The readily available administrative or political definitions applied are unlikely to correspond to real-world arenas of exposure for highly mobile persons (Perchoux et al., 2013). Indeed, Montello (2001) highlighted the discordance between analysis scale – the scale at which administrative units are defined – and phenomenon scale, the scale where phenomena exist in social structure(s). Technical developments have helped to address some of the inadequacies of ‘off-the-shelf’ measures (Owen et al., 2016). Boundary issues can be overcome by creating eco-centric bespoke areas for each individual participant (Hedman et al., 2013). Modelling spatial dependencies and spillovers in multi-level analysis gives an element of porosity to areal units and can help to better understand the phenomenon scale (Chaix et al., 2005; Owen et al., 2016). Additionally, a wider range of contexts beyond the residential environment can be examined in studies through the use of cross-classified multi-level models. For example, Aminzadeh et al. (2013) employed a model of individuals nested within both neighbourhoods and schools for their evaluation of social capital and adolescent wellbeing.

In aiming to more adequately capture contexts and exposures, the exposome draws upon the logic of Hägerstrand’s time geography,
understanding individual movements and immobilities as continuous trajectories through space-time (Schaerström, 2014). This perspective privileges movement and relational thinking and echoes arguments made in the geographic and health literatures for the use of ‘people-based’ exposure measures (Kwan, 2009). These have been driven by understandings of the personal nature of place definitions (Milton et al., 2015) and the undeniable role of movement in shaping the ‘dosage’ of particular environments (Galster, 2012). Space-time geographic approaches alongside growing technologies for capturing movement have helped to inform new operationalisations of context.

Activity-based approaches to defining context are a growing method for revealing the varied environments of quotidian experience. Neighbourhood effects research in particular has been criticised for privileging the residential environment (Perchoux et al., 2013). Tools such as the interactive mapping application presented by Chaix et al. (2012) can be employed to collect spatial information based on regularity of destinations, establishing habitual patterns of locations by which to construct activity-space contextual definitions (Kwan, 2012; Perchoux et al., 2013).

Global Positioning Systems (GPS) are an increasingly popular tool to access spatio-temporal activity patterns. For example, Yoo et al. (2015) utilised GPS measures to characterise individual time-activity patterns, using the frequency and density of timepoints to define habitual mobility. GPS technology provides data-rich information on continuous space-time trajectories, and in combination with other sensing technologies such as portable and personal sensors, momentary and self-report assessments and methods like social network analysis, it is possible to create detailed exposure datasets (Kwan, 2012; Turner et al., 2017). For example, in a pilot study by Steinle et al. (2015), contextual and time-activity information was gathered with diaries and used in conjunction with GPS-linked personal air quality data to assign activity patterns to particular microenvironments of importance, such as home, work and transport. These technical developments in measurement enable researchers to more closely align their data with the theoretical background of continual, shifting exposure. There is also the potential to reveal momentary pathways of exposure to both subjective and biological responses. For instance, Shoval et al. (2018) demonstrate the use of traditional survey methods alongside sensors of electrodermal activity to characterise emotional responses of tourists in Jerusalem.

The exposome presents the lifecourse and temporality as of central importance for comprehending multiplicitous exposures, lending the exposome to assessments of biosocial models. Geographers have long understood it is highly informative to track the contexts in which people live throughout their lifecourse. For instance, Glass and Bilal (2016) showed that the environment at birth has a high degree of ‘stickiness’: people tend to persist within the same type of socioeconomic contexts as those they are born into. Long-standing and emerging knowledge on biological processes also continues to highlight how exposures in early life and periods of developmental change can carry influence throughout the lifecourse. Tracking the migration patterns of people between areas (or not) over the lifecourse also helps researchers to access the role of selection effects (Hedman and Van Ham, 2012; Jokela, 2014, 2015), and the opportunity structures within which individuals are embedded. For example, Coulter et al. (2016) proposed a conceptual framework for investigations of residential mobility using a lifecourse approach alongside insights from the ‘new mobilities’ literature. They positioned residential mobility and immobility as relational, active practices, linking lives through time and space, and connecting people to structural conditions that may be enabling or constraining (Coulter et al., 2016).
residential mobility as a relational practice acting over the lifecourse, such a framework showcases the benefit of lifecourse geographies to understanding the development and maintenance of inequalities.

Clearly, it is not feasible to evaluate individuals for every moment of their lives, indeed it may not be desirable; researchers must use assessments at different timepoints, covering critical events of developmental change, as well as important life stages (Wild, 2012). It remains a particularly difficult task to capture local area and social characteristics over the lifecourse. In a lot of cases this is due to the data constraints of particular studies and research contexts. However, the growth of longitudinal cohort and panel datasets across and within national contexts, as well as rich population register data from countries such as Denmark, Sweden and the Netherlands, is providing an expanding longitudinal data resource. For example, Gustafsson et al. (2014) capitalised on Swedish cohort data linked to residence information, demonstrating a cumulative impact of neighbourhood disadvantage on allostatic load in midlife for men, but not for women. Residential histories have been used to implicate an environmental risk factor for Amyotrophic Lateral Sclerosis, helping to reveal the interplay of genetic and environmental factors in the aetiology of the disease (Sabel et al., 2009). Removing the privilege usually given to current environments and accepting the possibility for space-time lags between exposure and response (Schærström, 1996) was an important theoretical underpinning to this work.

