Chapter 11

Syndemics

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11.1 Introduction

Recognising how early experiences frame and impact later health is a central focus of DOHaD. However, rarely in DOHaD studies are the synergistic characteristics of diseases throughout the lifecourse a central focus. Syndemic theory can enhance our understanding of health over the lifecourse by integrating a more synergistic understanding of early stressors and long-term adverse health, often caused by the interactions of health and social conditions. Syndemic theory posits that disease concentrations (where diseases cluster together) and disease interactions (what adverse effects result from the clustering) cause more health adversity due to their synergistic dynamics. Moreover, because the clusters and interactions of health conditions share upstream drivers, designing interventions to mitigate one condition may have larger-scale impacts on health and well-being. In this way, syndemic theory can contribute meaningfully to DOHaD studies because it considers how and why diseases occur, cluster, and interact across the lifecourse. Further, DOHaD thinking is inherent to syndemic theory, which recognises how chronic stress and inflammation over the lifecourse can play central roles in the interaction and exacerbation of certain infectious and/or non-infectious health conditions. Recognising how and why health conditions cluster together, and what factors from early life through adolescence may have a major impact on adult multimorbidities, can advance both DOHaD and syndemic thinking.

In this chapter, we consider how syndemic thinking can advance DOHaD scholarship by critically engaging with the synergistic underlying conditions of early life that profoundly affect health and disease in later life. In what follows, we describe the history of the syndemics framework and provide a few examples of how the framework has been used in other studies. We discuss the synergies of syndemic and DOHaD theory. We draw on our work with the 'Birth to Thirty' birth cohort based at the Developmental Pathways for Health Research Unit (DPHRU) at the University of the Witwatersrand to provide some examples of how social, psychological, and biological factors cluster and drive health and disease over a lifetime, and demonstrate how the syndemic framework may benefit DOHaD research.

11.2 History of Syndemic Theory

The term syndemics was first proposed by Merrill Singer [1] to demonstrate how socioeconomic, political, or environmental factors influenced the frequently co-occurring problems of substance abuse, violence, and HIV. Singer and Clair [2] defined syndemics as a set of intertwined and mutually enhancing epidemics involving disease interactions at the

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biological level that develop and are sustained in a community/population because of harmful social conditions and injurious social connections. Singer argued that the *syn*ergies of epi*demics* are crucial for understanding what diseases emerge, where, and why. Specifically, syndemics theory focuses on disease concentration (the where) and disease interactions (the how) and provides a framework for understanding what drives disease clusters and for designing interventions that might mitigate these effects. Others have described syndemics by thinking about interactions of 'people, place, and time' and as a 'constellation of affliction' [3]. In many ways, the syndemics framework provides a clear way of thinking about disease: rarely does an individual or population experience a disease in isolation from other conditions – such as social, political, or historical contexts where people live.

Singer first proposed the SAVA Syndemic, showing how substance abuse, violence, and AIDS cannot be understood in isolation among inner-city residents of Hartford, Connecticut. Singer argued that the local HIV epidemic could not be dissociated from the local epidemic of substance abuse and that the pathways of transmission were inextricably linked and deepened by structural violence [1]. In this way, Singer emphasised that understanding local history and social context was fundamental for understanding the social life of an infectious disease. The SAVA syndemic framework is now widely used to develop interventions in the field of HIV/AIDS, while recognising that the interactions between and concentration of diseases have a history and may share an origin. This framing provides clear pathways for intervention, such as through integrating mental health and substance use interventions for the prevention of and living with HIV.

Three rules frame syndemic thinking [1, 2], and these rules are crucial for defining what comprises a syndemic and what does not [4]. First, two or more diseases concentrate within a population. In many cases, this relationship is well documented in the epidemiological literature, often cited as a comorbid or multi-morbid relationship. Second, disease interactions are measurable through bio-bio, bio-social, or bio-psychological pathways, which may include anything from well-documented interactions in biology (such as inflammation) to cultural dynamics (like stigma). Third, macro-scale forces precipitate disease clustering, framed by factors at the macro-level (such as structural violence) to meso-level (such as immigration or gender-based policy) and micro-level (such as interpersonal violence or chronic food insecurity). DOHaD takes a similarly integrative approach, recognising how early exposures to adversity and chronic stress, particularly in relation to nutrition, can profoundly shape disease risk later in life. It is this adversity and the diseases that emerge that often become syndemic; chronic stress and inflammation are closely linked to non-communicable diseases, and these conditions increase the risk for or compromise health when one confronts infections like HIV. It is these underlying conditions, and the weakening of immune function, that compromise one's ability to fight off or live well when multiple serious conditions concentrate together within individuals and communities. The elevated risk of morbidity and mortality among people with such conditions, who are socially and economically marginalised, was exemplified by the recent COVID-19 crisis.

