RESEARCH ARTICLE

Global research on syndemics: a meta-knowledge analysis (2001-2020) [version 1; peer review: 2 approved with reservations]

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Abstract

Background: Syndemics or synergies of cooccurring epidemics are widely studied across health and social sciences in recent years.

Methods: We conducted a meta-knowledge analysis of articles published between 2001 to 2020 in this growing field of academic scholarship.

Results: We found a total of 830 articles authored by 3025 authors, mostly from high-income countries. Publications on syndemics are gradually increasing since 2003, with rapid development in 2013. Each article was cited more than 15 times on average, and most (n = 604) articles were original studies. Syndemics research focused on several areas, including HIV/AIDS, substance abuse, mental health, gender minority stressors, racism, violence, chronic physical and mental disorders, food insecurity, social determinants of health, and coronavirus disease 2019. Moreover, biopsychosocial interactions between multiple health problems were studied across medical, anthropological, public health, and other disciplines of science.

Conclusions: The limited yet rapidly evolving literature on syndemics informs transdisciplinary interests to understand complex coexisting health challenges in the context of systematic exclusion and structural violence in vulnerable populations. The findings also suggest applications of syndemic theory to evaluate clinical and public health problems, examine the socioecological dynamics of factors influencing health and wellbeing, and use the insights to alleviate

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Any reports and responses or comments on the article can be found at the end of the article.

health inequities in the intersections of synergistic epidemics and persistent contextual challenges for population health.

Keywords

Syndemics; Multimorbidity; Health inequity; Health disparity; Health Promotion; Health Policy; Global Health; Meta-knowledge Analysis

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Introduction

Addressing health inequities in marginalized populations requires a complex understanding of the epidemiological burden of multiple health problems and associated factors that determine the health statuses and outcomes in that context.^{1–3} Theoretical frameworks may help in examining different dimensions of population health, adopting intellectual inspirations from scholarly concepts that emerged in the past across scientific discipline.^{4,5} Amongst many contemporary theories, “syndemic(s) theory” offers critical perspectives on the relationships between diseases and biopsychosocial factors that not only explain the high burden of diseases in populations but also sustain a series of adverse health and social outcomes.^{6,7} Conceptually, syndemics have three fundamental components that characterize them.^{6,8,9} Firstly, two or more health problems cluster together that can be assessed epidemiologically or described as co-morbidity or multimorbidity. Secondly, syndemic diseases or conditions interact among themselves using biological, psychological, or social pathways. Lastly, syndemics are associated with social, structural, and contextual forces that precipitate disease clustering and progression in the first place, which may include but are not limited to poverty, segregated housing, systematic exclusion from opportunities, enslavement, colonialism, neo-colonialism, and neo-liberal economic measures that result in disproportionate distribution of wealth, lack of access to resources and services that may improve health and wellbeing, and other socioeconomic inequalities.^{6,8–10}

Since its conceptualization by Merrill Singer in the 1990s,^{10–12} syndemic(s) theory has become one of the eminent ideas that has influenced scholarly discourses in different disciplines, including social epidemiology and medical anthropology, investigating the dynamics of persistent health inequities in disadvantaged population groups such as homeless, racial and ethnic minorities, and people affected by chronic diseases or social problems.^{6,9} One of the earliest examples used in theorizing syndemics was substance abuse, violence, and HIV/AIDS (SAVA).^{8,10} The case of the SAVA syndemic illustrated the clustering of these three health problems where a high burden of substance abuse and violence were prevalent in people living with HIV/AIDS, predominantly in the systematically oppressed communities in the United States.¹⁰ Most of them were urban poor, people of color, and deprived of opportunities to live healthy lives in the first place. Another syndemic of HIV and Hepatitis C virus (HCV) is recognized in people who use drugs (PWUD).^{9,13} Nearly 2.3 million out of 36.7 million people living with HIV in 2015 were infected with HCV. The co-infection of HIV and HCV significantly increases the risks of advanced liver disease and associated adverse health outcomes compared to those with HCV infection alone.^{9,14,15} Moreover, HCV facilitates the pathogenesis and disease progression of HIV, thus interacting with each other in multiple pathways that may result in adverse health outcomes among the affected individuals.¹⁴ These infections are highly prevalent in PWUD, who are more likely to share syringes and engage in other high-risk health behaviors. In addition to these pathological and psychological challenges, these people share similar socioeconomic marginalization driven by structural forces that transform their life choices, health behaviors, and biopsychosocial outcomes.^{9,14} Rather than presenting the disease burden and their correlates only, syndemic(s) theory highlights the complicated relationships between these co-existing health problems that can be biological, psychological, or social in nature. More importantly, studying these problems in the context of their shared determinants and interactions between multiple constructs provides a broader understanding to address the problems, which is less probable if these problems are examined individually without exploring their synergistic characteristics.^{9,13}

A growing body of literature indicates that the academic and professional interests in syndemics have increased over the past three decades.^{6–8} A review of syndemics associated with HIV/AIDS identified 60 articles published in 2019 alone,⁶ which reported co-conditions such as substance abuse (n = 40; 67%), high-risk sexual behavior (n = 36; 60%), depression (n = 36; 60%), interpersonal violence (n = 35; 58%), stigma (n = 19; 32%), sexually transmitted infections (STIs) (n = 16; 27%), trauma (n = 14; 23%), and noncommunicable diseases (NCDs) (n = 6; 10%). Such inclusive nature of those syndemics literature informs the scope of interdisciplinary research using tools from diverse sources to answer common questions of interest in different contexts and populations. The increasing recognition of research on syndemics can potentially specify, describe, and explain bio-social interactive pathways advancing both science and practice. Another review identified 143 journal articles, 23 book chapters, and 29 other types of publications.⁹ In this review, the authors reported five thematic categories of studies that included syndemics (12%) with cooccurring diseases with bio-bio and bio-social interactions, potential syndemics (18%) where those interactions are referred but not fully articulated, socially determined heightened health burden of diseases (15%) that described social conditions associated with poor health without identifying disease clusters or interactions, harmful disease clusters (17%) that identified disease clusters and social factors without mentioning their interactions, and adverse additive co-morbidities (38%) describing diseases and social determinants through an additive approach to adverse health outcomes without examining the evidence on interactions. Furthermore, a systematic literature review assessed a potential syndemic comprising of HIV, HCV, intimate partner violence, and posttraumatic stress disorder (PTSD).¹⁶ In this review, the authors reported childhood physical and sexual abuse and intimate partner violence as social sources of trauma, which was associated with elevated unsafe health behavior leading to a higher burden of HIV infections and subsequent health outcomes. Existing literature provides an overview of diverse health problems and methodological measures adopted by different authors to study

syndemics and associated conditions,^{6,9} which highlight both the complexity of the current evidence base and the necessity of improving our understandings of syndemics applied in different frontiers of knowledge.

Primary studies and analytical reviews offer syntheses of evidence focusing on specific research questions relevant to a field or a problem of interest, which are useful for evaluating evidence in that scenario. However, such focused approaches may not provide a comprehensive overview of the entire scientific landscape or describe how research on a domain or topic evolved over time. In this regard, meta-knowledge analyses offer quantitative assessments of research identifying the overall status and characteristics of research. Through scientometric and bibliometric measures, meta-knowledge studies identify top contributing scholars, institutions, journals, and countries that may promote further research collaborations. In addition, meta-knowledge studies aim to identify research hotspots where most studies have emphasized previously, thus inform research trends and explore research areas that are not examined extensively. Recognizing areas that require further studies is one of the many goals of knowledge development in a field or topic of interest. To the best of our knowledge, there is no meta-level study on syndemics, which informs an overview of the current status and the evolution of global knowledge on syndemics-related research. Such studies, if conducted systematically, can inform the scholars and practitioners to understand the historical development of knowledge in this field, explain the status of intellectual advancements, and guide future research and scientific advancements in this area of growing interest in health sciences research.