Increasing efforts at geographic linkage and methodological innovations in lifecourse place research are also opening new avenues for longitudinal geographic health research. The collaborative geographic linkage project being undertaken by Cohort and Longitudinal Studies Enhancement Resources (CLOSER, 2016) is aiming to provide geographic information for a range of longitudinal studies. The developing arena of historical geographic information systems is also expanding opportunities for analysing people and places over time (Pearce, 2015). For example, Pearce et al. (2016) demonstrate the construction of an urban green space measure covering a 100-year period for the Edinburgh region in Scotland, drawing upon historical and contemporary resources such as maps, aerial photographs and land-use data. Developments in lifecourse and longitudinal research will help to expand the temporal restrictions placed on our comprehension of health and place processes by cross-sectional and short-run analyses. Moreover, alongside geographic linkage and GIS developments which are improving the quantitative assessment of health and place over time, qualitative methods such as oral histories (Bornat et al., 2000) offer a complementary resource for accessing the accumulation of different exposures over time.

Qualitative methods help to reveal the messy complexities of people and places over time, and through personal accounts of experience can provide insight into factors and potential pathways important in shaping the trajectories of individual lifecourses (O’Campo et al., 2009; Temelová and Slezáková, 2014). Interviews and participatory methods may get closer to the grain of the interplay of lived experience, the accumulation of experience across varied personal landscapes, and states of health and well-being. By recognising the non-quantifiable, insights from qualitative methods would also help prevent deterministic employments of the exposome.

However, qualitative methods are not able to capture the interplay of the biological and the social over time, which biosocial theory and the exposome concept demonstrate are vitally important for comprehending health inequalities. Indeed, part of the value of exploring bio-processes such as epigenetics and allostatic load is their ability to offer a record of social exposure by which to trace the reproduction of
disadvantage over time. Additionally, providing quantitative evidence for exposomic health and place relations, in relation to specific, measurable health outcomes, helps to strengthen the evidence base to bring forward to policymakers. It is important to use larger cohort and panel studies to expose biosocial geographies of disadvantaged groups who are constrained to particular exposure environments across their lifecourse.

The exposome reminds researchers of the inextricability of the body and the external world by proposing a genome-plus view of the environment, where exposures and processes within and without the body are intertwined. One mode to implement assessments of the biosocial, to get closer to accessing the permeability of the body to social relations, is to use mediation analysis. Mediation is conceived as a causal phenomenon, whereby the relationship between two variables is accounted for by an intervening variable – a mediator (Baron and Kenny, 1986; Hayes and Preacher, 2014). It is a method for exploring potential mechanisms linking factors of interest (Mackinnon et al., 2007). Therefore, mediation analysis, which incorporates techniques such as path analysis and structural equation modelling, offers a methodological framework for accessing the processes by which contexts manifest in health states (Hayes and Preacher, 2010; Pardo and Román, 2013). Conceptually, mediators are used to explain how external events become expressed in the physiological and psychological state of bodies (Baron and Kenny, 1986).

The explicit investigation of intervening pathways using mediation analysis techniques is also relatively uncommon in health geography, particularly in the assessment of biologically plausible pathways in health and place studies. For example, the concept of allostatic load presents a means through which the bodily response to stress exposures can be accessed. However, the two studies which have investigated whether allostatic load mediated individual-level socio-economic gradients in health status have not provided in-depth assessment of the mediating pathways and their action. They rely instead on the attenuation of a previous relationship which may also occur if a variable is a confounder (Hu et al., 2007; Sabbah et al., 2008) – the primary difference of a mediator to a confounder being that a mediator is positioned in a causal chain between the independent and dependent variable; for a confounder there is not the same directionality of the relationship. There is a mismatch between the aim of understanding the pathways through which the environment may manifest in differently healthy bodies and the methodological approach taken. In particular, studies of health and place should make more use of the technical and methodological developments in mediation analysis which are facilitating the investigation of more complex models incorporating multiple mediators, heterogeneity of associations, multiple levels and longitudinal data (Bind et al., 2016; Loeys et al., 2013; Preacher et al., 2007, 2010; Selig and Preacher, 2009; Valeri and VanderWeele, 2013; Zhang et al., 2009). Utilising such techniques will help to elucidate exposomic and biosocial geographies of place and health over time and ally with a relational lens that points towards the analysis of dynamic process and relationships.

V Conclusion
To uncover the how and when of health and place relationships, health geographers need to engage with biosocial ideas. The missing insight into how exposure to the varied social and physical features of places come to be imprinted on and manifest in differentially healthy bodies can be gained through an understanding of biosocial relations. Integrating biosocial thought with the established social determinants of health model will allow health geographers to move the agenda forward to investigating not only the interacting processes
from the macro socio-economic climate to individual characteristics, but also to exploring biological process and its inherent connection to social context. Biosocial theorisations enable both body and environment to be repositioned as active components in fluid health and place relationships, acting in interchange and accumulation over time. In this way health geographers, and particularly quantitative researchers, can move beyond static, at times uncritical understandings of the determining power of place to more nuanced, critical theorisations for the marginalisation of different groups over time.

Our growing insight into the processes of epigenetics and of allostatic pathways for the embodiment of context provide novel avenues for feeding into discourses on health inequalities. These processes offer links between socially structured relations over the lifecourse and patterns of group and population health. By engaging with the expanding biodata resource across large-scale social surveys and through collaboration with epidemiologists and the biomedical community, health geographers can inform discussion on the biological embedding of disadvantage. The geographic lens is needed in this discussion to provide the more-than-individual, social perspective which has so far been largely lacking in bio-studies. The complex temporality and plasticity of bodies indicated by processes such as epigenetics invites an integration with relational theorisations of space, place and the social.

It will be beneficial to employ the concept of the exposome within health geographies. The exposome can provide a holistic framework in which to position the investigation of dynamic relationships between heterogeneous and multi-scalar exposures, their biological imprint and health outcomes. It will be a complex and difficult task to compile biosocial geographies of health and place through the exposome. Researchers will have to take up and integrate methodological and theoretical developments in the assessment of exposures and context, of modelling lifecourse relationships, and of investigating the mechanisms of embodiment, to reveal histories of exposure, vulnerability and marginalisation to inform and act on inequalities in health.

