## Syndemic thinking to address multimorbidity in the context of social and structural determinants

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The authors declare no competing interests.

The concept of syndemics specifies which, where, and how disease concentrations and interactions emerge and persist. Recognizing multimorbidity within a population or region is fundamental to syndemics because multimorbid conditions often share upstream drivers, including social inequalities. Applying syndemics to healthcare can inform clinical and policy interventions.

The concept of syndemics (*synergies* of epi*demics*) focuses on both concentrations (clusters) of diseases and interactions of diseases, which together worsen health. Although individual-level analysis of disease interactions are crucial to understand syndemic conditions, generally a syndemic is evaluated at the population-level. These disease concentrations are driven by mutually exacerbating upstream factors, such as inequality, inadequate housing, climate-related stress and/or racism, as well as the iatrogenic effects of maladaptive medical systems.<sup>1,2</sup> The concept places multimorbidity – the co-occurrence of two or more long-term conditions in one individual<sup>3</sup> – at its theoretical center. Multimorbidity is among the most pressing threats to health systems globally and has been welcomed as a more realistic understanding of disease. Research and care in this framework pushes boundaries beyond the siloed diagnosis and treatment domains of singular conditions, acknowledging disease clusters and their shared upstream determinants.<sup>3–5</sup> Syndemics also takes into account where these multiple conditions come from, how and why they occur together, and where to intervene.

The increasing focus on multimorbidity in clinical studies points to the need for more holistic, upstream, and integrated approaches to health and care. However, defining multimorbidity in purely biomedical terms is limited and inadvertently sidelines other concepts that have labelled, analyzed, and precipitated action on this challenge over the past half century. Following the Whitehall Studies, which were among the first efforts to rigorously demonstrate the association between socio-economic status and disease, several theories referred to and, in some cases, explicitly named multimorbidity as emergent within larger social and ecological constructs. These theories include, for example, eco-social theory, fundamental cause theory, local biologies, recursive cascades, and syndemics. These frameworks emphasize how multiple conditions emerge and interact, often with social, ecological, and political domains, albeit to different degrees.

Among these theories, syndemics provides a useful bridge between the social and medical sciences because of its biological focus. Syndemics involve a set of intertwined and mutually enhancing epidemics involving disease interactions at the biological level that develop and are sustained in a community or population because of harmful social conditions and injurious social connections. By emphasizing where disease concentrations emerge geographically and how diseases interact biologically, syndemic thinking also highlights the need to design interventions that might mitigate these effects. For example, the Soweto Syndemics study, conducted in Soweto, an urban township in Johannesburg, South Africa, demonstrated that patients with comorbid disease who experienced high stress levels reported considerably lower quality of life than patients with fewer stressors and the same comorbidities<sup>2</sup>. This study indicates how social and structural interventions might improve the health of people living with multimorbidity more than medical interventions alone.

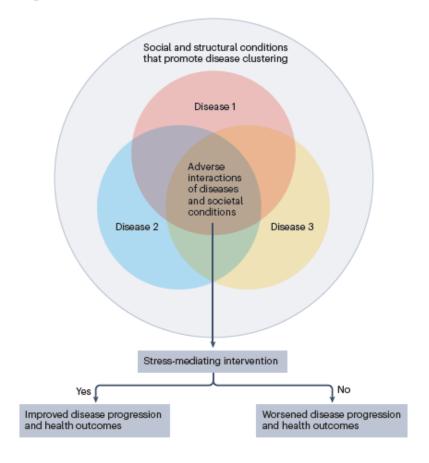
Syndemic thinking can be understood using three orientating rules that define what is a syndemic and what is not (Figure 1). The first rule involves identifying multimorbidity, where two or more diseases concentrate within a population, for example, through epidemiological analysis of co-occurring diseases within the same individual and/or the same population. In the Soweto Syndemics study, type 2 diabetes mellitus (T2DM) clustered primarily with one or more conditions (primarily hypertension, depression, and HIV infection) within six neighborhoods of Soweto. This was measured using standard survey and biological measures to evaluate glucose, blood pressure, HIV status, and depressive symptoms in a large sample. The second rule requires identification of disease interactions that are measurable through biological pathways and interact with social, psychological, or concurrent biological disturbances, which may include anything from well documented biological interactions (such as inflammation) to cultural dynamics (such as stigma). In Soweto, earlier clinical research illustrated how closely these conditions interact (for example, diabetes with depression and/or hypertension) and ethnographic work highlighted how HIV infection and T2DM are linked through stigma. Finally, the third rule considers how upstream or macro-scale forces precipitate disease concentration, such as policies around food, housing, rights, education, and healthcare, which may impede an individual from living a healthy and secure life. The Soweto Syndemics study evaluated how these factors affected health and well-being, such as stress related to finances, safety, housing, family, knowing someone who can lend you money, or having someone to rely on in a crisis. Hence, investigations of the third rule clarify what factors may perpetuate not only disease concentrations but also disease interactions that make people sick. By identifying specific pathways through which upstream factors cause syndemics, the third rule emphasizes how interventions for multimorbidity require a combined effort of both clinical (downstream) and policy (upstream) interventions because clinical interventions cannot address the root cause of disease clusters.

Syndemic care provides a practical conceptual interface between policy and clinical interventions. It involves a shift in emphasis from curative care to active screening for conditions known to interact syndemically in a particular setting. This approach may include, for example, integrated mental health and HIV screening (as is increasingly practiced in HIV care) as

well as screening for social vectors of mental health conditions, such as discrimination, stigma, domestic violence, and chronic poverty. The example in Soweto emphasizes how social dynamics may be an important space for intervention: ethnographic data revealed how health interventions through church groups and meetings might be effective in improving health. In this way, screening and care in non-medical settings may be an effective intervention on a patient's own terms. Patients may subsequently be more open to attending coordinated medical visits for multiple conditions at once in medical or non-medical settings, including home visits. Thus, syndemic care conceptualizes patients receiving treatment that addresses their conditions as one unit in contrast to an approach of managing discrete diseases. Health workers devising treatment plans are trained in holistic health models that integrate management of physical, mental, and social ills. This requires an expanded view of 'generalism' – well-recognized as crucial for multimorbidity care – to emphasize the importance of structural competency within training curricula and continuous professional development. On the structural competency within training curricula and continuous professional development.

Today, people live within a complex, changing world where diseases cluster, interact, and become embedded in their everyday lives. Multimorbidity emphasizes how multiple conditions cluster within individuals and populations, but the dominant biological concept of multimorbidity tends to stop short of meaningfully incorporating non-medical factors in health and wellbeing. Syndemic care meets people where they are: spaces where they feel safe, treatment plans that include their various symptoms and diagnoses, and recognition of the social and emotional dynamics that drive their ill or good health. Syndemic care can, therefore, help reinvigorate long-standing calls for more upstream, integrated, and person-centered approaches by putting the coexistence of multiple social and health conditions at the center of care.

Fig 1



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Figure 1 | The syndemic model

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Syndemic thinking integrates social and medical sciences by taking into account social conditions where disease concentrations emerge and how diseases interact biologically. Syndemic care aims to provide upstream and person-centered management approaches, integrating clinical and structural[Au: Or "policy"?] interventions.

