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Co-occurring epidemics, syndemics, and population health

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Introduction

As originally theorised, three concepts underlie the notion of a syndemic: disease concentration, disease interaction, and the large-scale social forces that give rise to them.[1, 2] The concept of *disease concentration* holds that two or more epidemics co-occur in particular temporal or geographical contexts due to harmful social conditions. This aspect of the theory of syndemics is not necessarily what makes its contribution distinctive. For example, anthropologists have long called attention to the manner in which large-scale political, economic, and cultural forces have given rise to clustered epidemics of various infectious diseases, most prominently HIV and tuberculosis[3–5]; and the theory of fundamental causes highlights the roles of these forces in driving concentrated health disadvantage.[6–8] Rather, what makes the theory notable are its predictions about how interactions between epidemics amplify disease burden and about how public health planners can (or cannot) effectively intervene to mitigate this burden. Although the theory of

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Conflicts of interest

We declare that we have no conflicts of interest.

Ethics statement

Preparation of this manuscript required no research involving human subjects. Therefore, no ethical approval was sought.

syndemics is principally a theory about population health, the past two decades' worth of quantitative literature motivated by the theory has generally focused on studying individuals, rather than populations -- and consequently has had very little to say about population health. Our aim in this *Viewpoint* is to critically review the literature on syndemics and to introduce key concepts for measuring their impacts on population health.

Measuring syndemics

The concept of *disease interaction* in the theory of syndemics holds that co-occurring epidemics interact at the level of populations and individuals, with mutually enhancing deleterious consequences for health. Compared with the other tenets of the theory, the concept of disease interaction has received less empirical support in the literature, perhaps owing to its complexity. At times, its framing language has focused specifically on interaction (or synergism): the disease burden attributable to health risks in combination exceeds the sum of the disease burden of the health risks when considered separately.[9] The most highly cited précis of the theory of syndemics[10] describes numerous exemplars that draw exclusively on the language of interaction, e.g., the risk of hepatocellular carcinoma is greater among persons with chronic hepatitis C virus infection who also consume alcohol (compared with persons who either have hepatitis or consume alcohol, and compared with persons who neither have hepatitis nor consume alcohol). Other statements of the theory have instead adopted the language of mutual causality (or bidirectionality). The canonical elaboration of the unhappy triad of substance abuse, violence, and HIV,[1] for example, focuses on the ways in which substance abuse increases the risk of violence and HIV acquisition, violent victimisation increases the risk of HIV acquisition and begets further substance abuse, and persons with HIV are often subjected to violence specifically because of their seropositivity.

These two different models of co-occurring epidemics are represented, without reference to the social forces conditioning exposure, in the Figure. Notably, these two models imply different treatment or prevention strategies -- but the conceptual distinctions between the two have largely been blurred. In the field of HIV treatment and prevention, appeals to the theory of syndemics are near-universally used to justify calls for complex, integrated and/or multi-component interventions targeting all of the co-occurring epidemics in concert.[11–13] Operario and Nemoto, [11] for example, have argued that "Multicomponent interventions are necessary to mitigate the HIV syndemic dynamics in transgender communities… In order for multiple services to form a meaningful bundle, they must be complementary, synergistic in their health benefit, cost-effective, and accepted by target audiences" (p.S92).

Two significant observations can be made about such recommendations.

First, the empirical foundation underlying enthusiasm for multi-component interventions is limited. Since its original conceptualization, the theory of syndemics has received scant empirical support either for its concept of disease interaction or for the model of mutually causal epidemics. Rather, the overwhelming majority of studies[14] have employed an empirical specification similar to that which has predominated in the literature on childhood adversity, i.e., a sum score of exposures.[15–18] While helpful, in some instances, for

understanding the health effects of cumulative adversities, the sum score sheds light on the co-dynamics of neither interaction nor mutual causality.[19] Studies in the literature published more recently have largely adopted a similar approach (Panel).