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References
Amin A (2004) Regions unbound: Towards a new politics of place. Geografiska Annaler 86 B(1): 33–44.
Aminzadeh K, Denny S, Utter J, Milfont TL, Ameratunga S, Teevale T and Clark T (2013) Neighbourhood social capital and adolescent self-reported wellbeing in New Zealand: A multilevel analysis. Social Science and Medicine 84: 13–21.
Arcaya MC, Tucker-Seeley R, Kim R, Schnake-Mahl A, So M and Subramanian SV (2016) Research on neighborhood effects on health in the United States: A systematic review of study characteristics. Social Science and Medicine 168: 16–29.
Bambra C, Gibson M, Sowden A, Wright K, Whitehead M and Petticrew M (2010) Tackling the wider social determinants of health and health inequalities: Evidence from systematic reviews. *Journal of Epidemiology and Community Health* 64(4): 284–291.

Barker DJP (1995) Fetal origins of coronary heart disease. *British Medical Journal* 311: 171–174.

Barker DJP, Eriksson J, Forsén T and Osmond C (2002) Fetal origins of adult disease: strength of effects and biological basis. *International Journal of Epidemiology* 31: 1235–1239.

Barker DJP, Gluckman PD, Godfrey KM, Harding JE, Owens JA and Robinson JS (1993) Fetal nutrition and cardiovascular disease in adult life. *The Lancet* 341(8850): 938–941.

Barker DJP, Winter PD, Osmond C, Margetts B and Simmons SJ (1989) Weight in infancy and death from ischaemic heart disease. *The Lancet* 2(8663): 577–580.

Barrington WE, Stafford M, Hamer M, Beresford SAA, Koepsell T and Steptoe A (2014) Neighborhood socioeconomic deprivation, perceived neighborhood factors, and cortisol responses to induced stress among healthy adults. *Health and Place* 27: 120–126.

Bell SL, Wheeler BW and Phoenix C (2017) Using geonarratives to explore the diverse temporalities of therapeutic landscapes: Perspectives from ‘green’ and ‘blue’ settings. *Annals of the American Association of Geographers* 107(1): 93–108.

Bellatorre A, Finch BK, Phuong Do D, Bird CE and Beck AN (2011) Contextual predictors of cumulative biological risk: Segregation and allostatic load. *Social Science Quarterly* 92(5): 1338–1362.

Ben-shlomo Y and Kuh D (2002) A life course approach to chronic disease epidemiology: Conceptual models, empirical challenges and interdisciplinary perspectives. *International Journal of Epidemiology* 31: 285–293.

Bind M-AC, VanderWeele TJ, Coull BA and Schwartz JD (2016) Causal mediation analysis for longitudinal data with exogenous exposure. *Biostatistics* 17(1): 122–134.

Biobank UK (2016) Biobank UK improving the health of future generations. UK Biobank Limited. Available at: http://www.ukbiobank.ac.uk/ (accessed 21 May 2017).

Bissonnette L, Wilson K, Bell S and Shah TI (2012) Neighbourhoods and potential access to health care: The role of spatial and aspatial factors. *Health and Place* 18(4): 841–853.

Boggs JS and Rantisi NM (2003) The ‘relational turn’ in economic geography. *Journal of Economic Geography* 3: 109–116.

Bornat J, Perks R, Thompson P and Walmsley J (eds.) (2000) *Oral History, Health and Welfare*. London: Routledge.

Bosma H, Van de Mheen HD, Borsboom GJ and Mackenbach JP (2001) Neighborhood socioeconomic status and all-cause mortality. *American Journal of Epidemiology* 153(4): 363–371.

Bourdieu P (1986) The forms of capital. In: Richardson JG (ed.) *Handbook of Theory and Research for the Sociology of Education*. New York: Greenwood Press, 241–258.

Braveman P and Gruskin S (2003) Poverty, equity, human rights and health. *Bulletin of the World Health Organization* 81(7): 539–545.

Bridle-Fitzpatrick S (2015) Food deserts or food swamps?: A mixed-methods study of local food environments in a Mexican city. *Social Science and Medicine* 142: 202–213.

Brooker RJ, Davidson RJ and Goldsmith HH (2016) Maternal negative affect during infancy is linked to disrupted patterns of diurnal cortisol and alpha asymmetry across contexts during childhood. *Journal of Experimental Child Psychology* 142: 274–290.

Brown T, McLafferty S and Moon G (2010) *A Companion to Health and Medical Geography*. Chichester: Wiley-Blackwell.

Brown T, Andrews GJ, Cummins S, Greenhough B, Lewis D and Power A (2017) *Health Geographies: A Critical Introduction*. Chichester: Wiley-Blackwell.

Cattell V (2001) Poor people, poor places, and poor health: The mediating role of social networks and social capital. *Social Science and Medicine* 52(10): 1501–1516.

Chaix B, Merlo J, Subramanian SV, Lynch J and Chauvin P (2005) Comparison of a spatial perspective with the multilevel analytical approach in neighborhood studies: The case of mental and behavioral disorders due to psychoactive substance use in Malmö, Sweden, 2001. *American Journal of Epidemiology* 162(2): 171–182.

Chaix B, Kestens Y, Perchoux C, Karussi N, Merlo J and Labadi K (2012) An interactive mapping tool to assess individual mobility patterns in neighborhood studies.
Clark CAC, Espy KA and Wakschlag L (2016) Developmental pathways from prenatal tobacco and stress exposure to behavioral disinhibition. Neurotoxicology and Teratology 53: 64–74.