Objectives

In the current study, we primarily aimed to analyze the characteristics and trends of the global research literature on syndemics. Secondly, we evaluated the most prolific authors, institutions, journals, affiliating countries, and funding institutions contributing to syndemics-related research. Lastly, we mapped the major knowledge domains on syndemics highlighting the intellectual development in this field.

Methods

Data source

In this study, we adopted meta-knowledge methods that have been used in previous research.^{17,18} To retrieve scientometric data on syndemics, we accessed the Web of Science (WoS) core collection that included multiple citation sources such as Science Citation Index-Expanded (SCI-Expanded), the Social Sciences Citation Index (SSCI), the Arts & Humanities Citation Index (A&HCI), and the Emerging Sources Citation Index (ESCI). The selection of WoS as the data source was informed by several advantages that it offers. Firstly, WoS provides extensive coverage of more than 20,000 journals, making it one of the most widely used databases for bibliometric studies.¹⁹ Moreover, WoS includes publications not only from biomedical sources but also social sciences and other scholarly disciplines, thus making the bibliographic collective more inclusive in nature.^{20,21} As syndemics are associated with a wide range of biopsychosocial issues relevant to different scientific disciplines,^{9,22} WoS is likely to provide a transdisciplinary overview of the research landscape in this topic.

Data criteria and extraction

We used “syndemic*” keyword in the topic field for searching the titles, abstracts, and keywords in the WoS database collection. The search process was structured using several eligibility criteria. First, we included citations published from January 1, 2000, to December 31, 2020. Second, we reviewed the titles and abstracts of the retrieved citations and excluded studies on topics such as “parasyntheticolpate” OR “syndemicolpate” that could have provided false positive entries. Third, we limited our search in citations published in English language, thus we excluded citations published in languages other than English. Lastly, we included all publication types such as original articles, reviews, commentaries, editorials, letters, and book chapters considering a low number of citations in the emerging field of knowledge. For all eligible citations, the complete bibliometric data on publication records, authorship, institutional affiliations, funding information, keywords, and citations data were extracted for subsequent analytic steps. No alterations were made for the primarily collected data.

Data analysis

The corpus of the eligible literature was used for descriptive analysis, social network analysis, and conceptual structure analysis using measures that have been used in previous knowledge mapping studies.^{17,19,23,24} The descriptive analyses on the key bibliometric characteristics such as total citations, publication trends, top ten cited articles, prolific authors, h-index and g-index of the authors, contributing journals, research institutions, affiliating countries of the authors were analyzed using Microsoft Excel 2021 and R software (version 4.1.2).²⁵

Knowledge mapping offers visual representations of the social connectedness among affiliating authors, institutions, and countries that reflect the research collaborations in a topic. We used a free software called the *VOSviewer* (version 1.6.16)

that applies a natural language processing algorithm (NLP), which represents the units of analysis as a circular node within the map.²⁶ The size of the node portrays the volume (e.g., number of publications in a dataset) and the position represents the resemblance with other nodes in the same set. As a result, closer nodes are more alike than nodes far apart from each other in the final map. The lines connecting multiple nodes represent the relationships among those nodes, whereas the thickness of those lines indicate the strength of that relationship. Finally, the color of the node indicates the cluster to which each node has been allocated to. In this way, all nodes in the map are clustered together based on their affiliation.²⁶ To make the map, *VOSviewer* uses the SMACOF algorithm,²⁷ which minimizes the function:

$$V(X_1, \dots, X_n) = \sum_{i < j} S_{ij} \|X_i - X_j\|^2$$

under the constraints:

$$\frac{2}{n(n-1)} \sum_{i < j} S_{ij} \|X_i - X_j\| = 1$$

where:

n —the number of nodes in a given network,

X_i —the locations of node i within a two-dimensional space,

$\|X_i - X_j\|$ —the Euclidean distance between nodes i and j .

VOSviewer builds clusters of nodes by maximizing the following function:

$$V(c_1, \dots, c_n) = \sum_{i < j} \delta(c_i, c_j) (s_{ij} - \gamma)$$

where:

c_i —the cluster to which node i is assigned,

$\delta(c_i, c_j)$ —a function that equals one if $c_i = c_j$; and zero otherwise,

γ —a resolution parameter that determines the level of detail of the clustering (the higher γ is, the higher the number of clusters).

This method uses a distance-based approach to construct the bibliometric maps in three steps.^{26,28} At the first step, it normalizes the differences between multiple nodes. At the next step, it builds a two-dimensional map where the distance between multiple nodes reflects the similarities between those nodes. Further, it combines closely related nodes into clusters sharing similar bibliometric properties allowing visual representation of the research field. Moreover, we conducted a co-occurrence analysis of keywords to evaluate the conceptual relationships between multiple topics. The frequency of co-occurrence of two or more keywords indicated the strength of their association, whereas multiple keywords appearing within a cluster highlighted the topical foci or knowledge base within the research landscape. This approach was used to map multiple clusters with an overview of research domains and a graphical evolution of those domains across years. Lastly, we developed a three-field plot connecting the current literature with cited references using *KeyWords Plus* in the WoS database. This was used to generate the most frequently appearing words or phrases in cited sources, depicting the intellectual linkages between the existing studies on syndemics and cited research articles. This meta-knowledge study is registered in the Open Science Framework, and the data on eligible studies can be found in the underlying data.

Results

Overview of the publications

We found a total of 830 articles eligible for this bibliometric study, including 604 original articles, 75 reviews, and 151 other types of publications from 314 scholarly sources (Table 1). These documents were authored by 3025 individual authors, on average most articles were authored by more than three authors. Most ($n = 750$) articles had multiple authors, whereas 80 articles were authored by a single author. The collaboration index was 4.03 suggesting more than four co-authors per article index calculated only using the multi-authored article set. Figure 1 shows the citation retrieval process.

Table 1. Summary of the bibliographic findings.

Description	Frequency
No. of total documents	830
No. of scholarly sources	314
No. of original articles	604
No. of review articles	75
No. of other publications (letters, editorial etc.)	151
No. of author's keywords	1492
No. of authors	3025
No. of single authored documents	80
No. of cited references	30189
Mean citations per document	15.09
Mean annual citations per document	2.35
Mean authors per documents	3.64
Mean documents per author	0.274
Collaboration index	4.03

Table 2 provides an overview of the top 10 cited articles on syndemics published from 2003 to 2019, with the average citation per article per year ranging from 12.81 to 124.67. Seven of these articles focused on HIV-related syndemics, whereas the remaining articles discussed HIV in syndemic-related discourses emphasizing other health issues such as substance abuse, tuberculosis, violence, nutritional disorders, chronic diseases, and social determinants of health.

Publication trends

Figure 2 highlights an increasing trend of scholarly publications on syndemics since 2003. Only 33 articles were published before 2010, whereas the frequency of publication increased significantly since 2013. The annual growth rate of the scholarly publications on syndemics was calculated as 10.47%.

Top contributors in syndemics research

Table 3 provides an overview of the top ten contributing authors who contributed to the published manuscripts on syndemics. Among the authors, Safren S.A. had the highest number of publications ($n = 26$), followed by Singer M ($n = 24$) and Halkitis P.N. ($n = 17$). Moreover, Singer M. had the highest number of citations ($n = 949$), followed by Stall R. ($n = 679$) and Mendenhall E. ($n = 555$). Singer M. also had the highest h-index (12) and g-index (24) among the top authors.

Most articles on syndemics were published in AIDS and Behavior journal (7.23%, $n = 60$), followed by Annals of Behavioral Medicine (3.73%, $n = 31$) and AIDS Care (2.89%, $n = 24$). Four out of the top ten journals were associated with AIDS and STI-related topics, whereas all journals were related to epidemiological, behavioral, anthropological, social, and public health sciences (**Table 4**).