Panel

Systematic review of empirical tests of the disease interaction concept

In a pair of recently published critiques of quantitative studies on syndemics, Tsai and colleagues[14, 19] highlighted the problematic ways in which the literature has deviated from its theoretical underpinnings. First, Tsai and Burns [14] systematically reviewed the literature and showed that most studies claiming to test the disease interaction concept actually use an empirical specification (i.e., the "syndemic count variable," or a sum score corresponding to the total number of psychosocial problems) that sheds light on neither syndemic synergy nor mutual causality; *viz.,* the models depicted in the Figure. Tsai and Venkataramani [19] then explored the implicit assumptions embedded in the sum score approach, highlighting the consequential ways in which programme implementers and public health policymakers might be led astray in their efforts to counter the large-scale forces leading to concentrated health disadvantage.

Systematic review

Here we update the systematic review to include new studies that have appeared in the literature since its publication. Our systematic evidence search was conducted on July 2, 2016 with the aim of identifying empirical studies testing the disease interaction concept in the theory of syndemics. Interested readers are referred elsewhere for a full description of the methods.[14] In brief, the search "syndemic [all fields] OR syndemics [all fields]" was applied to PubMed, with retrieval restricted to articles published on or after January 1, 2015. The search "allintitle:syndemic OR syndemics" was also applied to Google Scholar, with a similar date restriction, to identify additional publications not indexed in PubMed. Of 87 records returned in the PubMed search, 23 met criteria for inclusion; of 119 records returned in the Google Scholar search, after excluding duplicates an additional 4 conference presentations, 2 journal articles, and 1 doctoral dissertation met criteria for inclusion. These 31 newly identified studies were combined with the 40 studies identified in the original systematic review, and their summary characteristics are shown in the Table.

All of the included studies were based on data collected at the individual level (71 [100%]). The most frequently used specification to test the disease interaction concept was the sum score (57 [80%]). Compared to studies that used other specifications (e.g., a product term in a multiplicative model), the studies that employed the sum score approach were much more likely to characterise their findings as demonstrating that psychosocial problems had "additive associations" with the outcomes of interest (28/57 [49%] vs. 1/14 [7%]; $\chi 2=8{\cdot}20$, $P=0{\cdot}004$). Although no formal tests of interaction were used, these studies were also much more likely to adopt language about "synergy" or "interaction": 20/57 (35%) of these studies employed such language, compared to 0/14 (0%) of the others ($\chi 2=6{\cdot}84$, $P=0{\cdot}009$).

In terms of any observed changes in the literature before and after the publication of the review by Tsai and Burns, [14] minor differences were noted. First, the proportion of studies based solely on data collected in the U.S. has declined (32/40 [80%] vs. 21/31 [68%]; $\chi 2=1{\cdot}39$, P=0·24). Second, the percentage of studies describing "additive associations" has also declined (20/40 [50%] vs. 9/31 [29%]; $\chi 2=3{\cdot}18$, P=0·08). The Web Appendix Table provides more detail on the 31 newly identified studies.

Interpretation

Most quantitative studies that aim to test the disease interaction concept in the theory of syndemics have adopted an empirical specification that sheds light on neither syndemic interactions nor mutually causal epidemics. None have been based on ecological, multilevel, or experimental/quasi-experimental study designs. These findings illustrate important methodological gaps in the literature. Since the publication of the systematic review, there have been minimal signs of progress: although the estimated associations are not statistically significant, the quantitative literature on syndemics is diversifying -- incorporating data on vulnerable populations and those living in resource-limited settings outside of the U.S. -- while simultaneously becoming more accurate in its representations and increasingly discarding the uninformative[19] language of "additive associations." Future studies should incorporate data from multiple levels of analysis, which will provide additional opportunities to understand how epidemics interact both at the level of populations and at the level of individuals, and to understand how syndemics evolve across space and time. In doing so, they will generate evidence to support appropriate interventions to improve the health and psychosocial wellbeing of vulnerable populations worldwide.

Second, the conceptual foundation underlying the bias against single-component interventions does not necessarily follow from a close reading of the theory of syndemics. It is true that, in the setting of mutually causal epidemics, single-component intervention strategies targeting a single epidemic would likely be ineffective, because the other epidemics ignored by the intervention would continue to exert their reciprocal, driving forces on the epidemic of focus. On the other hand, if a syndemic is characterised by synergistically interacting epidemics that are not mutually causal, then there may be opportunities to implement efficient single-component interventions that could potentially have a greater impact on the HIV epidemic than would otherwise be expected if no synergy were present (Web Appendix Panel). The preventive impact of the single-component intervention would likely be less than the impact of the multi-component intervention, but implementing the single-component intervention may nonetheless be a prudent decision if resources are limited and if there is some uncertainty about the effectiveness of the multi-component intervention.