Another example is the syndemic of violence, racist immigration policy, diabetes, depression, and abuse (verbal, emotional, physical, or sexual) among Mexican immigrant women living in the Chicago metropolitan area, as described by Emily Mendenhall [5]. In a mixed-methods study consisting of data collected through life history narrative interviews, biological specimens, and validated psychiatric instruments, Mendenhall describes how interpersonal violence and fear (bound to immigration policy) drove

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distress. These experiences linked stress and trauma from undocumented migration and navigating a racist immigration system to the deleterious effects of living with chronic illness (type 2 diabetes) amidst financial uncertainty. In this case, the adverse health effects of these larger forces, often obscured, could be observed in the epidemiological data demonstrating the close biological and psychological links between depression and type 2 diabetes [5, 6]. A central focus of this work was to describe how study participants, despite seeking care for diabetes or being identified by the state as having diabetes (e.g. via Medicaid), could not become well without psychological healing and overcoming structural barriers like a lack of safety and food [7]. In this way, their diabetes was entangled in a feedback loop with traumatic memories, family stress, chronic financial uncertainty, and untreated depression that required nuanced care and support from the clinic, their community, and their families [5].

These examples illustrate how syndemic co-factors build throughout a lifetime. DOHaD studies can emphasise at what time and in what ways interventions for one aspect of a syndemic may elevate overall health and well-being by lessening the interactions within and among syndemic problems [8] – in this way, syndemic and DOHaD theories are complementary and synergistic.

11.3 How Syndemics Thinking and DOHaD Studies Are Inherently Synergistic

Understanding the social and biological histories of people is as fundamental to the syndemic framework as it is for DOHaD studies. Histories of disease have long engaged with a 'disease biography' approach – where diseases are viewed as biological entities, overlooking how diseases become interconnected and co-occur through social and political processes [9, 10]. Thinking about the rise and decline of syndemics across time, as well as intergenerationally, provides an opportunity to recognise the fundamental role of contexts and driving forces that underlie how and why diseases interact within bodies and populations in a certain time and place. Studies central to driving DOHaD scholarship, such as of the 1944 Dutch Hunger Winter famines [11] and other famines such as in China and Nigeria [12, 13], can provide situational evidence for why and how socio-political contexts may have affected biological risk for disease later in life or across generations. DOHaD studies emphasise how experiences of deprivation can provoke multiple and overlapping chronic conditions later in life, but rarely do they emphasise how these synergistic interactions occur and why. In many ways, DOHaD studies are already thinking syndemically, but making these links clearer, with a focus on interactions that perpetuate disease experiences, can provide clearer modes for intervention [14]. Using syndemic theory in DOHaD research could push forward an understanding of the connectedness of synergistic conditions through time and across space. This allows for syndemics to be studied historically and may allow researchers to fundamentally understand current syndemics and anticipate future ones.

Another attractive aspect of syndemics framework is its broad applicability to conditions or diseases that commonly cluster together such as malnutrition, obesity, and diabetes; HIV and TB; and HIV and non-communicable diseases such as diabetes and mental health [15]. This provides a chance to develop interventions that respond to these diseases concurrently and in an integrative manner as opposed to dealing with individual diseases. Further, preventing syndemics requires not only prevention or control of each disease, respectively, but also understanding and controlling the forces

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that tie the diseases together. Insights gained from understanding syndemics (e.g. HIV syndemics research) can then be transferred and applied to other syndemics.

Syndemics often emphasise how deleterious social and political conditions such as poverty, food insecurity, inequalities, or political instabilities expose populations to disease clustering and interactions across the lifecourse [16]. These factors further shape disease burden, from immune responses to healthcare access. The reverse is also true; disease burden and limited access to healthcare may influence social and economic conditions or processes [17]. For DOHaD research, the syndemic framework may allow researchers to understand diseases holistically by examining how biological synergisms cluster and are worsened by social and structural forces. In other words, the syndemics framework may shed some light on inequalities in diseases and health and why some people suffer more than others within or outside the same geographical locations. For instance, although conditions like type 2 diabetes have been associated with old age [18], we know that insulin resistance can emerge and afflict younger people in part because economic pressures and intensified economic inequalities cause increasing stress, and viral and metabolic conditions are increasingly linked [19–22]. This may best be exemplified in countries such as South Africa that have experienced extraordinary social and political changes [23]. Metabolic disease appears to emerge at earlier ages in South Africa and makes people sicker faster compared to other developed countries [24, 25].