Institutional research collaborations

Table 5 shows the top 10 institutions that were affiliated with syndemics-related research. The majority of the studies were authored by scholars from the University of California System (11.93%, $n = 99$), followed by Harvard University (8.19%, $n = 68$), and the Johns Hopkins University (6.63%, $n = 55$). **Figure 3** shows extensive collaborations between the key affiliating institutions with a higher publication frequency ($n = 5$ or above), which highlights the interconnectedness of top contributing institutions in collaborative research on syndemics.

Global research collaborations

Global contributors at the country level show 76 countries that published at least one document on syndemics-related topics. Among those countries, the top 10 contributors are listed in **Table 6**. Most articles originated from the United States (74.46%, $n = 618$), followed by Canada (11.93%, $n = 99$) and UK (6.14%, $n = 51$). **Figure 4** shows global collaborations among participating countries (with at least one publication), highlighting a high volume of syndemics research from high-income countries compared to low- and middle-income countries. Moreover, North American and

Figure 1. Citation retrieval process.

other high-income countries had stronger collaborative ties on syndemics research that informs higher cumulative production of scientific research from these regions.

Research areas on syndemics

Several research areas were identified within the broader umbrella of syndemics using clusters of keywords that overlapped with each other. We mapped keywords that had a frequency of 5 and above across the collective bibliography. A total of 104 top keywords were identified and clustered to generate common areas of research in multiple clusters highlighted in the same color. [Figure 5](#) shows the distribution of keyword clusters where the greater size of a circle represents a higher number of publications on that keyword and the thickness of connecting line between circles represents the intensity of coexistence of these terms in the literature.

Amongst multiple research hotspots, the first cluster highlighted in red consisted of keywords related to syndemic theory and associated concepts such as syndemic, substance use, intimate partner violence, depression, health disparities, transgender, gay, bisexual, food insecurity, and intersectionality ([Figure 5](#)). Several studies were identified that used these

Table 2. Top ten cited articles on syndemics research.

Title	Authors	Journals	Publication year	Total citations	Average citations per year
Syndemics and public health: Reconceptualizing disease in bio-social context	Singer, M; Clair, S	Medical Anthropology Quarterly	2003	480	25.26
The Global Syndemic of Obesity, Undernutrition, and Climate Change: The Lancet Commission report	Swinburn, B A. et al.	Lancet	2019	374	124.67
Psychosocial health problems increase risk for HIV among urban young men who have sex with men: preliminary evidence of a syndemic in need of attention	Mustanski, B. et al.	Annals of Behavioral Medicine	2007	328	21.87
HIV and Tuberculosis: a Deadly Human Syndemic	Kwan, C.K.; Ernst, J.D.	Clinical Microbiology Reviews	2011	310	28.18
Antiretroviral Therapy for Prevention of Tuberculosis in Adults with HIV: A Systematic Review and Meta-Analysis	Suthar, A.B.	Plos Medicine	2012	233	23.3
Syndemics and the biosocial conception of health	Singer, M. et al.	Lancet	2017	229	45.8
Sexual Compulsivity, Co-Occurring Psychosocial Health Problems, and HIV Risk Among Gay and Bisexual Men: Further Evidence of a Syndemic	Parsons, J.T. et al	American Journal of Public Health	2012	206	20.6
Syndemics, sex and the city: Understanding sexually transmitted diseases in social and cultural context	Singer, M. et al.	Social Science & Medicine	2006	205	12.81
Syndemic Theory and HIV-Related Risk Among Young Transgender Women: The Role of Multiple, Co-Occurring Health Problems and Social Marginalization	Brennan, J. et al.	American Journal of Public Health	2012	199	19.9
Substance Abuse, Violence, and HIV in Women: A Literature Review of the Syndemic	Meyer, J. et al.	Journal of Women's Health	2011	178	16.18

Figure 2. Trends of scholarly publications on syndemics.

Table 3. Top ten authors contributing to syndemics research.

Author	Number of Publications	Year of first publication	h-index	g-index	Total citations
Safren SA	26	2010	9	22	497
Singer M	24	2003	12	24	949
Halkitis PN	17	2010	11	17	484
Mayer KH	14	2015	6	14	229
Stall R	14	2005	11	14	679
Mendenhall E	13	2014	8	13	555
O'Cleirigh C	12	2015	6	12	200
Gilbert M	9	2017	4	6	45
Pitpitan EV	9	2013	6	9	102
Reisner SL	9	2009	8	9	349

Table 4. Top ten journals publishing syndemics research.

Journal's name	Total publications on syndemics	Percentage	Impact factor (Journal citations reports 2019)
AIDS and Behavior	60	7.22%	3.147
Annals of Behavioral Medicine	31	3.73%	4.475
AIDS Care Psychological and Socio-medical Aspects of AIDS HIV	24	2.89%	1.894
Archives of Sexual Behavior	18	2.17%	3.131
Social Science Medicine	17	2.05%	3.616
American Journal of Public Health	16	1.93%	6.464
BMC Public Health	15	1.81%	2.521
Global Public Health	15	1.81%	1.791
Journal of Acquired Immune Deficiency Syndromes	15	1.81%	3.475
Annals of Anthropological Practice	14	1.69%	N/A

Table 5. Top ten institutions affiliated with syndemics-related publications.

Name of the institutions	Number of publications	Percentage
University of California System	99	11.93%
Harvard University	68	8.19%
Johns Hopkins University	66	7.95%
Pennsylvania Commonwealth System of Higher Education	55	6.63%
Yale University	45	5.42%
University of Toronto	43	5.18%
University of Miami	42	5.06%
University of Pittsburgh	38	4.58%
New York University	37	4.46%
University of Connecticut	35	4.22%

Figure 3. Institutional collaborations on syndemics-related research.**Table 6. Top contributing countries on syndemics research.**

Countries	Number of publications	Percentage
USA	618	74.46%
Canada	99	11.93%
UK	51	6.14%
South Africa	44	5.3%
Australia	28	3.37%
Peoples' Republic of China	27	3.25%
Mexico	20	2.41%
India	19	2.29%
Brazil	17	2.04%
Netherlands	11	1.33%

VOSviewer VOSviewer

keywords, indicating their relevance to this research cluster. For example, Couture *et al.*, adopted the syndemic framework to evaluate the effects of comorbid psychosocial problems on the risk of physical and sexual violence on female entertainment and sex workers (FESW) in Cambodia.²⁹ They reported a high burden of client-perpetuated violence that was associated with housing insecurity, substance use, and psychological distress. FESW with two psychosocial conditions had twice the odds (adjusted odds ratio [AOR] = 2.08; 95% confidence interval [CI] 1.00-4.31), whereas women with 5-6 psychosocial conditions had eightfold higher odds (AOR = 8.10; 95% CI 3.4-19.31) of violence, highlighting a syndemic model of cooccurring psychosocial problems. Another study examined the prevalence and correlates of trauma in South African youth living in syndemic HIV risk.³⁰ More than 99% of the participating youths experienced at least one potentially traumatic event (PTE), whereas a high PTE score associated with high food insecurity among adolescent men (AOR 2.63, 95% CI = 1.36-5.09) and women (AOR = 2.57, 95% CI = 1.55-4.26, respectively). This study reported biopsychosocial pathways including depression and inconsistent condom use as pathways of syndemic of trauma and HIV in that context.

