ABSTRACT

Introduction Men who have sex with men (MSM) are disproportionately affected by a number of health conditions that are associated with violence, stigma, discrimination, poverty, unemployment or poor healthcare access. In recent years, syndemic theory provided a framework to explore the interactions of these health disparities on the biological and social levels. Research in this field has been increasing for the past 10 years, but methodologies have evolved and sometimes differed from the original concept. The aim of this paper is to provide an overview of the existing literature on syndemic theory applied to MSM in order to identify knowledge gaps, inform future investigations and expand our understanding of the complex interactions between avoidable health conditions in a vulnerable population.

Methods and analysis The proposed scoping review will follow the methodological framework developed by Arksey and O’Malley with subsequent enhancements by Levac et al, Colquhoun et al and Peters et al as well as the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping review. A systematic search of MEDLINE, PsycINFO, Scopus, Cochrane Central Register of Controlled Trials and ProQuest Sociological Abstracts will be conducted. Reference lists of the included studies will be hand-searched for additional studies. Screening and data charting will be achieved using DistillerSR. Data collating, summarising and reporting will be performed using R and RStudio. Tabular and graphical summaries will be presented, alongside an evidence map and a descriptive overview of the main results.

Ethics and dissemination This scoping review does not require ethical approval. Data and code will be made accessible after manuscript submission. Final results will be disseminated through publication in a peer-reviewed journal and collaboration with grassroots Lesbian, Gay, Bisexual, Transgender, Queer, Intersex and Asexual (LGBTQIA+) organisations.

Registration This protocol was registered on manuscript submission on the Open Science Framework at the following address: https://osf.io/jwxtd; DOI: 10.17605/OSF.IO/JWXTD.

Strengths and limitations of this study

► This proposed review will be the first scoping review to map the current knowledge in Syndemic Theory applied to men who have sex with men (MSM), an important topic to understand the complex interactions between avoidable health conditions within an already vulnerable population group.

► A comprehensive search strategy of electronic databases was developed with the help of the director of health sciences library of our institution; this will be combined with a secondary hand-search of reference lists of included studies.

► We plan to conduct a fully transparent and reproducible study so that another researcher could reproduce our analysis using our open-access data and codes.

► Grassroots LGBTQIA+ and community health organisations will be the focus of the dissemination phases as part of a larger project to improve the health of MSM in Belgium.

► Usual limitations of scoping reviews will apply, such as the lack of risk of bias and strength of evidence assessment. However, we feel that the heterogeneity of research in the field of syndemics means a scoping review is the most appropriate methodology at this time.

INTRODUCTION

Background

Men who have sex with men (MSM) suffer disproportionately from a wide range of health conditions. The most studied of them being their susceptibility to HIV infection. Indeed, MSM represent 70% of new HIV diagnoses in the United States of America and more than half of new HIV diagnoses in the European Union-European Economic Area (among those for whom the route of transmission was known). Furthermore, they are also more prone to contract other sexually transmitted diseases, and gonococcal isolates from MSM are more likely to exhibit...
antimicrobial resistance than samples taken from heterosexual men.3

In addition to the burden of HIV and other sexually transmitted infections, MSM are also more likely to suffer from mental health conditions: depression, anxiety, suicide attempts and self-harm are more prevalent among MSM.4–6 Substance use is also higher in the MSM population.7 Moreover, all of these negative and often avoidable health outcomes are associated with experiences of homophobic violence, stigma, discrimination, internalisation of negative assumptions and attitudes about MSM by MSM themselves8–12 as well as with poverty, unemployment, unstable housing and poor healthcare access.13–16

Unfortunately, social factors such as these are often overlooked in the conventional frameworks of comorbidity and multimorbidity17 even though our understanding of diseases clustering demonstrates the need to incorporate social and environmental elements.18 To offer meaningful improvements to the health of marginalised populations, public health researchers and clinicians must move beyond a reductionist understanding of disease causation to more complex models of diseases interaction taking into account the social forces driving health inequalities.18–20

Syndemic theory draws attention to how social, economic and environmental factors affect the health of individuals.18 A syndemic refers to two or more mutually reinforcing epidemics interacting to produce an excess burden of disease in a population because of harmful social conditions.21 The main appeal of syndemic theory is that it considers health with a holistic point of view, describing interactions at two levels: (1) between diseases themselves and (2) between diseases and the social environment that contributes to their emergence, clustering and spread.18 One example of biological interaction between diseases would be the HIV/hepatitis B virus coinfection that results in a faster course of the liver disease and an increase in the risk of hepatocellular carcinoma.22

For biosocial interactions relevant to our population of interest, we may cite the heightened stress due to the stigmatisation and various forms of violence MSM encounter that may lead to unhealthy coping mechanisms such as drug and alcohol abuse as well as mental health disorders including depression and anxiety.23 These dysfunctional coping strategies and mental health issues may in turn trigger sexual risk behaviours, increasing the risk of infections such as HBV and HIV,18–24 to return to our previous example.

