

## Editorial

# A Syndemic Model: COPD, Multimorbidity, and Poverty

Sophia A. Hayes, MD, MS<sup>1,2</sup> Ananya L. Bhatia-Lin, MD<sup>3</sup> Jai-la Campbell, MD<sup>4</sup> Aaron Baugh, MD<sup>5</sup>

1. Center of Innovation for Veteran-Centered and Value-Driven Care, VA Puget Sound Health Care System, Seattle, Washington, United States
2. Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, University of Washington, Seattle, Washington, United States
3. Department of Medicine, University of Washington, Seattle, Washington, United States
4. Department of Medicine, Henry Ford Macomb Hospital, Macomb Township, Michigan, United States
5. Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, University of California-San Francisco, San Francisco, California, United States

### Abbreviations:

**COPD**=chronic obstructive pulmonary disease

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### Address correspondence to:

Sophia Hayes, MD  
University of Washington  
Division of Pulmonary, Critical Care, and Sleep Medicine  
1959 Northeast Pacific Street, Box 356522  
Seattle, WA 98195  
shayes4@uw.edu

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## Introduction

A well-known proverb tells us that the poor will always be with us. Disappointingly, despite sustained clinical attention and research funding, it can sometimes feel that the same

is true of chronic obstructive pulmonary disease (COPD). What explains the lack of progress in improving disease outcomes? One possibility is that the persistence of these 2 problems is connected. In a recent perspective by Fabbri and colleagues, COPD is described as part of a syndemic of multiple co-occurring chronic conditions.<sup>1</sup> This builds on existing guideline statements and the reality that individuals with COPD suffer from an average of 5 chronic diseases.<sup>1-3</sup> However, we believe that the value of this model is more than incremental. Heretofore, syndemic theory has mostly been applied to diseases that disproportionately impact those of low socioeconomic status. It moves away from a single-disease management approach to place multimorbidity and social justice at its theoretical core.<sup>4</sup> We extend Fabbri's proposal to explore its clinical and policy implications and propose the next steps to ground the theory through empirical evaluation.

## Syndemic Theory

Syndemic theory posits that diseases cluster due to mutually exacerbating upstream factors such as racism, structural injustice, and maladaptive medical systems.<sup>4,5</sup> To qualify as a syndemic, 2 or more diseases must co-occur within a specific population and share common causative contextual and social factors. The final criterion is that involved diseases must synergistically and bidirectionally multiply each other's burden.<sup>4,6-8</sup> Like the eco-social and fundamental cause theories, syndemic theory highlights how health conditions emerge within their social, ecological, and political domains. Uniquely, syndemic theory focuses on biological mechanisms, thereby, bridging the medical and social sciences. For those interested in reducing health disparities in COPD, syndemic thinking offers a roadmap for upstream policy and downstream clinical interventions.

## COPD, Multimorbidity, and Poverty – A Proposed Syndemic

Instead of identifying one or more single diseases in their proposed syndemic, Fabbri et al<sup>1</sup> identified multimorbidity itself as the syndemic associated with COPD. Commonly co-occurring conditions with COPD include cardiovascular

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and other respiratory diseases, osteoporosis, muscle wasting, metabolic disorders, and neuropsychiatric disorders.<sup>1,9</sup> For several of these, they developed phenotypic descriptions for unique patterns of clinical and biomarker expressions in COPD. Examining these phenotypes can demonstrate how multiple comorbidities concentrate with COPD in temporal or geographic contexts, and interactively influence disease burden.<sup>1,9</sup> For instance, among both tobacco-smoking and nonsmoking patients with COPD, cardiovascular mortality is positively associated with airflow obstruction.<sup>10,11</sup> Conversely, compared to individuals with COPD alone, those with cardiovascular disease have a significantly higher risk of mortality,<sup>12</sup> suggesting a bidirectional interaction. Similarly, the degree of airflow obstruction in COPD is independently associated with reduced bone mineral density,<sup>13</sup> while low bone mineral density is associated with increased COPD-specific and all-cause mortality, even after controlling for airflow obstruction and physical activity.<sup>14,15</sup> While warranting further empiric confirmation, Fabbri's theory emphasizes that beyond chance, multimorbidity appears to be a fundamental feature of many individuals who develop COPD.<sup>1</sup>

The syndemic theory, grounded in the biosocial conception of health, posits that social and environmental conditions contribute to the development, clustering, and progression of diseases within a population.<sup>6</sup> COPD develops from complex and cumulative gene-environment interactions that begin in conception and continue through adulthood (see Figure 1).<sup>16</sup> Exposure to stress across the lifespan, referred to as the exposome, leads to epigenetic changes, alterations in gene expression, and changes in the immune system that alter organ development and cellular aging.<sup>16,17</sup> Examples of early life stressors proposed to impact COPD include exposure to second-hand smoke, childhood respiratory infections, asthma, poor nutrition, and air pollution.<sup>17,18</sup> In addition to these factors, the stress associated with adverse childhood experiences leads to alterations in biological function through a process known as embodiment and increases the risk of developing chronic lung disease later in life.<sup>19,20</sup> Throughout adulthood, further exposure to tobacco smoke, environmental pollution, occupational toxins, and stress compound with early life risk to influence the age at COPD presentation, disease severity, and speed of progression.<sup>18</sup> Many of these risk factors are not unique to COPD and contribute to the synchronous development of comorbid chronic conditions.<sup>1,16,18</sup> All are hazards associated with marginalization and low socioeconomic status.