The second cluster illustrated in green includes keywords on syndemics of infectious diseases such as HIV, AIDS, tuberculosis, STIs, hepatitis c, antiretroviral therapy, adherence, comorbidity, and coinfection. For example, Dyer *et al.*, conducted a cohort study among 301 men who have sex with men (MSM) to assess syndemic relationships.³¹ They reported that depression symptoms were associated with sexual compulsiveness (odds ratios [OR]: 1.88, 95% CI = 1.1, 3.3) and stress (OR: 2.67, 95% CI = 1.5, 4.7); sexual compulsiveness was associated with stress (OR: 2.04, 95% CI = 1.2, 3.5); substance misuse was associated with intimate partner violence (IPV) (OR: 2.57, 95% CI = 1.4, 4.8); stress was associated with depression symptoms (OR: 2.67, 95% CI = 1.5, 4.7), sexual compulsiveness (OR: 2.04, 95% CI = 1.2, 3.5) and IPV (OR: 2.84, 95% CI = 1.6, 4.9). Also, men who reported three or more syndemic constituents (three or more conditions) were engaged in high-risk sexual behavior compared to men who had two or fewer health conditions (OR: 3.46, 95% CI = 1.4-8.3). Moreover, a review by Meyer and colleagues identified 45 articles that emphasized SAVA syndemic and associated conditions such as HIV-associated risk-taking behaviors, mental health, utilization of health services and medication adherence, and a bidirectional relationship between violence and HIV/AIDS.³² This review highlighted the complex relationships and associated outcomes of poor decision making and high-risk behavior in the context of the SAVA syndemic.

In the third cluster highlighted in blue, several keywords were identified, including mental health, MSM, sexual compulsivity, stigma, resilience, internet, and aging. Studies in this cluster focused on health behavior and syndemic relationships in gay and bisexual men. For example, a study by Parsons and colleagues examined 1,033 HIV-negative gay and bisexual men living in the U.S. and found that more than 62% of men reported having at least one syndemic condition.³³ Also, HIV-related risk behavior was associated with polydrug use, sexual compulsivity, being single, and being Latino. Moreover, the risk was highest among participants with three or more syndemic conditions. Another study from Mexico conducted by Pitpitan *et al.* found that MSM with a high number of syndemic conditions showed an increased prevalence of sexual risk-taking.³⁴ Moreover, MSM who were out to more people showed a weaker association between high-risk sexual behavior and syndemic conditions suggesting outness or disclosure of same-sex preference as a resilience factor from a syndemic perspective.

A fourth cluster highlighted in yellow included keywords related to psychosocial and health behavior-related keywords such as violence, substance abuse, HIV testing, homophobia, and suicide. This research cluster emphasized the growing number of studies that examined the psychosocial health of MSM and associated syndemic conditions and relationships. For example, a study by Herrick and colleagues recruited 1551 MSM and found that different life-course predictors such as internalized homophobia and victimization were significantly associated with syndemic condition as well as psychosocial health conditions including stress, depressive symptomology, substance abuse, compulsive sexual behavior, and intimate partner violence.³⁵ Moreover, the authors used a nested negative binomial analysis and found that the overall life course significantly explained the variability in syndemic outcomes ($\chi^2(2) = 247.94$; $P < .001$; $df = 22$). Another study by Ferlatte and colleagues examined the data from a survey of 8382 Canadian gay and bisexual men and found that suicidal ideation and attempts were associated with individual marginalization and psychosocial health problems such as mental disorders, substance use, STIs, and HIV risks.³⁶ In addition, individuals with three or more psychosocial problems had higher odds of experiencing suicidal ideation [6.90 (5.47-8.70) times] and suicide attempts [16.29 (9.82-27.02)] compared to participants with no such problems. These relationships show the complex nature of syndemic relationships among people living under psychosocial stressors that impacts their health and wellbeing.

The fifth research cluster highlighted in purple color consisted of keywords including coronavirus disease 2019 (COVID-19), obesity, diabetes, chronic disease, poverty, and social determinants of health. This cluster emphasizes a research domain that includes noncommunicable diseases and contemporary health problems such as the COVID-19 pandemic. For example, Mendenhall and colleagues conducted a study in Kenya and found that adults with diabetes shared a complex social and medical framework associated with their health conditions. People with diabetes also had

Evolution of knowledge in the field of syndemics research

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Figure 7. Intellectual contributions of influential articles and authors on commonly cited topics related to syndemics.

publications on syndemics. These keywords are marked in purple, which included HIV/AIDS, substance abuse, prevention, syndemic theory, coinfection, social determinants, social inequality, internet, mortality, sexually transmitted diseases, and health policy. Moreover, keywords colored in bluish-purple show a transition of those topics being used in publications around 2016, which include syndemics, tuberculosis, obesity, harm reduction, health disparities, poverty, and aging. Furthermore, keywords used across publications during 2017-18 are presented in green color, where most keywords such as syndemic, men who have sex with men, gay and bisexual men, diabetes, domestic violence, food insecurity, global health, public health, drug use, intimate partner violence, HIV risk, testing, and prevention were identified. Lastly, keywords in yellow represent topics used in articles published around and after 2019. These recent topics included COVID-19, pandemic, social determinants of health, noncommunicable diseases, network analysis, latent class analysis, pre-exposure prophylaxis, and climate change.

An assessment of the cited references provided another perspective on how the current research publications cited and used previous scholarly items. Figure 7 represents the cited sources on the left, the most widely used keywords from the titles of cited publications in the middle, the top contributing authors on the right. Common keywords from cited sources inform the most relevant topics used from previous research, which included psychosocial health problems, gay, united states, substance use, risk, united states, prevalence, depression, health, women, and syndemics. Across these cited sources, Singer *et al.* authored five articles published from 1994 to 2017.^{7,8,10,12,40} One of earliest articles that was widely cited across syndemics literature was the article describing the development and psychometric assessment of the Center for Epidemiological Studies-Depression (CES-D) scale by Radolf, published in 1977.³⁸ Furthermore, top published authors such as Singer and Stall have been contributing to syndemics research across most topics that are frequently cited across current publications.

Discussion

This study evaluated the global scientific landscape of syndemics research using bibliometric measures. The findings of this study suggest a slow yet gradual increase in syndemics-related publications, which has accelerated since 2013. In recent years, syndemic conditions are increasingly examined in both primary and review articles that draw intellectual inspirations from biopsychosocial literature, highlighting a transdisciplinary trend in syndemics research. Moreover, a higher proportion of original articles rather than reviews and other publication types indicates a rising body of empirical research on syndemic(s) theory and associated concepts. Furthermore, syndemics-related publications were published in general and specialty journals emphasizing the intersection of coexisting diseases, their shared determinants, and complex relationships between biosocial constructs as commonly seen in social medicine and allied fields of knowledge.

Most of the syndemics-related publications were affiliated with authors and institutions from high-income countries, and the U.S. had the highest contributions. In addition, heavy collaborations among authors and institutions in high-income countries indicate active research across major research entities. While some of the low- and middle-income countries (LMICs) such as Brazil, Mexico, China, South Africa, and India are engaged in syndemics research, their individual and collective contributions appeared to be limited, which informs a critical research gap in LMICs. This is consistent with previous research that reported a low scholarly output from LMICs in different areas of health sciences.^{41–44} In the case of syndemics research, the historical and persistent gaps in research capacities in LMICs are likely to be compounded by the fact that syndemics have been primarily conceptualized and extensively studied by scholars and institutions in high-income countries. It is necessary to increase the research capacities in LMICs with a focus on syndemics, as those countries experience a high burden of infectious and noncommunicable diseases and poor social determinants of health. As the key concepts of syndemic(s) theory suggest,^{6,7,10} studying syndemics in such underprivileged contexts can potentially offer unique and diverse scientific perspectives on the biopsychosocial formation of health and illness in respective populations. It may enrich the current knowledge base on syndemics and inform the future transformations of medical and social care as well as disease prevention globally.