CLOWER (2016) Closer: Promoting excellence in longitudinal research. Available at: https://www.closer.ac.uk/ (accessed 21 May 2017).

Connell R (2012) Gender, health and theory: Conceptualizing the issue, in local and world perspective. Social Science and Medicine 74: 1675–1683.

Coulter R, Van Ham M and Findlay AM (2016) Re-thinking residential mobility: Linking lives through time and space. Progress in Human Geography 40(3): 352–374.

Crimmins E, Kim JK and Vasunilashorn S (2010) Biodemography: New approaches to understanding trends and differences in population health and mortality. Demography 47–Supplement: S41–S64.

Cummins S, Stafford M, Macintyre S, Marmot M and Ellaway A (2005) Neighbourhood environment and its association with self-rated health: Evidence from Scotland and England. Journal of Epidemiology and Community Health 59(3): 207–213.

Cummins S, Curtis S, Diez Roux AV and Macintyre S (2007) Understanding and representing ‘place’ in health research: A relational approach. Social Science and Medicine 65(9): 1825–1838.

Dahlgren G and Whitehead M (1991) Policies and strategies to promote social equity in health. Background document to WHO – Strategy paper for Europe. No 2007: 14. Arbetsrapport, Institute for Futures Studies.

Diez Roux AV (2001) Investigating neighborhood and area effects on health. American Journal of Public Health 91(11): 1783–1789.

Diez Roux AV and Mair C (2010) Neighborhoods and health. Annals of the New York Academy of Sciences 1186: 125–145.

Diez Roux AV, Mujahid MS, Hirsch JA, Moore K and Moore LV (2016) The impact of neighborhoods on CV risk. Global Heart 11(3): 353–363.

Duncan C, Jones K and Moon G (1999) Smoking and deprivation: are there neighbourhood effects? Social Science and Medicine 48: 497–505.

Elder GH (1998) The life course as developmental theory. Child Development 69(1): 1–12.

Elwood S, Lawson V and Sheppard E (2017) Geographical relational poverty studies. Progress in Human Geography 41(6): 745–765.

Finlay J, Franke T, McKay H and Sims-Gould J (2015) Therapeutic landscapes and wellbeing in later life: Impacts of blue and green spaces for older adults. Health and Place 34: 97–106.

Flinn MV, Nepomnaschy PA, Muehlenbein MP and Ponzi D (2011) Evolutionary functions of early social modulation of hypothalamic-pituitary-adrenal axis development in humans. Neuroscience and Biobehavioral Reviews 35: 1611–1629.

Franklin TB, Russig H, Weiss IC, Gräff J, Linder N, Michalon A, Vizi S and Mansuy IM (2010) Epigenetic transmission of the impact of early stress across generations. Biological Psychiatry 68(5): 408–415.

Galster GC (2012) The mechanism(s) of neighbourhood effects: Theory, evidence, and policy implications. In: Van Ham M, Manley D, Bailey N, Simpson L and Maclellan D (eds) Neighbourhood Effects Research: New Perspectives. Dordrecht: Springer, 23–56.

Gatrell AC and Elliott SJ (2009) Geographies of Health: An Introduction. 2nd Edition. Chichester: Wiley-Blackwell.

Gesler WM (1992) Therapeutic landscapes: Medical issues in light of the new cultural geography. Social Science and Medicine 34(7): 735–746.

Glass TA and Bilal U (2016) Are neighborhoods causal? Complications arising from the ‘stickiness’ of ZNA. Social Science and Medicine 166: 244–253.

Gould MI and Jones K (1996) Analyzing perceived limiting long-term illness using U.K. Census microdata. Social Science and Medicine 42(6): 857–869.

Gruenewald TL, Karlamangla AS, Hu P, Stein-Merkin S, Crandall C, Koretz B and Seeman TE (2012) History of socioeconomic disadvantage and allostatic load in later life. Social Science and Medicine 74(1): 75–83.

Gustafsson PE, Janlert U, Theorell T and Hammarström A (2010) Life-course socioeconomic trajectories and diurnal cortisol regulation in adulthood. Psychoneuroendocrinology 35(4): 613–623.

Gustafsson PE, San Sebastian M, Janlert U, Theorell T, Westerlund H and Hammarström A (2014) Life-course...
accumulation of neighborhood disadvantage and allostatic load: Empirical integration of three social determinants of health frameworks. *American Journal of Public Health* 104(5): 904–910.

Guthman J and Mansfield B (2012) The implications of environmental epigenetics: A new direction for geographic inquiry on health, space, and nature-society relations. *Progress in Human Geography* 37(4): 486–504.

Hales CN and Barker DJP (2001) The thrifty phenotype hypothesis. *British Medical Bulletin* 60: 5–20.

Hall E and Wilton R (2017) Towards a relational geography of disability. *Progress in Human Geography* 41(6): 727–744.

Harvey D (1996) *Justice, Nature and the Geography of Difference*. Oxford: Blackwell.

Hayes AF and Preacher KJ (2010) Quantifying and testing indirect effects in simple mediation models when the constituent paths are nonlinear. *Multivariate Behavioral Research* 45(4): 627–660.

Hayes AF and Preacher KJ (2014) Statistical mediation analysis with a multicategorical independent variable. *British Journal of Mathematical and Statistical Psychology* 67: 451–470.

Hayes M (1999) ‘Man, disease and environmental associations’: From medical geography to health inequalities. *Progress in Human Geography* 23(2): 289–296.

HEALS (2017) *Health and Environment-wide Associations based on large population surveys: The largest research project in Europe on environment and health*. EU: HEALS. Available at: http://www.heals-eu.eu (accessed 21 May 2017).