Most striking is the inconsistency between the calls for multi-component interventions and the statistical models used to support such recommendations. Tsai and Venkataramani [19] showed, for example, that one of the most commonly employed specifications in the literature essentially encodes an assumption that epidemics A and B have null main effects and exert a joint effect on the HIV epidemic only when both A and B are present. Response

patterns of this type might be considered a special case of the syndemic model in the left panel of the Figure and are often referred to as a "sufficient cause interaction."[20, 21] We are unaware of any such examples in the literature on syndemics. Moreover, the presence of sufficient cause interaction does *not* militate for a multi-component intervention targeting both epidemics A and B for effective HIV prevention. Rather it suggests the opposite: that a single-component intervention targeting either epidemic A or B would suffice (because if either exposure were to be eliminated then the outcome could not occur). Yet researchers and programme implementers drawing on the theory of syndemics rarely, if ever, advocate for single-component interventions; rather, calls for multi-component interventions are typically the norm.[11–13]

While there may be few examples of sufficient cause interactions in the literature on syndemics, less rare are scenarios in which there are multiple sufficient risk factors for disease. Enteric pathogens, for example, have multiple sufficient pathways to diarrhoea that may overlap and interact at multiple levels of analysis.[22–25] Under such conditions, multi-component intervention strategies targeting all of the pathways in concert are necessary for effective diarrhoeal disease control.[26] But the force of this programmatic recommendation is not contingent upon an appeal to syndemic synergy.

Syndemics and the "individualistic fallacy"

The theory of syndemics -- and, specifically, its concept of disease interaction -- involves multiple levels of analysis.[10] For example, Singer [27] notes: "Recently, in our efforts to further delineate the concept of syndemic [*sic*], we have drawn attention to the fact that disease interaction occurs at both the population and individual levels" (p.39). By implication, data from multiple levels of analysis should be mobilised in order to gain purchase on validating the theory. The field, however, has largely focused on investigating how individual-level outcomes can be explained by individual-level covariates.[14] The omission of population-level studies is significant -- representative of the "individualistic fallacy"[28, 29] -- because it has led the field away from investigating the distal syndemic causes that, if eliminated, hold even greater potential for efficient prevention strategies.

To take a specific example: power imbalances within relationships[30, 31] and men's beliefs about gender roles[32] are thought to be risk factors for cases of violence against women. These risk factors might be most likely to elevate the risk of violence in settings where women are structurally disadvantaged, either by law or by tradition, relative to men in terms of land ownership and access to other factors of production,[33] or in settings where violence against women is normative.[34, 35] And when these adverse structural conditions are mitigated through economic[36] or legislative[37, 38] changes, the individual-level risk factors might matter less or (in the extreme, e.g. in settings of perfect gender equality) might cease to matter entirely.

To invoke Geoffrey Rose,[39, 40] even though the individual-level risk factors are generally accepted as more proximate causes (e.g., of violence against women) and therefore more amenable to causal attribution, the field can achieve more efficient population-level prevention of the disease burden wrought by syndemics if attention is shifted toward

eliminating the large-scale social forces that condition the distributions of individual-level risk factors or expedite their interaction and translation into diseased states. In the literature on syndemics, large-scale social forces like mass incarceration,[41, 42] gender-inequitable norms,[43] the home foreclosure epidemic,[44] and racial segregation[45] may be discussed but have largely gone un-modeled.

The individualistic fallacy therefore leads the field to miss critical opportunities to understand how epidemics interact both at the level of populations and at the level of individuals. Given the explicitly multilevel emphasis of the theory of syndemics,[10, 27] multilevel models could provide a needed bridge between ecological study designs and cohort/case-control/cross-sectional study designs to show how epidemics (e.g., violence[46–48]) and large-scale social forces (e.g., foreclosure and neighborhood degradation, [44, 49] or lack of economic opportunity[50–54]) interact at both the population and individual levels to worsen the burden of disease. Studies that ignore interactions with ecological influences to focus exclusively on how individual-level risk factors interact to affect disease outcomes within relatively homogeneous populations may erroneously conclude that interactions between individual-level risk factors are the principal determinants of disease.