Syndemics research focused on diverse topics, among which HIV-related syndemics were extensively studied across the literature. As evident in research hotspots, HIV/AIDS and associated health behaviors and outcomes were common in more than one cluster of keywords. This frequent appearance of HIV/AIDS in the syndemics research landscape can be attributable to several factors. First, HIV/AIDS-related conditions were amongst the earliest syndemics that were conceptualized and examined in the history of the syndemic theory. For this reason, many articles focusing on non-HIV syndemics also referred to the case of previous HIV syndemics such as SAVA.^{9,10} Secondly, syndemics literature from the US and other developed countries present studies and cases of multiple health problems and their synergies within a syndemic framework,^{6,9} where the study populations were urban poor from inner-city neighborhoods. As we learn from social epidemiological and anthropological studies,^{9,33} biosocial challenges associated with HIV/AIDS were highly prevalent in these population groups. Therefore, the academic discourses on the social reality of health and wellbeing in these marginalized people would remain incomplete without studying HIV/AIDS and related issues. Lastly, literature from the global context, particularly from Sub-Saharan countries, highlighted the burden of HIV/AIDS in the context of the continued burden of infectious and chronic diseases in those contexts.^{6,9} For this reason, we can find studies that provide national and regional assessments of HIV/AIDS-related syndemics from those countries, which also compared their findings with what was known from similar studies conducted in developed nations. As many scholars described HIV/AIDS as a pandemic rather than just a disease outbreak,^{45,46} global studies comparing and connecting the concepts and associated evidence revealed the worldwide relevance of HIV/AIDS in syndemics research.

In addition to HIV/AIDS, syndemics literature also discussed infectious diseases such as tuberculosis and COVID-19. While tuberculosis research was often studied as a comorbid condition in people living with HIV/AIDS,^{6,9} recent literature examined the relevance of comorbid diseases that are relevant to susceptibility to COVID-19 and subsequent health outcomes.^{39,47–49} Given the growing burden of biopsychosocial challenges associated with COVID-19,^{38,50–55} it is necessary to investigate bio-bio and bio-social interactions between coexisting health problems in COVID-19 patients and survivors. Such research may reveal the true burden of disease clustering, biopsychosocial relationships, shared determinants, and health outcomes in the context of this pandemic. Despite a growing body of evidence that is mostly epidemiological and predominantly cross-sectional in nature, transdisciplinary and longitudinal investigations would be necessary to understand syndemic aspects of this pandemic. Furthermore, COVID-19 has demonstrated the vulnerability of people with noncommunicable diseases who are more likely to have adverse outcomes.^{38,39,49} Limited literature exists on syndemics of non-HIV chronic diseases,⁹ which necessitates a more comprehensive yet inclusive study of communicable and noncommunicable diseases from a syndemic perspective.

Social determinants of health constituted a significant proportion of syndemics research. This is consistent with the fundamental idea of syndemic conditions that have common social factors and bio-social interactions.^{9,10,12} However, there were distinct patterns in research on social factors that influenced health status, disease development, and subsequent outcomes in study populations. As evident in research hotspots, sexual and gender minorities such as men who have sex with men, bisexuals, and transgender people were frequently studied in the syndemics literature. Although many of those studies examined health problems and associated factors in the context of HIV/AIDS,⁶ studies have also presented their psychosocial vulnerability due to minority stressors such as social stigma and other determinants of health in the affected individuals. The added value of those studies may include, but are not limited to, a broader understanding of how gender roles and norms may have biosocial interactions with pre-existing health conditions, contribute to the progression of diseases, and impact their health and wellbeing at the individual and population level. Such research findings must be translated to clinical and social decision-making addressing the stressors that affect health outcomes in gender minorities. Moreover, future syndemics research may need to extend the scope and depth of conceptual and

empirical investigations on other psychosocial stressors such as racism, poverty, lack of education, unemployment, inadequate access to health and social care, xenophobia, and other means of marginalization. In recent years, public interests in those issues reflect not only their relevance to the social oppression experienced by minorities but also inform a critical need to examine the biopsychosocial dynamics of such stressors to understand how they may determine health and social outcomes in respective populations.

Directions for future research

The current literature emphasizes diseases and their interactions among individuals in the social context. However, socioecological perspectives may inform the need for research in several under-investigated areas that may provide a more accurate understanding of how syndemics work in individuals and populations.^{56,57} For example, the role of caregivers and family members is critical for the psychosocial wellbeing of the affected individuals.^{44,58,59} Moreover, caring for someone with one or more chronic diseases is reported to be associated with adverse health and social outcomes among family caregivers.^{60,61} Since they share the same or similar social and contextual factors relevant to the respective syndemics, future research should investigate the roles of and impacts on informal caregivers alongside primarily affected individuals in syndemic scenarios. Furthermore, syndemic conditions, as well as their determinants and consequences, may not have equal impacts on people of different age groups. Disease dynamics and associated social forces are likely to be different in children, adolescents, young adults, and older adults with varying sociodemographic characteristics.^{9,62,63} Future research should examine syndemics in different population groups, associated biopsychosocial relationships, and multiple outcomes.

From a health services perspective, syndemics may impose unique challenges to the affected individuals requiring personalized care that may address multiple health concerns at a time. The recent technological advancements have facilitated the digitalization of health services with a focus on personalized or precision health.^{64–66} Syndemics research in the digital age should explore avenues of integrating interventions that target intersections of coexisting diseases and associated factors in specific contexts. Such integrative technological measures may inform spatial and temporal challenges through real-time measurements,^{67,68} and enable the practitioners to mitigate the burden of multimorbidity using evidence-based digital and traditionally delivered interventions.

Given the complex nature of syndemics, implementation research on coexisting diseases, common determinants, cumulative impacts, and shared sociocultural aspects should be conducted, and the findings should be incorporated in public health and social welfare policymaking. Despite a growing need for translating the current evidence to transform clinical and social care for syndemics, it is necessary to acknowledge that the current literature does not emphasize implementation dimensions of complex health and social problems. Researchers and decision-makers should recognize this gap as the persistence of comorbid disease would be critical for common healthcare operations such as patient-provider interactions and the delivery of health services. Institutional measures, including sensitizing the stakeholders and establishing evidence translation systems for practitioners, should be prioritized for minimizing knowledge-to-practice gaps in this regard.

Syndemics research highlights global health disparities by emphasizing the roles of context-specific forces and determinants of health.^{9,13} Therefore, local and global health systems should be examined from a syndemic perspective, which may enable health system strengthening that results in a better understanding of concurrent syndemics, future population health challenges, and how to respond to the same in a systematic way. Such insights on syndemics would also necessitate the active participation of global health organizations and member countries to use their collective resources to combat global health crises such as infectious disease outbreaks, food insecurity, climate migration, and health inequities that continue to affect populations. In these processes, the role of political commitment and collaborations will be of paramount importance.

From a health promotion perspective, it is critical to engage communities who are vulnerable to syndemics to increase their awareness on social determinants of cooccurring diseases.^{69,70} The public should be informed through targeted and mass media interventions regarding common challenges and preventive measures. However, empowering community-based organizations to assess their risks and address the same using local resources would be far more impactful. Such efforts may require technical assistance and external support, which should be organized through public health institutions. As syndemics researchers argue that context-specific factors and biopsychosocial interactions make syndemics unique to individuals and populations,^{9,40,48} participatory research and action plans may create opportunities to exchange knowledge and develop context-appropriate interventions for syndemics.

Syndemics research highlights an intersection of academic contributions from multiple scholarly disciplines, including medical anthropology, social epidemiology, health policy, health promotion, clinical sciences, and social sciences.^{6,30,57,69}

The combined use of multiple quantitative and qualitative methods has complemented the investigations of complex syndemic problems in current literature, which couldn't have been understood using any single-best method.^{6,9,16} Arguably, syndemics necessitate transdisciplinary approaches to integrate multiple research methodologies to answer complex research questions. Such integrative measures may help the scholars to apprehend the ontology and phenomenology of syndemics from shared epistemological perspectives.