Hedman L and Van Ham M (2012) Understanding neighbourhood effects: Selection bias and residential mobility. In: Van Ham M, Manley D, Bailey N, Simpson L and Maclennan D (eds) *Neighbourhood Effects Research: New Perspectives*. Dordrecht: Springer, 79–100.

Hedman L, Manley D, Van Ham M and Östl J (2013) Cumulative exposure to disadvantage and the intergenerational transmission of neighbourhood effects. *Journal of Economic Geography* 15(1): 195–215.

Hooper CM, Ivory VC and Fougere G (2015) Childhood neighbourhoods as third places: Developing durable skills and preferences that enhance wellbeing in adulthood. *Health and Place* 34: 34–45.

Hordyk SR, Hanley J and Richard É (2015) ‘Nature is there; its free’: Urban greenspace and the social determinants of health of immigrant families. *Health and Place* 34: 74–82.

Horvath S (2013) DNA methylation age of human tissues and cell types. *Genome Biology* 14: R115.

Hu P, Wagle N, Goldman N, Weinstein M and Seeman TE (2007) The associations between socioeconomic status, allostatic load and measures of health in older Taiwanese persons: Taiwan social environment and biomarkers of aging study. *Journal of Biosocial Science* 39(4): 545–556.

Hwang A-C, Peng L-N, Wen Y-W, Tsai Y-W, Chang L-C, Chiou S-T and Chen L-K (2014) Predicting all-cause and cause-specific mortality by static and dynamic measurements of allostatic load: A 10-year population-based cohort study in Taiwan. *Journal of the American Medical Directors Association* 15(7): 490–496.

Ivory VC, Blakely T, Pearce J, Witten K, Bagheri N, Badland H and Schofield G (2015) Could strength of exposure to the residential neighbourhood modify associations between walkability and physical activity? *Social Science and Medicine* 147: 232–241.

Jacquez GM, Sabel CE and Shi C (2015) Genetic GIScience: Toward a place-based synthesis of the genome, exposome, and behavome. *Annals of the Association of American Geographers* 105(3): 454–472.

Jokela M (2014) Are neighborhood health associations causal? A 10-year prospective cohort study with repeated measurements. *American Journal of Epidemiology* 180(8): 776–784.

Jokela M (2015) Does neighbourhood deprivation cause poor health? Within-individual analysis of movers in a prospective cohort study. *Journal of Epidemiology and Community Health* 69(9): 899–904.

Jones K and Moon G (1992) *Health, Disease and Society: An Introduction to Medical Geography*. London: Routledge.

Jones K and Moon G (1993) Medical geography: Taking space seriously. *Progress in Human Geography* 17(4): 515–524.

Jones M (2009) Phase space: Geography, relational thinking, and beyond. *Progress in Human Geography* 33(4): 487–506.

Juster R-P, McEwen BS and Lupien SJ (2010) Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neuroscience and Biobehavioral Reviews* 35(1): 2–16.

Kakinami L, Séguin L, Lambert M, Gauvin L, Nikiema B and Paradis G (2013) Comparison of three lifecourse
models of poverty in predicting cardiovascular disease risk in youth. *Annals of Epidemiology* 23(8): 485–491.

Kawachi I and Berkman LF (eds) (2003) *Neighborhoods and Health*. New York: Oxford University Press.

Kearns R and Moon G (2002) From medical to health geography: Novelty, place and theory after a decade of change. *Progress in Human Geography* 26(5): 605–625.

Kearns RA (1993) Place and health: Towards a reformed medical geography. *The Professional Geographer* 45(2): 139–147.

Kearns RA (1995) Medical geography: Making space for difference. *Progress in Human Geography* 19(2): 251–259.

Kim D, Subramanian SV and Kawachi I (2008) Social capital and physical health: A systematic review of the literature. In: Kawachi I, Subramanian SV and Kim D (eds) *Social Capital and Health*. New York: Springer, 139–190.

Kobrosly RW, Van Wijngaarden E, Seplaki CL, Cory-Slechta DA and Moynihan J (2014) Depressive symptoms are associated with allostatic load among community-dwelling older adults. *Physiology and Behavior* 123: 223–230.

Krieger N (1994) Epidemiology and the web of causation: Has anyone seen the spider? *Social Science and Medicine* 39(7): 887–903.

Krieger N (1999) Sticky webs, hungry spiders, buzzing flies, and fractal metaphors: On the misleading juxtaposition of ‘risk factor’ versus ‘social’ epidemiology. *Journal of Epidemiology and Community Health* 53: 678–680.

Kuipers MAG, Van Poppel MNM, Van Den Brink W, Wingen M and Kunst AE (2012) The association between neighborhood disorder, social cohesion and hazardous alcohol use: A national multilevel study. *Drug and Alcohol Dependence* 126(1–2): 27–34.

Kurka JM, Adams MA, Todd M, Colburn T, Sallis JF, Cain KL, Glanz K, Frank LD and Saelens BE (2015) Patterns of neighborhood environment attributes in relation to children’s physical activity. *Health and Place* 34: 164–170.

Kuzawa CW and Sweet E (2009) Epigenetics and the embodiment of race: Developmental origins of US racial disparities in cardiovascular health. *American Journal of Human Biology* 21: 2–15.

Kwan M-P (2009) From place-based to people-based exposure measures. *Social Science and Medicine* 69(9): 1311–1313.

Kwan M-P (2012) The uncertain geographic context problem. *Annals of the Association of American Geographers* 102(5): 958–968.

Kwan M-P (2013) Beyond apace (as we knew it): Toward temporally integrated geographies of segregation, health, and accessibility. *Annals of the Association of American Geographers* 103(5): 1078–1086.

Lekkas P, Paquet C, Howard NJ and Daniel M (2017) Illuminating the lifecourse of place in the longitudinal study of neighbourhoods and health. *Social Science and Medicine* 177: 239–247.