Conclusion

The theory of syndemics is a notable conceptual instrument in population health science that has the potential to help policymakers and programme implementers in their endeavours to improve the health of populations. As theorised, syndemics are a complex, multilevel phenomenon. There remain important opportunities to investigate how epidemics interact both at the level of populations and at the level of individuals. The field will need to move forward beyond the first generation of studies to mobilise evidence to support appropriate interventions to improve the health and psychosocial wellbeing of vulnerable populations worldwide.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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BIBLIOGRAPHY

1. Singer M. A dose of drugs, a touch of violence, a case of AIDS: conceptualizing the SAVA syndemic. Free Inq Creative Sociol. 1996; 24(2):99–110.
2. Singer M. Toward a critical biosocial model of ecohealth in southern Africa: the HIV/AIDS and nutrition insecurity syndemic. Annals of Anthropological Practice. 2011; 35(1):8–27.
3. Farmer P, Kleinman A. AIDS as human suffering. Daedalus. 1989; 118(2):135–60.

4. Farmer P, Lindenbaum S, Good MJ. Women, poverty and AIDS: an introduction. Cult Med Psychiatry. 1993 Dec; 17(4):387–97. [PubMed: 8112083]
5. Farmer P. Social inequalities and emerging infectious diseases. Emerg Infect Dis. 1996 Oct-Dec; 2(4):259–69. [PubMed: 8969243]
6. Link BG, Phelan J. Social conditions as fundamental causes of disease. J Health Soc Behav. 1995; 35(Extra Issue):80–94.
7. Phelan JC, Link BG, Tehranifar P. Social conditions as fundamental causes of health inequalities: theory, evidence, and policy implications. J Health Soc Behav. 2010; 51(Suppl):S28–40. [PubMed: 20943581]
8. Lutfey K, Freese J. Toward some fundamentals of fundamental causality: socioeconomic status and health in the routine clinic visit for diabetes. American Journal of Sociology. 2005; 110(5):1326–72.
9. Rothman KJ. Synergy and antagonism in cause-effect relationships. Am J Epidemiol. 1974 Jun; 99(6):385–8. [PubMed: 4841816]
10. Singer M, Clair S. Syndemics and public health: reconceptualizing disease in bio-social context. Med Anthropol Q. 2003; 17(4):423–41. [PubMed: 14716917]
11. Operario D, Nemoto T. HIV in transgender communities: syndemic dynamics and a need for multicomponent interventions. J Acquir Immune Defic Syndr. 2010 Dec; 55(Suppl 2):S91–3. [PubMed: 21406995]
12. Li R, Cai Y, Wang Y, Sun Z, Zhu C, Tian Y, et al. Psychosocial syndemic associated with increased suicidal ideation among men who have sex with men in Shanghai, China. Health Psychol. 2016 Feb; 35(2):148–56. [PubMed: 26462059]
13. Chakrapani V, Newman PA, Shunmugam M, Logie CH, Samuel M. Syndemics of depression, alcohol use, and victimisation, and their association with HIV-related sexual risk among men who have sex with men and transgender women in India. Glob Public Health. in press. Epub ahead of print 12 Oct 2015.
14. Tsai AC, Burns BFO. Syndemics of psychosocial problems and HIV risk: a systematic review of empirical tests of the disease interaction concept. Soc Sci Med. 2015; 139(1):26–35. [PubMed: 26150065]
15. Sameroff AJ, Seifer R, Barocas R, Zax M, Greenspan S. Intelligence quotient scores of 4-year-old children: social-environmental risk factors. Pediatrics. 1987 Mar; 79(3):343–50. [PubMed: 3822634]
16. Turner RJ, Lloyd DA. Lifetime traumas and mental health: the significance of cumulative adversity. J Health Soc Behav. 1995 Dec; 36(4):360–76. [PubMed: 8719054]
17. Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. Am J Prev Med. 1998 May; 14(4):245–58. [PubMed: 9635069]
18. Montez JK, Hayward MD. Cumulative childhood adversity, educational attainment, and active life expectancy among U.S. adults. Demography. 2014 Apr; 51(2):413–35. [PubMed: 24281740]
19. Tsai AC, Venkataramani AS. Syndemics and health disparities: a methodological note. AIDS Behav. 2016 Feb; 20(2):423–30. [PubMed: 26662266]
20. VanderWeele TJ. Sufficient cause interactions and statistical interactions. Epidemiology. 2009 Jan; 20(1):6–13. [PubMed: 19234396]
21. VanderWeele TJ, Robins JM. Empirical and counterfactual conditions for sufficient cause interactions. Biometrika. 2008; 95(1):49–61.
22. Wagner, EG., Lanoix, JN. Excreta disposal for rural areas and small communities. Geneva: World Health Organization; 1958. WHO monograph series no. 39
23. Briscoe J. Intervention studies and the definition of dominant transmission routes. Am J Epidemiol. 1984 Sep; 120(3):449–55. [PubMed: 6475919]
24. VanDerslice J, Briscoe J. Environmental interventions in developing countries: interactions and their implications. Am J Epidemiol. 1995 Jan 15; 141(2):135–44. [PubMed: 7817969]
25. Curtis V, Cairncross S, Yonli R. Domestic hygiene and diarrhoea - pinpointing the problem. Trop Med Int Health. 2000 Jan; 5(1):22–32. [PubMed: 10672202]