Thereby, syndemic theory provides an appropriate framework to study the health disparities among MSM and the links between these disparities and averse social conditions such as homophobia and structural heterosexism.

Rationale
As promising as syndemic theory is to explain health disparities among MSM and to propose multidisciplinary interventions, empiric data supporting this theory remain limited.25–26 Indeed, in a systematic review conducted in 2015 on psychosocial problems and HIV risk, Tsai and Burus25 showed that although the concept of interaction is central to the theory, statistics used to assess interaction vary considerably across studies and are often inadequate to prove the existence of an interaction. Moreover, in a scoping review of syndemic-related publications performed by Singer et al.27 published in 2020, the authors found only a limited number of citations meeting the definition of a true syndemic among the recent research in the field. Indeed, most publications related to syndemic theory failed to articulate the biological and biosocial interactions necessary to account for a true syndemic.25 These findings highlight the challenges faced by researchers interested in this approach to describe and empirically support a syndemic arrangement as well as a deviation from the original conceptualisation of the syndemic theory.27

A scoping review of systematic reviews on HIV prevention research on MSM published between 1988 and 2017 found that syndemics were an understudied topic.28 Mapping current knowledge in this field is important given the evolving variation in methodological approaches in syndemic research and the potential of the syndemic framework to address health inequalities and improve care and prevention services for this vulnerable population.

Objectives
The goal of this scoping review is to provide an overview of the existing literature on syndemic theory applied to MSM. We seek to map:
1. The different study designs employed;
2. The subpopulations of MSM studied;
3. The outcomes measured;
4. The psychosocial conditions evaluated and how they were defined;
5. The statistics used to evaluate the concept of interaction;
6. How many studies proposed a hypothesis for biological and sociobiological interactions and to collect the hypotheses proposed when applicable;

The information gathered will allow us to better understand the state of affairs in this topic, to identify the current knowledge gaps and to suggest recommendations to guide future research in the field in order to expand our understanding of the complex interactions between avoidable health conditions in a vulnerable population.

METHODS AND ANALYSIS
Design
Scoping reviews have been defined as : ‘a form of knowledge synthesis that addresses an exploratory research question aimed at mapping key concepts, types of evidence, and gaps in research related to a defined area or field by systematically searching, selecting, and synthesising existing knowledge’.29 This kind of review is relatively new and has become increasingly...
popular in recent years. It is a suitable approach for our research, given that we do not intend to evaluate the quality of the included studies nor the strength of their findings. The methodology of our scoping review will apply the framework suggested by Arksey and O’Malley with enhancements from Levac et al. We will also take into account the recommendations from Colquhoun et al and Peters et al. Furthermore, we will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews. The completed checklist can be found in online supplemental table S1.

Screening and data charting will be completed using DistillerSR (Evidence Partners, Ottawa, Canada). Statistics, charts, tables and final report will be generated using R and relevant packages.

We took several measures to ensure full transparency and reproducibility of our research, and the complete Data Management Plan can be found in the supplementary materials. This protocol was registered on manuscript submission on the Open Science Framework (https://osf.io/jwxted) and every important protocol amendment that may happen will be documented there.

**Stage 1: identifying the research questions**

The overarching research question of this scoping review is: ‘What is known about Syndemic Theory applied to MSM?’. To better explore this main question, we identified three subquestions:

1. ‘How are studies concerning Syndemic Theory applied to MSM conducted?’
2. ‘How is the concept of interaction explored in syndemic research applied to MSM?’
3. ‘What were the key findings of these studies?’

The questions 1 and 3 allow us to explore the full scope of the field and to summarise the way research is done and what was found so far. It is worth mentioning that, as stated earlier, we seek to map the field, not to assess the strength of the evidence and the risk of bias.