Loeys T, Moerkerke B, De Smet O, Buysse A, Steen J and Vansteelandt S (2013) Flexible mediation analysis in the presence of nonlinear relations: Beyond the mediation formula. *Multivariate Behavioral Research* 48(6): 871–894.

Macintyre S and Ellaway A (2003) Neighbourhood and health: An overview. In: Kawachi I and Berkman LF (eds) *Neighbourhoods and Health*. New York: Oxford University Press, 20–42.

Macintyre S, Ellaway A and Cummins S (2002) Place effects on health: How can we conceptualise, operationalise and measure them? *Social Science and Medicine* 55: 125–139.

Mackinnon DP, Fairchild AJ and Fritz MS (2007) Mediation analysis. *Annual Review of Psychology* 58: 593–614.

Mair C, Diez Roux AV and Galea S (2008) Are neighborhood characteristics associated with depressive symptoms? A review of evidence. *Journal of Epidemiology and Community Health* 62(11): 940–946.

Malambo P, Kengne AP, De Villiers A, Lambert EV and Puoane T (2016) Built environment, selected risk factors and major cardiovascular disease outcomes: A systematic review. *PLoS ONE* 11(11): e0166846.

Malmstrom M, Johansson S and Sundquist J (2001) A hierarchical analysis of long-term illness and mortality in socially deprived areas. *Social Science and Medicine* 53(3): 265–275.

Margerison-Zilko CE, Li Y and Luo Z (2017) Economic conditions during pregnancy and adverse birth outcomes among singleton live births in the United States, 1990–2013. *American Journal of Epidemiology* 186(10): 1131–1139.

Marmot M (2007) Achieving health equity: From root causes to fair outcomes. *Lancet* 370: 1153–1163.

Massey D (1991) A global sense of place. *Marxism Today* 38: 24–29.
Massey D (1994) *Space, Place and Gender*. Cambridge: Polity Press.

Matheson FI, White HL, Moineddin R, Dunn JR and Glazier RH (2012) Drinking in context: The influence of gender and neighbourhood deprivation on alcohol consumption. *Journal of Epidemiology and Community Health* 66(4): 1–9.

McEwen BS (2008) Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. *European Journal of Pharmacology* 583(2–3): 174–185.

McEwen BS and Seeman T (1999) Protective and damaging effects of mediators of stress: Elaborating and testing the concepts of allostasis and allostatic load. *Annals of the New York Academy of Sciences* 896: 30–47.

McEwen BS and Stellar E (1993) Stress and the individual: Mechanisms leading to disease. *Archives of Internal Medicine* 153: 2093–2101.

Milton S, Pliakas T, Hawkesworth S, Nanchahal K, Grundy C, Amuzu A, Casa J-P and Lock K (2015) A qualitative geographical information systems approach to explore how older people over 70 years interact with and define their neighbourhood environment. *Health and Place* 36: 127–133.

Mishra G, Nitsch D, Black S, De Stavola B, Kuh D and Hardy R (2009) A structured approach to modelling the effects of binary exposure variables over the life course. *International Journal of Epidemiology* 38(2): 528–537.

Montello DR (2001) Scale in geography. In: Smelser NJ and Baltes PB (eds) *International Encyclopedia of Social and Behavioral Sciences*. Oxford: Elsevier Science, 13501–13504.

Murayama H, Nishi M, Nofuji Y, Matsuo E, Taniguchi Y, Amano H, Yokoyama Y, Fujiiwara Y and Shinkai S (2015) Longitudinal association between neighborhood cohesion and depressive mood in old age: A Japanese prospective study. *Health and Place* 34: 270–278.

Murdoch J (2006) *Post-Structuralist Geography: A Guide to Relational Space*. London: SAGE.

Nakamura J, Mutlu E, Sharma V, Collins L, Bodnar W, Yu R, Lai Y, Moeller B, Lu K and Swenberg J (2014) The endogenous exposome. *DNA Repair* 19: 3–13.

Ngamini Ngui A, Perreault M, Fleury MJ and Caron J (2012) A multi-level study of the determinants of mental health service utilization. *Revue d'épidémiologie et de Santé Publique* 60(2): 85–93.

O’Campo P, Salmon C and Burke J (2009) Neighbourhoods and mental well-being: What are the pathways? *Health and Place* 15(1): 56–68.

Owen G, Harris R and Jones K (2016) Under examination: Multilevel models, geography and health research. *Progress in Human Geography* 40(3): 394–412.

Pardo A and Román M (2013) Reflections on the Baron and Kenny model of statistical mediation. *Anales de psicologia* 29(2): 614–623.

Pearce J (2015) Invited commentary: History of place, life course, and health inequalities-historical geographic information systems and epidemiologic research. *American Journal of Epidemiology* 181(1): 26–29.

Pearce J, Shortt N, Rind E and Mitchell R (2016) Life course, green space and health: Incorporating place into life course epidemiology. *International Journal of Environmental Research and Public Health* 13(3): E331.

Perchoux C, Chaix B, Cummins S and Kestens Y (2013) Conceptualization and measurement of environmental exposure in epidemiology: Accounting for activity space related to daily mobility. *Health and Place*, 21: 86–93.

Philo C (2016) ‘Healthy debate’ and ‘healthy ferment’: Medical and health geographies. *Progress in Human Geography*: 1–21. DOI: 10.1177/0309132516678343.

Pickett KE and Pearl M (2001) Multilevel analyses of neighbourhood socioeconomic context and health outcomes: A critical review. *Journal of Epidemiology and Community Health* 55(2): 111–122.

Ploubidis GB, Benova L, Grundy E, Laydon D and DeStavola B (2014) Lifelong socio economic position and biomarkers of later life health: Testing the contribution of competing hypotheses. *Social Science and Medicine* 119: 258–265.