Global research on syndemics informs the deteriorating effects of cooccurring health problems in populations living under chronic social stressors.^{8,10,31,56} Understanding these complex scenarios may offer insights on humanitarian challenges that are infrequently studied and discussed in contemporary health and social policy discourses. Notably, the production of health in a population reflects its commitment to improve people's wellbeing and maximize public welfare through regulating factors that may be harmful to individual and social health. Such initiatives may also include mandates for better access to health services irrespective of social, economic, cultural, geographic, and other differences across individuals and communities. However, many high-income countries such as the United States are far behind in ensuring equitable access to health.⁷¹ Previous research on political determinants of health informs critical challenges such as systematic racism, implicit bias, environmental injustice, and other structural factors that share the policy responses to public health problems.⁷¹⁻⁷⁴ From an ethical perspective, it is a shared responsibility of healthcare providers, researchers, and organizations to advocate for using science for bringing social justice through meaningful changes in the socio-political determinants of syndemics and health disparities in marginalized populations.

Limitations

There are several limitations of this meta-knowledge study, which are necessary to understand the scope and findings of this study. Also, the limitations of this study would inform future research addressing the theoretical, methodological, and empirical shortcomings of the current findings. One such limitation is the choice of the database; although WoS is one of the most inclusive sources of bibliographic data, it may not contain all articles published on syndemics. Therefore, this study could not include potential studies that may exist elsewhere. Although this limitation is very common across knowledge mapping studies,^{17,19,23} we encourage methodologists and other scholars to continue intellectual discourses on how the global knowledge community can find opportunities to harmonize citations data across databases. This is extremely challenging as journals are not universally indexed, and databases do not contain bibliographic data on all key variables of interest. This challenge necessitates an integration of technological advancements and cooperation between database authorities to facilitate a uniform distribution of scholarly resources globally. Another challenge was the framing of syndemics in the published literature. As found in the previous synthesis of empirical research,⁹ many scholars do not examine all criteria of syndemics in their studies. For example, the coexistence of multiple health problems without specifying the bib-bio or bio-social relationships is often studied within the syndemic framework. Also, it is possible to describe all criteria of syndemic without using the framework, which is perhaps a major challenge leading to a limited observation of literature on complex health problems. We recommend wide scholarly communication of syndemic theory and adoption of relevant keywords and explanations whenever possible. This may eliminate the existing knowledge biases and improve future mapping of the global knowledge landscape. Lastly, despite using contemporary knowledge mapping approaches, this study may not inform population-level estimates or determinants of syndemics. As we discussed earlier, the field of syndemics research is evolving, and this study highlighted key research areas within this growing field of knowledge. We recommend further primary studies and evidence synthesis on disease clusters that have synergistic effects, interactions, and shared sociocultural factors that may inform specific insights on context-specific syndemics.

Conclusions

In this meta-knowledge study on global research on syndemics, we found a limited yet growing body of scientific literature on syndemics and associated population health problems. Most studies on syndemics were published from high-income countries, and they included diverse topics ranging from STIs to various social determinants of health. Further research is needed to understand the dynamics of multiple coexisting infectious and noncommunicable diseases across global populations with a focus on cumulative disease burden, biopsychosocial relationships, and common structural forces that are associated with health and wellbeing. The findings of this study highlight the scope of syndemics to inform advanced research, health policymaking, and practices, not only through focusing on a single disease but also addressing health inequities in the intersections of multiple health problems through inclusive, context-specific, socioculturally appropriate, and evidence-based approaches.

Data availability

Underlying data

Open Science Framework: A meta-analysis of global research on syndemics (2001-2020). <https://doi.org/10.17605/OSF.IO/8N9R6>.

This project contains the following file:

- DataFile-Authors-DOI-Titles.xlsx
- Flowchart of the citations retrieval process (1).pdf

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

Competing interests

No competing interests were disclosed.

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Version 1

Reviewer Report 29 March 2022

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Ashley V. Hill

Department of Epidemiology, University of Pittsburgh School of Public Health, Pittsburgh, PA, USA

The authors of the present article provided a robust review of the literature examining “Syndemics” in multiple areas of emphasis and with various health indicators and outcomes. This article attempts to provide an overview of syndemic named literature published in the past 20 years and highlights both the researchers, institutions, and countries within which this work is being conducted.

An understanding of the scope of syndemic work being conducted globally is helpful, however, the article lacks any examination of the statistical approaches used across the articles included and overlooks the relatively robust discourse in the literature on criticisms of commonly used analytical approaches to syndemic research. As mentioned by the previous reviewer, the article would be significantly strengthened by a discussion of Tsai and colleagues’ recommendations for analytical approaches and a true discussion of the types of additive or interactive evaluations in the studies listed.

- Tsai, A. C., & Burns, B. F. (2015). Syndemics of psychosocial problems and HIV risk: A systematic review of empirical tests of the disease interaction concept. *Social Science & Medicine*, 139, 26-35.¹
- Stall, R., Coulter, R. W., Friedman, M. R., & Plankey, M. W. (2015). Commentary on “Syndemics of psychosocial problems and HIV risk: A systematic review of empirical tests of the disease interaction concept” by A. Tsai and B. Burns.²
- Tsai, A. C., & Venkataramani, A. S. (2016). Syndemics and health disparities: a methodological note. *AIDS and Behavior*, 20(2), 423-430.³
- Tsai, A. C. (2018). Syndemics: a theory in search of data or data in search of a theory?. *Social Science & Medicine*, 206, 117-122.⁴
- Mendenhall, E., Newfield, T., & Tsai, A. C. (2021). Syndemic theory, methods, and data. *Social science & medicine (1982)*.⁵

The inclusion of academic institutions, authors, and countries in the assessment is lacking recommendations. What are the authors hoping readers do with this information? How does it facilitate or foster collaboration? How would the authors recommend better support of syndemic

research in low- and middle-income countries? At present, this information does not add additional value to the study.

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3. Tsai AC, Venkataramani AS: Syndemics and Health Disparities: A Methodological Note. *AIDS Behav.* 2016; **20** (2): 423-30 [PubMed Abstract](#) | [Publisher Full Text](#)
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Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: I am a reproductive epidemiologist and have published research examining social determinants of sexually transmitted infections, some which apply a syndemic framework.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 25 Jan 2023

Samia Tasnim, EviSyn Health, Khulna, Bangladesh

Comment:

The authors of the present article provided a robust review of the literature examining “Syndemics” in multiple areas of emphasis and with various health indicators and outcomes. This article attempts to provide an overview of syndemic named literature published in the past 20 years and highlights both the researchers, institutions, and countries within which this work is being conducted.

An understanding of the scope of syndemic work being conducted globally is helpful, however, the article lacks any examination of the statistical approaches used across the articles included and overlooks the relatively robust discourse in the literature on criticisms of commonly used analytical approaches to syndemic research. As mentioned by the previous reviewer, the article would be significantly strengthened by a discussion of Tsai and colleagues’ recommendations for analytical approaches and a true discussion of the types of additive or interactive evaluations in the studies listed.

- Tsai, A. C., & Burns, B. F. (2015). Syndemics of psychosocial problems and HIV risk: A systematic review of empirical tests of the disease interaction concept. *Social Science & Medicine*, 139, 26-35.¹
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- Tsai, A. C. (2018). Syndemics: a theory in search of data or data in search of a theory?. *Social Science & Medicine*, 206, 117-122.⁴
- Mendenhall, E., Newfield, T., & Tsai, A. C. (2021). Syndemic theory, methods, and data. *Social science & medicine* (1982).⁵

Response:

The goal of a scientometric study is to examine the meta-knowledge development in a given topic in terms of research growth and trends and in this study we evaluated the scientific development of syndemics and related health and social issues. We have reviewed the methodology of the studies identified including the statistical approaches. Critical evaluation of the approaches was not possible as it was out of the scope of the present study.