26. Eisenberg JN, Scott JC, Porco T. Integrating disease control strategies: balancing water sanitation and hygiene interventions to reduce diarrheal disease burden. Am J Public Health. 2007 May; 97(5):846–52. [PubMed: 17267712]
27. Singer M. A dose of drugs, a touch of violence, a case of AIDS, part 2: further conceptualizing the SAVA syndemic. Free Inq Creative Sociol. 2006; 34(1):39–53.
28. Riley, MW. Sociological research I: a case approach. New York: Harcourt, Brace & World, Inc; 1963. Special problems of sociological analysis; p. 700-25.
29. Diez-Roux AV. Bringing context back into epidemiology: variables and fallacies in multilevel analysis. Am J Public Health. 1998 Feb; 88(2):216–22. [PubMed: 9491010]
30. Conroy AA, Tsai AC, Clark GM, Boum Y, Hatcher AM, Kawuma A, et al. Relationship power and sexual violence among HIV-positive women in rural Uganda. AIDS Behav. 2016 Apr 6; 20(9): 2045–53. [PubMed: 27052844]
31. Hatcher AM, Tsai AC, Kumbakumba E, Dworkin SL, Hunt PW, Martin JN, et al. Sexual relationship power and depression among HIV-infected women in Rural Uganda. PLoS One. 2012; 7(12):e49821. [PubMed: 23300519]
32. Shannon K, Leiter K, Phaladze N, Hlanze Z, Tsai AC, Heisler M, et al. Gender inequity norms are associated with increased male-perpetrated rape and sexual risks for HIV infection in Botswana and Swaziland. PLoS One. 2012; 7(1):e28739. [PubMed: 22247761]
33. Heise LL, Kotsadam A. Cross-national and multilevel correlates of partner violence: an analysis of data from population-based surveys. Lancet Global Health. 2015 Jun; 3(6):e332–40. [PubMed: 26001577]
34. Tsai AC, Subramanian SV. Proximate context of gender-unequal norms and women's HIV risk in sub-Saharan Africa. AIDS. 2012; 26(3):381–6. [PubMed: 22045344]
35. Tsai AC. Intimate partner violence and population mental health: why poverty and gender inequities matter. PLoS Med. 2013; 10(5):e1001440. [PubMed: 23667344]
36. Aizer A. The gender wage gap and domestic violence. Am Econ Rev. 2010; 100(4):1847–59. [PubMed: 25110354]
37. Beaman L, Duflo E, Pande R, Topalova P. Female leadership raises aspirations and educational attainment for girls: a policy experiment in India. Science. 2012 Feb 3; 335(6068):582–6. [PubMed: 22245740]
38. Beaman L, Chattopadhyay R, Duflo E, Pande R, Topalova P. Powerful women: does exposure reduce bias? Q J Econ. 2009; 124(4):1497–540.
39. Rose G. Sick individuals and sick populations. Int J Epidemiol. 1985 Mar; 14(1):32–8. [PubMed: 3872850]
40. Rose, G. The strategy of preventive medicine. Oxford: Oxford University Press; 1992.
41. Wildeman C. Parental imprisonment, the prison boom, and the concentration of childhood disadvantage. Demography. 2009 May; 46(2):265–80. [PubMed: 21305393]
42. Johnson R, Raphael S. The effect of male incarceration dynamics on AIDS infection rates among African-American women and men. Journal of Law and Economics. 2009; 52(2):251–93.
43. Jewkes R. Intimate partner violence: causes and prevention. Lancet. 2002 Apr 20; 359(9315): 1423–9. [PubMed: 11978358]
44. Tsai AC. Home foreclosure, health, and mental health: a systematic review of individual, aggregate, and contextual associations. PLoS One. 2015; 10(4):e0123182. [PubMed: 25849962]
45. Sharkey P. The intergenerational transmission of context. American Journal of Sociology. 2008; 113(4):931–69.
46. Sharkey P. The acute effect of local homicides on children's cognitive performance. Proc Natl Acad Sci U S A. 2010 Jun 29; 107(26):11733–8. [PubMed: 20547862]
47. Sharkey PT, Tirado-Strayer N, Papachristos AV, Raver CC. The effect of local violence on children's attention and impulse control. Am J Public Health. 2012 Dec; 102(12):2287–93. [PubMed: 23078491]
48. Papachristos AV, Wildeman C, Roberto E. Tragic, but not random: The social contagion of nonfatal gunshot injuries. Soc Sci Med. 2015 Feb 6; 125(1):139–50. [PubMed: 24560101]