Preacher KJ, Rucker DD and Hayes AF (2007) Addressing moderated mediation hypotheses: Theory, methods, and prescriptions. *Multivariate Behavioral Research* 42(1): 185–227.

Preacher KJ, Zyphur MJ and Zhang Z (2010) A general multilevel SEM framework for assessing multilevel mediation. *Psychological Methods* 15(3): 209–233.

Putnam RD (2000) *Bowling Alone: The Collapse and Revi- val of American Community*. New York: Simon and Schuster.

Rager JE, Strynar MJ, Liang S, McMahan RL, Richard AM, Grulke CM, Wambaugh JF, Isaacs KK, Judson R, Williams AJ and Sobus JR (2016) Linking high...
resolution mass spectrometry data with exposure and toxicity forecasts to advance high-throughput environmental monitoring. *Environment International* 88: 269–280.

Richardson R, Westley T, Gariépy G, Austin N and Nandi A (2015) Neighborhood socioeconomic conditions and depression: A systematic review and meta-analysis. *Social Psychiatry and Psychiatric Epidemiology* 50(11): 1641–1656.

Riva M, Gauvin L and Barnett TA (2007) Toward the next generation of research into small area effects on health: A synthesis of multilevel investigations published since July 1998. *Journal of Epidemiology and Community Health* 61(10): 853–861.

Rosenberg M (1998) Medical or health geography? Populations, people and places. *International Journal of Population Geography* 4: 211–226.

Rosenberg M (2014) Health geography I: Social justice, idealist theory, health and health care. *Progress in Human Geography* 38(3): 466–475.

Rosenberg M (2016) Health geography II: ‘Dividing’ health geography. *Progress in Human Geography* 40(4): 546–554.

Rosenberg M (2017) Health geography III: Old ideas, new ideas or new determinisms? *Progress in Human Geography* 41(6): 832–842.

Ross CE and Mirowsky J (2001) Neighbourhood disadvantage, disorder, and health. *Journal of Health and Social Behavior* 42(3): 258–276.

Ruijsbroek A, Droomers M, Hardyns W, Groenewegen PP and Stronks K (2016) The interplay between neighbourhood characteristics: The health impact of changes in social cohesion, disorder and unsafety feelings. *Health and Place* 39: 1–8.

Sabbah W, Watt RG, Sheiham A and Tsakos G (2008) Effects of allostatic load on the social gradient in ischaemic heart disease and periodontal disease: Evidence from the Third National Health and Nutrition Examination Survey. *Journal of Epidemiology and Community Health* 62(5): 415–420.

Sabel CE, Boyle P, Raab G, Löytönen M and Maasila P (2009) Modelling individual space-time exposure opportunities: A novel approach to unravelling the genetic or environment disease causation debate. *Spatial and Spatio-temporal Epidemiology* 1(1): 85–94.

Scharström A (1996) *Pathogenic Paths? A Time Geographical Approach in Medical Geography*. Lund: Lund University Press.

Scharström A (2014) The potential for time geography in health studies. In: Scharström A, Jørgensen SH, Kistemann T and Silvertun Å (eds) *Geography and Health – A Nordic Outlook*. Stockholm: The Swedish National Defence College, 324–338.

Schüle SA and Bolte G (2015) Interactive and independent associations between the socioeconomic and objective built environment on the neighbourhood level and individual health: A systematic review of multilevel studies. *PLoS ONE* 10(4): e0123456.

Schüle SA, Gabriel KMA and Bolte G (2017) Relationship between neighbourhood socioeconomic position and neighbourhood public green space availability: An environmental inequality analysis in a large German city applying generalized linear models. *International Journal of Hygiene and Environmental Health* 220(4): 711–718.

Selig JP and Preacher KJ (2009) Mediation models for longitudinal data in developmental research. *Research in Human Development* 6(2–3): 144–164.

Shoval N, Schvimer Y and Tamir M (2018) Real-time measurement of tourists’ objective and subjective emotions in time and space. *Journal of Travel Research* 57(1): 3–16.

Skapinakis P, Lewis G, Araya R, Jones K and Williams G (2005) Mental health inequalities in Wales, UK: Multilevel investigation of the effect of area deprivation. *The British Journal of Psychiatry* 186: 417–422.

Small ML and Feldman J (2012) Ethnographic evidence, heterogeneity, and neighbourhood effects after Moving to Opportunity. In: Van Ham M, Manley D, Bailey N, Simpson L and Maclennan D (eds) *Neighbourhood Effects Research: New Perspectives*, Dordrecht: Springer, 57–77.

Springer KW, Mager Stellman J and Jordan-Young RM (2012) Beyond a catalogue of differences: A theoretical frame and good practice guidelines for researching sex/gender in human health. *Social Science and Medicine* 74(11): 1817–1824.

Steenbeek W and Hipp JR (2011) A longitudinal test of social disorganization theory: Feedback effects among cohesion, social control, and disorder. *Criminology* 49(3): 833–871.

Steinle S, Reis S, Sabel CE, Semple S, Twigg MM, Braban CF, Leeson SR, Heal MR, Harrison D, Lin C and Wu H (2015) Personal exposure monitoring of PM 2.5 in indoor and outdoor microenvironments. *Science of the Total Environment* 508: 383–394.
Stein Merkin S, Basurto-Dávila R, Karlamangla A, Bird CE, Lurie N, Escarce J and Seeman T (2009) Neighborhoods and cumulative biological risk profiles by race/ethnicity in a national sample of U.S. adults: NHANES III. *Annals of Epidemiology* 19(3): 194–201.