“It is also crucial to highlight the existing debate within the field of syndemics is the framing and the statistical approaches used to establish relationships between the diseases and outcomes. Considering the complex multilevel involvement of syndemics Tsai et al and colleagues believe that most empirical studies purporting to validate the theory lack in statistical robustness. Tsai identified that most studies in the field of syndemics demonstrate a statistically significant association between psychosocial problems and health outcomes using simple linear models, very few studies assess the how these psychosocial problems interact to magnify the outcomes as they only use summative approach for measuring the effect. Additionally, the summative approach is only successful

to measure the changes when the effect sizes are small. Authors suggested to use the summative model using the count variable approach to conduct a latent factor analysis for confirming that a single parameter model is adequate. They emphasized on sharpening the theory's prediction approaches by incorporating advanced systems level approaches.

Stall argued in favor of the summative approach saying that majority of the existing data in this field comes from self-reported data from cross-sectional studies. Applying more rigorous data analysis method would require long-term cohort studies designed to establish the theory. However, considering the current nature of the fundings, implementing such resource intensive cohort study is not feasible. Due to the physical and psychological burden of these diseases (especially HIV) on highly vulnerable marginalized communities such as young gay black men or transgender women, the current approach is acceptable as it can demonstrate the dangerous existence of these co-morbidities highlighting the needs for prevention efforts from practitioners and policy makers."

Comment:

The inclusion of academic institutions, authors, and countries in the assessment is lacking recommendations. What are the authors hoping readers do with this information? How does it facilitate or foster collaboration? How would the authors recommend better support of syndemic research in low- and middle-income countries? At present, this information does not add additional value to the study.

Response:

Thank you for your insightful comment regarding the recommendation about research institutions, authors, and countries. We have added additional recommendations based on our findings in the discussion in the revised manuscript.

"It is critical to foster collaborative efforts among researchers across the globe to expand the ongoing research in the field of syndemics by including diverse perspectives. The present study has highlighted which institutions, mainly from high-income countries, have expertise in syndemics research. An ideal next step would be to focus on developing long-term collaboration by resource sharing and capacity building with scholars from LMICs to amplify their work. International public health organizations can establish global strategic planning groups that help fund collaborative work to address syndemics across nations. These groups could also concentrate on implementing multilevel strategies involving researchers, policymakers, health workers, and other key stakeholders to achieve a sustainable solution."

Competing Interests: No competing interests were disclosed.

Reviewer Report 11 March 2022

<https://doi.org/10.5256/f1000research.77914.r125796>

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Nicola Bulled

¹ InCHIP, University of Connecticut, Storrs, CT, USA

² School of Public Health, Brown University, Providence, RI, USA

The article, "Global research on syndemics: a meta-knowledge analysis (2001-2020)" for consideration in F1000 Research, offers a detailed meta-knowledge analysis of published syndemics literature from 2001-2020. Having conducted a review of syndemics literature myself, I agree with the approach taken by the authors regarding search engine, and generally agree with the analysis offered by the data generated. I do, however, feel the authors need to offer a more critical assessment of the analysis regarding what it reveals about the application of the theory, drawing on current conversations.

A couple of points of clarification are needed regarding how the data is analyzed. What is the relevance of bibliographic elements with reference to how the work is related? It is unclear to me how these elements are included or not in a network analysis of similarities. Incorporate the dates of the other reviews conducted. The reviews mentioned included fewer publications because their dates and in some cases topics were significantly narrower. Also include additional reviews that have not been mentioned, including that by Tsai and Burns 2015.

I encourage the authors to highlight the limitations of the approach at the outset of the methods rather than in a limitations section at the end. One of the primary limitations is that the authors do not identify what of the literature calling itself "syndemics" is actually a syndemic analysis. In one of the prior reviews of syndemic literature conducted (mentioned in this manuscript), only 12% of the literature reviewed actually met a syndemics definition. If that is the case in your analysis, then close to 90% of the literature included in this analysis is likely not syndemics at all. This needs to be considered as a limitation at the outset of the study. Or at least, the reader needs to be made aware of this problem. The discussion of the prior review did not lay this out clearly enough.

This is my primary concern for this study. While the results are very interesting, I feel that the story the results tell are not presented in the context of current syndemic theory conversations. The authors fail to include any of the work of A. Tsai, who has strongly critiqued syndemic theory as lacking evidence. A special issue of Social Science and Medicine published between 2019-2022 includes different work attempting to evidence syndemics. Many of these publications do not. What has been recognized is that the method to assess a syndemic arrangement introduced by R. Stall in 2005 actually is a summative score, with more "syndemic" factors present resulting in worse outcomes. This does not indicate a syndemic arrangement with synergy occurring between the factors. Stall himself has agreed that his analytical approach was wrong. The data presented in this study indicates the significant impact this work of Stall has had in directing syndemic literature, completely changing the trajectory of the theory and the approaches to assessing the theory. Stall is one of the top 10 authors and, as shown in Figure 7, has significantly impacted other key authors in the field. Many of the examples offered on pages 12-13 fall into this erroneous application of syndemics. While this may be where syndemics literature is at present, the authors should indicate the problem. Scholars appear to be using "syndemics" as a

fashionable new term to describe co-morbidities, with some acknowledging social elements, but many not offering much at all, and few considering evaluating synergistic rather than summative relationships.

The assessment of institutions also does not offer a great deal. I don't understand the network dynamic shown, how are these relationships determined? The statistics of frequency per institution need to be proportional to the number of scholars present in the institution or at least offer some indication of size. In this light, UCONN might be producing significantly more than other institutions, which would make sense given as that is where Merrill Singer is based. The authors offer no assessment of why these arrangements are the way they are. In which case, it isn't clear what the value of the data is. Similarly, the authors do not interrogate the bibliographic data presented. While it is interesting to consider number of authors, number of documents per author, and number of keywords. What does this really tell us? If the network is generated on these similarities, I don't see the value of the network.

One final point of note, in the top 10 articles listed, the Lancet piece on global obesity syndemic is second. This proved a highly contentious article in the field of syndemics researchers as it posited that a global syndemic could exist. For syndemics scholars that recognize the influence of social factors, this was not possible. An obesity epidemic in India is not socially the same as an obesity epidemic in the US or South Africa or Australia. What this study did, much like Stall's, was set syndemics theory on another course of inaccurate application.

The authors need to:

- Include the work of Tsai and the conversations he has provoked regarding the direction of syndemics' work.
- Interrogate the data presented in reference to Tsai's work, where has syndemic theory gone, and is this problematic.
- Don't use examples of syndemics literature that isn't presenting a syndemics arrangement, unless the aim is to indicate how it isn't a syndemic arrangement (references such as: 22, 29, 30, 31, 32, 33, 34, 35, 36, 37). Anything that indicates that more factors results in worse outcomes is using an additive/summative approach and not assessing for synergy between factors.
- Fix the typo "bib-bio", it comes up twice.
- Offer a richer analysis of the data presented, including discussing the relevance of bibliographic elements, presenting institutional publication records relative to institutional size, and assessing how different frameworks of understanding syndemic theory and evaluating syndemics influenced the literature.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: I am a syndemics researcher having published numerous syndemics papers with Merrill Singer, including the heavily cited Lancet piece noted in this manuscript as the 6th most cited syndemics article. I have worked on syndemics for close to 15 years. My primary focus area is infectious disease and syndemic theory development, including the evidencing of the theory.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 25 Jan 2023

Samia Tasnim, EviSyn Health, Khulna, Bangladesh

Comment:

The article, "Global research on syndemics: a meta-knowledge analysis (2001-2020)" for consideration in F1000 research, offers a detailed meta-knowledge analysis of published syndemics literature from 2001-2020. Having conducted a review of syndemics literature myself, I agree with the approach taken by the authors regarding search engines and generally agree with the analysis offered by the data generated. I do, however, feel the authors need to offer a more critical assessment of the analysis regarding what it reveals about the application of the theory, drawing on current conversations.