49. Wallace R. A synergism of plagues: “planned shrinkage,” contagious housing destruction, and AIDS in the Bronx. Environ Res. 1988 Oct; 47(1):1–33. [PubMed: 3168963]

50. Wilson M, Daly M. Life expectancy, economic inequality, homicide, and reproductive timing in Chicago neighbourhoods. BMJ. 1997 Apr 26; 314(7089):1271–4. [PubMed: 9154035]

51. Dow WH, Philipson TJ, Sala-i-Martin X. Longevity complementarities under competing risks. Am Econ Rev. 1999; 89(5):1358–71.

52. Ganz ML. The relationship between external threats and smoking in central Harlem. Am J Public Health. 2000 Mar; 90(3):367–71. [PubMed: 10705853]

53. Venkataramani AS, Chatterjee P, Kawachi I, Tsai AC. Economic opportunity, health behaviors, and mortality in the United States. Am J Public Health. 2016 Mar; 106(3):478–84. [PubMed: 26691108]

54. Venkataramani AS, Brigell R, O’Brien R, Chatterjee P, Kawachi I, Tsai AC. Economic opportunity, health behaviours, and health outcomes in the USA: a population-based cross-sectional study. Lancet Public Health. 2016; 1(1):e18–e25. [PubMed: 29253376]

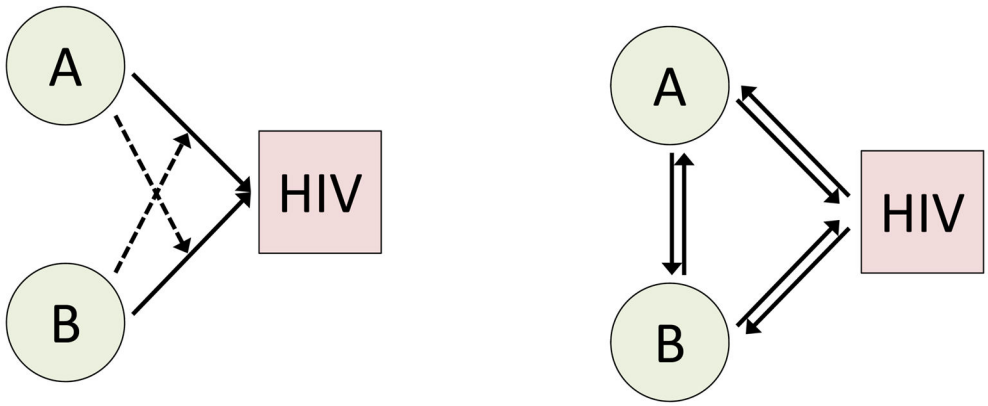

Figure. Models of epidemics co-occurring with HIV involving syndemic synergy (left) and mutual causality (right)