Question 2 aims to address the limitations already known on syndemic-related publications to explore how they apply to the publications restricted to the MSM population. As such, we will investigate both the statistics used to demonstrate an interaction and how the authors articulate the biological and biosocial interactions needed to account for a true syndemic arrangement.

**Stage 2: identifying relevant studies**

To identify the relevant studies, we employed a systematic search strategy with the help of the head librarian of our institution. We selected the following databases: MEDLINE, PsycInfo, Scopus, Cochrane Central Register of Controlled Trials and ProQuest Sociological Abstracts to allow us to obtain studies from different fields to have the most comprehensive corpus possible.

The main challenge we faced constructing the search strategy was the number of synonyms for ‘men who have sex with men’. To overcome this difficulty, we assembled a first list of keywords. Then we included additional keywords by selecting relevant entry terms for the MeSH term ‘Sexual and Gender Minorities’, which encompass MSM. The final list of keywords was approved by the authors and by our institution’s director of health sciences library. To limit the scope of the research to the studies focusing on syndemic and MSM, we decided to restrict the search to title, abstract and keywords. It seemed to be the best compromise between searching the full text, which may generate too much noise by returning studies that only mention MSM and/or syndemic and limit to the title only, which may be too restrictive. Likewise, we decided to only search articles containing ‘syndemic’ in their title, abstract or keywords. While we recognise that some earlier literature might be ignored, our goal is to examine how this concept in particular has been studied since it was conceived. Moreover, adding other search terms is likely to return too many references for the size of our team and our time constraints. No date limits will be applied, given the relative novelty of the syndemic literature and the expected low number of citations. Using this search strategy for MEDLINE via Ovid, we were able to generate 184 results. We then translated this search strategy for PsycInfo, Scopus, Cochrane Central Register of Controlled Trials and ProQuest Sociological Abstracts, which generated a total of 628 citations.

The full electronic search strategy can be found in online supplemental table S2.

Search results will be downloaded into .RIS files and imported into DistillerSR. Duplicates will then be immediately deleted before study screening for inclusion. After inclusion of relevant studies, we will hand-search the reference lists of the included studies to manually add pertinent studies that might have escaped our search strategy (eg, early articles did not yet use the term ‘syndemic’ but had a notable influence on syndemic literature). The same selection process outlined in stage 3 for the electronic search will be used. Relevant studies identified through these steps will be marked as ‘Additional records identified through other sources’ in the study selection flow diagram.

**Stage 3: selecting studies**

The screening process will be done using forms generated with DistillerSR by the authors. We will operate at two levels. A first wave of screening will be conducted on titles and abstracts. Articles that meet the inclusion criteria or for which eligibility is unclear will then pass through a second wave in which the full texts will be assessed for eligibility. A flow diagram will be generated to summarise the whole process, and exclusion reasons will be specified.

To embrace the full breadth of the research conducted on the field and considering the low number of existing studies, we decided to opt for broad inclusion criteria. Research will be included if they meet the following criteria:
Open access

► The main population studied must be MSM. For the inclusion criterion purpose, we consider as MSM every man who has sexual relationships with other men, independently from how they are defined in the study or how they define themselves. They will be considered eligible regardless if they have sexual relationships exclusively with men, with men and women or mostly with women.

► The syndemic framework must be the main focus of the study. Studies only mentioning syndemic theory will be excluded. Articles published in the early days of syndemic research that did not use the term yet will be included if they used a syndemic lens and had an impact on the field.

► Studies must be cohort, case–control, cross-sectional, controlled trials or qualitative studies.

► We will exclude letters, commentaries and editorials.

► Language must be English.

► Only peer-reviewed citations will be included.

No restriction will be applied concerning the location of the studies, the age of the participants nor the date of publication.

Because of the broadness and objectivity of our inclusion criteria, we do not consider it necessary for each paper to be reviewed by the all authors. Instead, 10% of the articles after deduplication will be randomly chosen and screened for eligibility by two reviewers. A Kappa inter-rater reliability score will be computed using DistillerSR to evaluate the agreement between the two reviewers. A score superior to 0.8 will be considered sufficient,37 and the rest of the screening process will then be conducted by the main investigator only. Throughout the two reviewers phase, discrepancy between the reviewers during the abstract screening will move the paper to full-text assessment. Any discrepancy after assessing the full text will be discussed to achieve consensus. If a consensus cannot be reached between the reviewers, a third reviewer may be consulted for arbitration.