Response:

We appreciate the valuable comments of the respected reviewer. The goal of a scientometric study is to examine the meta-knowledge development in a given topic in terms of research growth and trends¹⁻³. It is used for unraveling and mapping the cumulative scientific knowledge in well-established fields by objective analysis of large volumes of unstructured data. It aims to uncover emerging trends in the field by highlighting the article and journal performances, collaboration patterns, research constituents, along with the intellectual structure of a specific domain. In this current study, we evaluated the scientific development of syndemics and related health and social issues. This approach is significantly different than what can be done in a systematic review or a

critical review. However, the scope of critical evaluation of the research topics in light of the previous research and academic discourses remain relevant. In this revised version, we revisited those areas and provided updated information and explanations that may address the shared concerns. Reflection of our critical assessment can be found in the discussion section.

Comment:

A couple of points of clarification are needed regarding how the data is analyzed. What is the relevance of bibliographic elements with reference to how the work is related? It is unclear to me how these elements are included or not in a network analysis of similarities. Incorporate the dates of the other reviews conducted. The reviews mentioned included fewer publications because their dates and in some cases topics were significantly narrower. Also include additional reviews that have not been mentioned, including that by Tsai and Burns 2015

Response:

As mentioned in the methods section, we have included all the articles meeting the inclusion criteria indexed in Web of Science until 6/26/2022. The article by Tsai et al., might have been missed due to mismatched indexing. We have also mentioned in our limitation that due to lack of universal indexing of scientific journals there is a possibility of missing articles not indexed in this major database.

We have also reviewed the analyzed works and relevant literature as suggested. We found that some of the studies indexed outside of WoS were not included in the current study. However, adding them to the dataset from non-homogenous bibliographic sources would create further discrepancies on bibliometric indicators. Therefore, we confined our work within the scope of WoS collection and discussed this elaborately both in the methods and discussion sections of our manuscript. The rest of the network analyzes were revisited and they are consistent with the WoS collection on syndemics, which we believe cover the majority of, if not all, scientific publications on this topic.

Comment:

I encourage the authors to highlight the limitations of the approach at the outset of the methods rather than in a limitations section at the end. One of the primary limitations is that the authors do not identify what of the literature calling itself "syndemics" is actually a syndemic analysis. In one of the prior reviews of syndemic literature conducted (mentioned in this manuscript), only 12% of the literature reviewed actually met a syndemics definition. If that is the case in your analysis, then close to 90% of the literature included in this analysis is likely not syndemics at all. This needs to be considered as a limitation at the outset of the study. Or at least, the reader needs to be made aware of this problem. The discussion of the prior review did not lay this out clearly enough

Response:

Thank you for mentioning this critical problem. We acknowledge this issue and we have revised the methods and limitations accordingly to make the readers aware of this problem.

“Due to discrepancy in the framing of syndemics in the published literature, the coexistence of multiple health problems without specifying the underlying bio-bio or bio-social relationships is often studied within the syndemic framework.⁹ Thus studies titled syndemics can be included in the analysis despite the differences in the scope of their work. This issue has been elaborated in the limitations section.”

Comment:

This is my primary concern for this study. While the results are very interesting, I feel that the story the results tell are not presented in the context of current syndemic theory conversations. The authors fail to include any of the work of A. Tsai, who has strongly critiqued syndemic theory as lacking evidence. A special issue of Social Science and Medicine published between 2019-2022 includes different work attempting to evidence syndemics. Many of these publications do not. What has been recognized is that the method to assess a syndemic arrangement introduced by R. Stall in 2005 actually is a summative score, with more “syndemic” factors present resulting in worse outcomes. This does not indicate a syndemic arrangement with synergy occurring between the factors. Stall himself has agreed that his analytical approach was wrong. The data presented in this study indicates the significant impact this work of Stall has had in directing syndemic literature, completely changing the trajectory of the theory and the approaches to assessing the theory. Stall is one of the top 10 authors and, as shown in Figure 7, has significantly impacted other key authors in the field. Many of the examples offered on pages 12-13 fall into this erroneous application of syndemics. While this may be where syndemics literature is at present, the authors should indicate the problem. Scholars appear to be using “syndemics” as a fashionable new term to describe co-morbidities, with some acknowledging social elements, but many not offering much at all, and few considering evaluating synergistic rather than summative relationships.

Response:

We revisited our analyses and also retrieved the data again to cross-check if there was any discrepancies. We included all articles in Web of Science until 6/26/2022 and realized that a major proportion of Tsai’s work was published in 2021-22, whereas our primary analyses included studies up to 2020. By that time, Tsai had 7 publications on syndemics, whereas the last author mentioned in our list had 9 publications. This is the reason why we couldn’t mention Tsai from an objective viewpoint. Perhaps this is also the reason why our paper may not inform anything regarding articles that were published beyond the scope of our dataset.

As we explained in the methods section of our revised submission, we included any work related to syndemics irrespective of the definitions or frameworks used by the respective authors. We welcome the discussion on the references related to Stall and colleagues. We have presented arguments from both sides in the discussion to inform the readers. We have also mentioned the differences in the opinions and objectively reflected its impact on research synthesis in the discussion section of this revised submission.

“It is also crucial to highlight the existing debate within the field of syndemics is the framing and the statistical approaches used to establish relationships between the diseases and outcomes. Considering the complex multilevel involvement of syndemics Tsai et al and

colleagues believe that most empirical studies purporting to validate the theory lack in statistical robustness. Tsai identified that most studies in the field of syndemics demonstrate a statistically significant association between psychosocial problems and health outcomes using simple linear models, very few studies assess the how these psychosocial problems interact to magnify the outcomes as they only use summative approach for measuring the effect. Additionally, the summative approach is only successful to measure the changes when the effect sizes are small. Authors suggested to use the summative model using the count variable approach to conduct a latent factor analysis for confirming that a single parameter model is adequate. They emphasized on sharpening the theory's prediction approaches by incorporating advanced systems level approaches.

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Comment:

The assessment of institutions also does not offer a great deal. I don't understand the network dynamic shown, how are these relationships determined? The statistics of frequency per institution need to be proportional to the number of scholars present in the institution or at least offer some indication of size. In this light, UCONN might be producing significantly more than other institutions, which would make sense given as that is where Merrill Singer is based. The authors offer no assessment of why these arrangements are the way they are. In which case, it isn't clear what the value of the data is. Similarly, the authors do not interrogate the bibliographic data presented. While it is interesting to consider number of authors, number of documents per author, and number of keywords. What does this really tell us? If the network is generated on these similarities, I don't see the value of the network.

Response:

As mentioned in the method section of the paper we conducted descriptive analysis of key bibliometric characteristics, institutions conducting research are commonly considered as a key characteristics in the bibliometric analysis as it can provide ideas about distribution of resources and potential areas for collaboration between institutions across the globe ⁴⁻⁶. However, it was not possible to further the analysis at individual researcher level as this information was not included in the bibliometric data retrieved from the database. Moreover, there is a possibility for the researchers to change their work affiliation or hold more than one affiliation, thus analysis based on publications as proportional to the number of scholars will vary but publications from institutions will remain relatively constant. Our approach is consistent with previous bibliometric studies that offered aggregated outcomes for authors and institutions ^{7,8}. Lastly, the value of the network,

particularly those illustrating clusters of research nodes, are useful to visualize research hotspots and themes. As noted in earlier works^{9,10} those insights not only inform current research trends, but also provide critical insights on research gaps in a scientific area. Both in our results and discussion, we discussed those hotspots and potential gaps in syndemic literature, which can be considered as the added contributions of this study.

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Competing Interests: No competing interests were disclosed.

Comments on this article

Version 1

Reader Comment 22 Mar 2022

Habibullah Habibullah, National Research and Innovation Agency, Indonesia (BRIN), Jakarta,

Indonesia

Very interesting research using bibliometric analysis but indeed the research data in developing countries is less than in developed countries

Competing Interests: I have no conflict of interest with the author and am very interested in research using bibliometric analysis

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