In the syndemic model in the left panel, the two epidemics are not mutually causal but demonstrate synergy: epidemic A has a greater impact on the HIV epidemic in the presence of epidemic B, epidemic B has a greater impact on the HIV epidemic in the presence of epidemic A, and the combined effect of epidemics A and B on the HIV epidemic exceeds the sum of their independent effects were no synergy present. In the model of mutual causality in the right panel, the two epidemics do not demonstrate synergy but have reciprocal relationships with each other: epidemic A exacerbates epidemic B, which in turn worsens epidemic A, and both epidemics have similar bidirectional relationships with the HIV epidemic.

Table

Summary characteristics of quantitative studies in the literature on syndemics, 2003–16 (n=71)

	No. (%) or Median (Interquartile range)		
	Entire sample (n=71)	**Initial review (n=40)**	**Updated search (n=31)**
Year of publication			
2003–2008	3 (4)	3 (8)	-
2009–2013	18 (25)	18 (45)	-
2014–2015	34 (48)	19 (48)	15 (48)
2016	16 (23)	-	16 (52)
Study design			
Experimental or quasi-experimental	0 (0)	0 (0)	0 (0)
Observational	71 (100)	40 (100)	31 (100)
Cross-sectional	56 (79)	32 (80)	24 (77)
Longitudinal	15 (21)	8 (20)	7 (23)
Level of analysis			
Ecological	0 (0)	0 (0)	0 (0)
Individual	71 (100)	40 (100)	31 (100)
Multilevel	0 (0)	0 (0)	0 (0)
Study setting			
U.S.	53 (75)	32 (80)	21 (68)
Other	18 (25) [a]	8 (20)	10 (32)
Study population			
Men who have sex with men	36 (50)	21 (53)	15 (48)
Women	10 (14)	7 (18)	3 (10)
Persons with HIV	9 (13)	5 (13)	4 (13)
General	5 (7)	4 (10)	1 (3)
Adolescents	3 (4)	0 (0)	3 (10)
Other	8 (11)	3 (8)	5 (16)
Sample size	591 (301–1535)	596 (445–1425)	503 (212–1535)
Psychosocial problems			
Mental health	62 (87)	33 (83)	29 (62)

	No. (%) or Median (Interquartile range)		
	Entire sample (n=71)	**Initial review (n=40)**	**Updated search (n=31)**
Substance use	61 (86)	36 (90)	25 (81)
Violence	50 (70)	27 (68)	23 (74)
Other	44 (62) [b]	23 (58)	21 (68)
Outcomes of interest			
HIV transmission risk behavior	45 (63)	29 (73)	16 (52)
HIV-related health outcome	12 (17)	6 (15)	6 (19)
HIV infection	11 (15)	9 (23)	2 (6)
Mental health	6 (8)	4 (10)	2 (6)
Substance use	6 (8)	2 (5)	4 (13)

[a] Includes Canada (n=3), China (n=3), multiple countries (n=3), Mexico (n=2), Belgium (n=1), Ghana (n=1), India (n=1), Nepal (n=1), South Africa (n=1), Thailand (n=1), and Vietnam (n=1)

[b] Includes sexual compulsivity (n=10), homelessness (n=9), social isolation (n=8), HIV transmission risk behavior (n=7), poverty (n=7), food insecurity (n=5), HIV seropositivity (n=4), incarceration (n=4), sexual minority stigma (n=4), racism (n=3), condom use self-efficacy (n=2), educational attainment (n=2), HIV stigma (n=2), housing insecurity (n=2), self-esteem (n=2), caregiving responsibility (n=1), familial conflict tactics (n=1), health insurance (n=1), HIV treatment adherence (n=1), impulsivity (n=1), involuntary subordination (n=1), nuclear family structure (n=1), and quality of life (n=1)