Stage 4: charting the data

Data charting will be performed using forms generated in DistillerSR by the authors. Forms will be created to extract relevant information (see below) to answer the research questions as well as general study characteristics inspired by recommendations on data charting for scoping reviews.31,38

Study characteristics not directly related to our research questions consist of author(s), year of publication and the country (s) where the study took place.

To answer our first subquestion (‘How are studies concerning Syndemic Theory applied to MSM conducted?’), we will extract data regarding: study design; location of study; sample size; age of the sample; population and subpopulation of MSM studied, if any (eg, black MSM and men who have sex with men and women); conditions studied as part of a possible syndemic and how those conditions were defined and measured; and outcomes considered and how they were defined and measured and intervention type, comparator and duration of intervention (if applicable).

To answer question 2 (‘How is the concept of interaction explored in syndemic research applied to MSM?’), we will chart the statistics used to prove an interaction as well as if the study provided any articulation of biological interactions and biosocial interactions and what was the proposed articulation, if applicable.

Finally, we will summarise the key findings and recommendations to answer our last subquestion (‘What were the key findings of these studies?’).

The forms developed in DistillerSR for data charting may be adapted throughout the data collection process if new characteristics of interest emerge during the course of the study. Any departure from the present protocol, be it additional characteristics or removal of characteristics presented above, will be stated and justified in the final report.

Stage 5: collating, summarising and reporting the results

All data collected in stage 4 will be collated, summarised and reported using R,35 RStudio36 and relevant packages.

To answer the first subquestion, tables will be generated to offer a quantitative summary of the data collected. In addition, diagrams will be used to better visualise the breadth of conditions studied as plausible syndemics and the context in which they were studied. Doing so, we aim to provide an overview of the conditions most likely to represent a true syndemic, in order to inform future research by proposing recommendations to focus on those conditions.

For the second subquestion, we will generate a table summarising the key findings and recommendations for each study included, and we will provide an overview of these findings and recommendations in the discussion.

For studies proposing hypotheses of interaction, we will summarise said hypotheses in a dedicated table comprising the study identification, the level of interaction (biological and sociobiological) and the proposed hypothesis of interaction.

Finally, to address the question of knowledge gaps in syndemic theory applied to MSM, a visual evidence gap map will be created to help identify areas in which current evidences are lacking.39

Study timeline

The first stage of the proposed scoping review has already been completed to develop this protocol.

Stage 2 has been initiated and mostly completed, with regards to the electronic search. The .RIS files have not been downloaded yet, and the hand-search of the reference lists will only begin after completion of stage 3. The third stage will begin shortly after manuscript submission. We expect to complete this stage within a month before moving on to stages 4 and 5, which should take an additional 6 months. We expect to complete the scoping review by January 2021.

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PATIENT AND PUBLIC INVOLVEMENT

The first author (MO) is also the managing director of a LGBTQIA+ youth organisation. The relevance and potential of syndemic theory to the populations represented by the grassroots organisation has been extensively discussed internally and MO has been invited to give several presentations on the topic. Though LGBTQIA+ organisations have not been involved directly in the elaboration of the protocol, the relevance of the research objectives to the population in question has been established. LGBTQIA+ organisations and community health organisations will be extensively involved in the dissemination phases of this project as discussed below.

ETHICS AND DISSEMINATION

This study does not require ethics approval, as data will be collected through a review of published peer-reviewed literature. Dissemination of the findings will first occur via submission of the scoping review for peer-reviewed publication in a scientific journal. In order to promote transparency and reproducibility in scientific research, every file necessary to reproduce our research will be registered on the Open Science Framework and made accessible to be reusable with appropriate citation. Our full Data Management Plan can be found in the supplemental materials.

Following publication of the study, findings will be presented in an accessible format on the personal website of the main investigator and shared to the MSM population through grassroots LGBTQIA+ and health community organisations. This collaboration with grassroots organisation for the dissemination of our findings could then take the form of conferences, seminars or courses to draw attention to the syndemic theory. Moreover, this paper is intended to feed into an ongoing project on the health of MSM in Belgium.

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Contributors All authors contributed meaningfully to the preparation, drafting and editing of this scoping review protocol. BS suggested the idea and offered guidance throughout all stages of protocol development. MO, the main investigator and guarantor of the review, conceptualised the research questions and the research protocol as well as the data management plan. J-LB and LB participated in the elaboration of the protocol and proposed several improvements during the rounds of editing. All authors approved the final submitted manuscript.

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