Stingone JA, Buck Louis GM, Nakayama SF, Vermeulen RCH, Kwok RK, Cui Y, Balshaw DM and Teitelbaum SL (2017) Toward greater implementation of the exposome research paradigm within environmental epidemiology. *Annual Review of Public Health* 38: 315–327.

Sundquist K, Malmström M and Johansson S-E (2004) Neighbourhood deprivation and incidence of coronary heart disease: A multilevel study of 2.6 million women and men in Sweden. *Journal of Epidemiology and Community Health* 58: 71–77.

Szanton SL, Gill JM and Allen JK (2005) Allostatic load: A mechanism of socioeconomic health disparities? *Biological Research for Nursing* 7(1): 7–15.

Tehranifar P, Wu H-C, McDonald JA, Jasmine F, Santella RM, Gurrich I, Flom JD and Terry MB (2018) Maternal cigarette smoking during pregnancy and offspring DNA methylation in midlife. *Epigenetics* 13(2): 129–134.

Temelová J and Slezáková A (2014) The changing environment and neighbourhood satisfaction in socialist high-rise panel housing estates: The time-comparative perceptions of elderly residents in Prague. *Cities* 37: 82–91.

Thayer ZM and Kuzawa CW (2011) Biological memories of past environments: Epigenetic pathways to health disparities. *Epigenetics* 6(7): 1–6.

Theall KP, Drury SS and Shirtcliff EA (2012) Cumulative neighborhood risk of psychosocial stress and allostatic load in adolescents. *American Journal of Epidemiology* 176(Suppl): S164–S174.

Turner MC, Nieuwenhuijsen M, Anderson K, Balshaw D, Cui Y, Dunton G, Hoppin JA, Koutrakis P and Jerrett M (2017) Assessing the exposome with external measures: Commentary on the state of the science and research recommendations. *Annual Review of Public Health* 38: 215–239.

University of Bristol (2017) *Avon Longitudinal Study of Parents and Children*. Bristol: University of Bristol, Available at: http://www.bristol.ac.uk/alspac/ (accessed 21 May 2017).

University of Essex, Institute for Social and Economic Research (2017) *Understanding Society: The UK Household Longitudinal Study*. Colchester: University of Essex. Available at: https://www.understandingsociety.ac.uk/ (accessed 21 May 2017).

Valeri L and VanderWeele TJ (2013) Mediation analysis allowing for exposure-mediator interactions and causal interpretation: Theoretical assumptions and implementation with SAS and SPSS macros. *Psychological Methods* 18(2): 137–150.

Van Ham M and Manley D (2012) Neighbourhood effects research at a crossroads: Ten challenges for future research. *Environment and Planning A* 44: 2787–2793.

Van Ham M, Manley D, Bailey N, Simpson L and Maclennan D (2012) *Neighbourhood Effects Research: New Perspectives*. Dordrecht: Springer.

Vineis P, Chadeau-Hyam M, Gunderman H, Gulliver J, Herceg Z, Kleinjans J, Kogevinas M, Kyrtopoulos S, Nieuwenhuijsen M, Phillips DH, Probst-Hensch N, Scalbert A, Vermeulen R and Wild CP and The EXPOsOMICS Consortium (2017) The exposome in practice: Design of the EXPOsOMICS project. *International Journal of Hygiene and Environmental Health* 220: 142–151.

Voigtlander S, Berger U and Razum O (2010) The impact of regional and neighbourhood deprivation on physical health in Germany: A multilevel study. * BMC Public Health* 10(403): 1–12.

Vrijheid M, Slama R, Robinson O, Chatzi L, Coen M, Van Den Hazel P, Thomsen C, Wright J, Athersuch TJ, Avelan A, Basagaña X, Brochet C, Bucchini L, Casas M, Estivill X, Fairley L, Van Gent D, Gonzalez JR, Granum B, Grazulevičienė R, Gutzkow KB, Juvelz J, Keun HC, Kogevinas M, McEchan RRC, Meltzer HM, Sabidó E, Schwarze PE, Siroux V, Sunyer J, Want EJ, Zeman F and Nieuwenhuijsen MJ (2014) The human early-life exposome (HELIX): Project rationale and design. *Environmental Health Perspectives* 122(6): 535–544.

Weimann H, Rylander L, Albin M, Skärbäck E, Grahn P, Östergren P-O and Björk J (2015) Effects of changing exposure to neighbourhood greenness on general and mental health: A longitudinal study. *Health and Place* 33: 48–56.

Whitehead M and Popay J (2010) Swimming upstream? Taking action on the social determinants of health inequalities. *Social Science and Medicine* 71(7): 1234–1236.

Wild CP (2005) Complementing the genome with an “exposome”: The outstanding challenge of environmental exposure measurement in molecular...
epidemiology. Cancer Epidemiology, Biomarkers and Prevention 14(8): 1847–1850.
Wild CP (2012) The exposome: from concept to utility. International Journal of Epidemiology 41(1): 24–32.
Winning A, Glymour MM, McCormick MC, Gilsanz P and Kubzansky LD (2015) Psychological distress across the life course and cardiometabolic risk: Findings from the 1958 British Birth Cohort Study. Journal of the American College of Cardiology 66(14): 1577–1586.
World Health Organisation (2008) Closing the Gap in a Generation: Health Equity through Action on the Social Determinants of Health. Geneva: World Health Organisation.
Yoo E, Rudra C, Glasgow M and Mu L (2015) Geospatial estimation of individual exposure to air pollutants: Moving from static monitoring to activity-based dynamic exposure assessment. Annals of the Association of American Geographers 105(5): 915–926.
Zhang Z, Zyphur MJ and Preacher KJ (2009) Testing multilevel mediation using hierarchical linear models: Problems and solutions. Organizational Research Methods 12(4): 695–719.

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