While DOHaD interventions often focus on child, maternal, and preconception health as influential for health across the lifecourse, a syndemic lens is useful to foreground the social or environmental challenges that interact in the early life period to influence well-being. For example, part of our collaborative work in South Africa under the Healthy Life Trajectory Initiative (HeLTI) has suggested that women suffer considerably because of long-term exposure to hardships, poverty, and intergenerational conflicts at home [26]. Women may also frequently parent alone, in part due to parental separations and the early departure of the father in the context of women giving birth before marriage [26]. Women with girl children, fearing for their daughters' futures, sometimes exert undue pressure on their children to achieve educational goals and find secure employment before marriage or childrearing, but this can lead to significant intergenerational tensions. Daughters express stress, anger, anxiety, depression, and suicidal ideations [26], which may affect the risk of early pregnancy [27]. Patriarchal culture plays a crucial role in girls' experiences, where a hierarchy of power and privilege that typically favours men over women, and boys over girls, affects access to food, school, jobs, emotional support, and other crucial aspects of well-being. This then reinforces a systemic inequality that undermines the rights of women and girls and restricts the opportunity for women, men, and gender minorities to express their authentic selves.

This example illustrates the complex social dynamics that affect young people's health, from ways of thinking about sexuality and power to financial security, emotional support, and conceptualisations of a healthy life and well-being. Social, psychological, and biological conditions emerge and interact in different ways throughout the lifecourse. By disentangling how conditions interact and perpetuate one other, clinical programmes can integrate mental and physical healthcare, and policymakers can also prioritise community-based interventions, given that, as we have found in Soweto, people engage in health-seeking far beyond the clinic and can improve their overall health and well-being by engaging in activities that may be religious or relational [28].

Moreover, syndemic theory can advance DOHaD studies as it highlights where, when, and how disease concentration or interaction is likely to occur across the

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lifecourse. For example, households that are exposed to violence (e.g. gender-based violence including intimate partner violence, child maltreatment, or early marriages) may have consequential impacts in later life. Studies have shown that children born in households that experience violence may have developmental delays first seen in infancy; anxiety and mood disorder symptoms and poor peer relationships first seen in childhood; substance use, abuse, or addiction or a diagnosis of substance use disorder often first seen in adolescence; and increased risk for personality and other psychiatric disorders and relationship problems during adulthood [29]. Other research shows that among people exposed to major psychological stressors in childhood, there are elevated rates of morbidity and mortality from chronic diseases of ageing [30]. Understanding such factors can enable the development of timely interventions to ensure that disease clustering does not happen.

In sum, syndemic thinking in DOHaD studies can illuminate how macro-scale factors such as structural violence, meso-level factors such as health policies, and micro-level factors such as intimate partner violence influence disease clustering and interactions and produce poor health outcomes.

11.4 Conclusion

Syndemic theory facilitates an understanding of the cumulative effects of social and environmental influences, and how these interact with other variables such as demographic, biological, genetic, and epigenetic factors across the lifecourse. The syndemic framework underscores a need to focus on social inequality as a root cause of syndemic clustering and interactions and demonstrates that population-level disease prevention can only occur by addressing the large-scale social and structural forces that shape both individual and population health. In addition, addressing harmful or injurious forces at family, community, and population levels can help reduce disease clustering or interactions now and later in life. In this sense, the syndemic framework can highlight 'hotspots' where there is a high likelihood of disease clustering now or in the future and provide an opportunity to intervene before the clustering and interaction take place. Finally, the syndemic framework provides an avenue for interdisciplinary research – as it focuses on multi-layered factors that shape disease distribution at the population level. Thus, integrating syndemics in DOHaD studies may enhance cross-disciplinary research. The framework also enables researchers to address one of the greatest barriers to health improvements: the failure to examine linked phenomena. Syndemic theory allows researchers to move beyond understanding the proximate causes of diseases and draws attention to the processes that create clusters of disease and noxious living conditions for particular populations, affected by a particular condition. It is therefore imperative for DOHaD to think syndemically to understand disease patterns across different time periods.

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