Integrating life course epidemiology and the principles of gene-environment-time interactions, syndemic theory helps elucidate the causality between policy and COPD comorbidity. At the macro level, many of the aforementioned exposures cluster within areas of high socioeconomic disadvantage.<sup>21</sup> Racism, segregation,

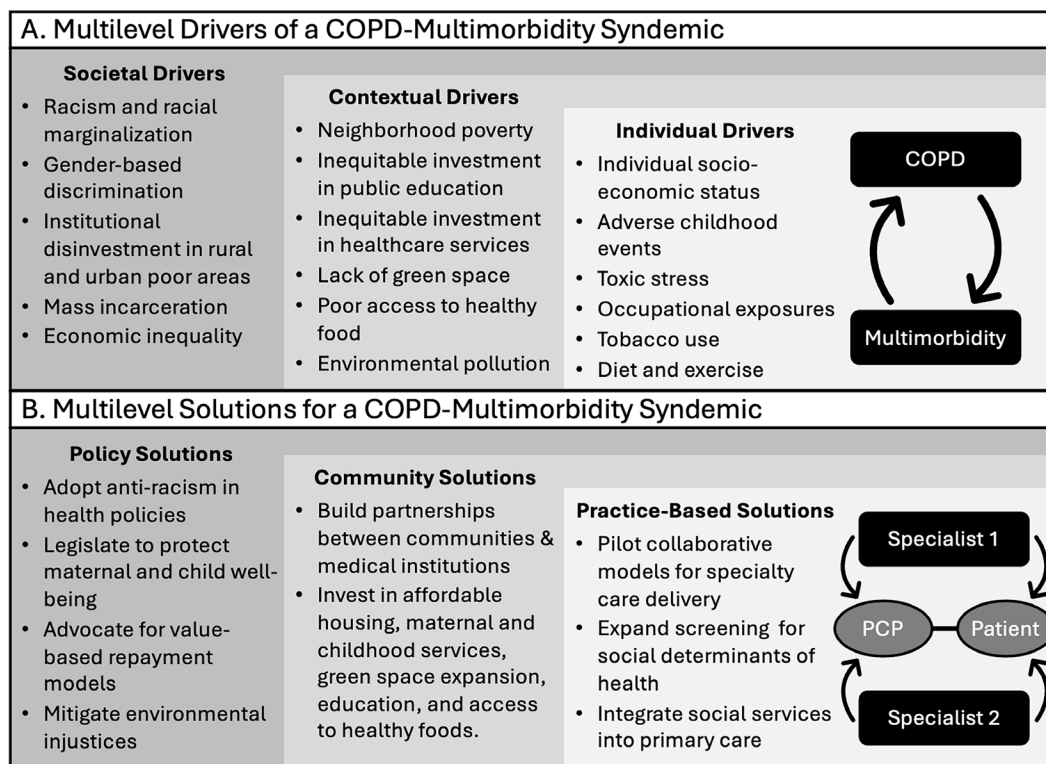
institutional disinvestment, and other forms of structural and interpersonal violence underpin much of the persistent concentration of poverty in these locales.<sup>22</sup> Individuals from more disadvantaged neighborhoods are more likely to reside near polluting industries, suffer occupational toxic exposures, have unsafe or inadequate housing, and experience daily and unremitting levels of toxic emotional stress.<sup>23-25</sup> The evidence base linking poverty to chronic disease, including COPD and its comorbidities,<sup>26-29</sup> is undeniable and staggering. As the rising terminology of “social drivers” of health suggests, this is not a predetermined fate but the result of deliberate and reversible policy choices.

## Treatment and Policy Implications

Individuals with COPD fall through the cracks at multiple levels within our health care system. It is estimated that up to 80% of people with COPD are undiagnosed, delaying interventions that could reduce the morbidity and mortality associated with disease progression.<sup>30,31</sup> Once diagnosed, the treatment approach to COPD remains largely dependent on overburdened primary care providers separately managing multiple comorbidities within a fragmented fee-for-service health care system.<sup>32</sup> Individuals diagnosed with COPD, even those on optimal guideline-concordant therapy, often suffer poor quality of life and increased mortality.<sup>33</sup> Multimorbidity exacerbates poor outcomes for individuals with COPD.<sup>10</sup> Applying syndemic theory encourages several points of intervention.<sup>34</sup>

First, it brings renewed attention to the poor and underserved. Guideline adherence in COPD care is chronically poor.<sup>35</sup> Cost is an important contributing factor.<sup>36</sup> Trials to address this concern, whether through direct subsidy or conversion to generic inhaled agents, have each demonstrated over 50% relative improvements in treatment adherence.<sup>37,38</sup> Aligned with these results, Illinois recently passed legislation<sup>39</sup> to cap copays for inhalers at \$25. Conceiving the disease in a way that centers its ties to poverty would clarify the need for broad adoption of such reforms. From a research perspective, the traditional, single-disease-focused system has collected too little data from racial/ethnic minorities and left unanswered questions about the ideal management of patients with comorbidities.<sup>40</sup> A syndemic-informed perspective that broadened inclusion criteria would align with current recommendations to improve clinical trial diversity.<sup>41,42</sup> In fact, because racial/ethnic minorities with COPD are more clinically impacted by comorbidities than their non-Hispanic White counterparts,<sup>43</sup> it would further incentivize intentional recruitment efforts.

Another major benefit of syndemic theory is encouraging a more holistic management approach that places the individual at the center of an integrated, collaborative care system.<sup>34</sup> Such models have already been

**Figure 1. Multilevel Drivers and Solutions for a COPD-Multimorbidity Syndemic**

shown to improve guideline-concordant care and quality of life for patients with COPD.<sup>44,45</sup> Nonetheless, they less commonly incorporate social services or community-level interventions. The syndemic framework expands traditional collaborative care to include accessible screening and management of comorbidities as well as identification of the specific social drivers of syndemic conditions.<sup>7</sup> It promotes the incorporation of alternate care providers (e.g., pharmacists, nurses, or population health specialists) into the workforce, thereby, expanding access to quality care.<sup>34</sup> Additionally, the population-based, collaborative systems of care promoted by the syndemic framework naturally align with value-based repayment models, which themselves promote health equity as a core tenant.<sup>46,47</sup>

Though such an integrative care system is daunting, it is not out of reach. The Veteran Affairs Whole Health initiative promotes a holistic approach that helps patients access medical and nonmedical interventions that can influence their health.<sup>48</sup> Partnerships with existing community leaders and organizations are another route for capacity-building to address upstream social determinants while piloting integrative care strategies.<sup>34</sup> This multipronged approach, though reliant on institutional support and individual advocacy, is likely to move the needle on COPD care and outcomes beyond what is achievable under our current single-disease paradigm.<sup>27</sup>

## Future Directions

Syndemic theory holds the potential to bridge the social sciences and biomedical research, align policymakers and health systems to improve population health, and inform the clinical care of individual patients. However, to serve as an effective heuristic for advocacy and reform, the theory must be rigorously and empirically validated.<sup>49</sup> Until now, evidence of a COPD-multimorbidity syndemic has been largely circumstantial. Potentially concordant evidence emerges from research designs but is nonetheless unable to affirm or falsify the underlying theoretical construct. Multiple analytic approaches have been recommended to fill this evidence gap.<sup>49,50</sup> Examples include multilevel modeling in population-level studies, path and social network analysis to map the temporal cascade of health risks, agent-based models to investigate the impact of interventions on disease dynamics, and mixed methods to enrich statistical and mathematical models. Syndemic localization, a mixed methods approach, combines quantitative analysis to test the existence of syndemics and qualitative methods to explore how “syndemic suffering”<sup>51</sup> manifests uniquely within different communities.<sup>49-52</sup> Leveraging publicly available datasets on area-level rates of COPD, other chronic diseases, as well as social determinants of health, may facilitate syndemic localization within the United States.<sup>53,54</sup> Purposeful recruitment of community members from across the urban and rural continuum as well as from

geographically diverse areas enriches our understanding of the lived experience of vulnerable individuals and communities<sup>49-52</sup> Syndemic theory relies on ethnography, a qualitative research technique that can be adapted to understand how COPD interacts uniquely with other diseases of poverty across and within different communities.<sup>34</sup> Such narratives may reveal not only maladaptive sociocultural factors but also community sources of strength and resilience to combat the burden of poverty and disease. Instead of simply representing a new avenue for descriptive health research, a mixed methods approach like syndemic localization orients the researcher towards the community and may identify targets and collaborators for interventions.

## Conclusions

We are in the midst of a nationwide reckoning on the entangled challenges of racism, structural injustice, and chronic disease. Researchers, health systems, and policymakers are mobilizing for health equity. Though much-needed and long overdue, this drive for health equity evades

a central challenge of American health care: that primary and preventative population health care are deprioritized in favor of revenue-generating procedural care.<sup>55</sup> Within the fee-for-service model, there is little incentive to be accountable for the upstream forces that perpetuate chronic disease. It is more profitable for health systems to treat a series of apparently incidental single diseases, leaving overburdened primary care providers with potentially conflicting recommendations, and the patient with growing medication lists, side effects, and disempowerment. Syndemic theory offers a meaningful alternative. Highlighting the role that unresolved social distress plays in undermining treatment success, it motivates research that gives voice to communities that disproportionately suffer from racist and discriminatory policies. Acknowledging the connections between chronic diseases, syndemic theory promotes value-based collaborative care models that integrate clinical care for the multimorbid state. And it calls on each of us, as researchers, clinicians, and leaders to advocate for policy reforms that address upstream social drivers of health inequities.

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