PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Theoretical explanations for socioeconomic inequalities in multimorbidity – A Scoping Review
AUTHORS	Fleitas Alfonzo, Ludmila; King, Tania; You, Emily; Contreras-Suarez, Diana; Zulkelfi, Syafiqah; Singh, Ankur

VERSION 1 – REVIEW

REVIEWER	Soley-Bori, Marina King's College London
REVIEW RETURNED	29-Jul-2021

GENERAL COMMENTS	Title: Theoretical explanations for socioeconomic inequalities in multimorbidity – a scoping review Manuscript ID: BMJOpen-2021-055264 General comments: This papers aims to assess the use of theoretical explanations for the relationship between socioeconomic disadvantage and multimorbidity. This research is relevant given the high prevalence of multimorbidity, its differential impact across sociodemographic groups, and the lack of theoretical explanations behind the observed inequalities. Gaining knowledge in this area could inform policies aimed at reducing health inequalities. I have some queries and suggestions to improve the paper. Major points: 1. The paper doesn't conceptually treat multimorbidity any different than a single condition in terms of how it may be affected by socioeconomic disadvantage. The theories listed in the introduction "are proposed to explain associations between social inequalities and health" (line 31, page 3). The authors in my opinion should indicate how each theory may be relevant to multimorbidity specifically. 2. The authors use inconsistent terminology to refer to socioeconomic disadvantage, including socioeconomic inequalities, socioeconomic position, social inequalities, social disadvantage. I think the authors should pick one term and use it consistently throughout the text. Also, a paragraph in the introduction explicitly providing a description for this term along with measurement approaches would be very useful. 3. The introduction should be more focused on the goal of the paper (socioeconomic inequalities and multimorbidity). Only a very general sentence is provided (lines 17 and 18). Some actual statistics would be useful to understand the magnitude of the problem. The authors mention reference 4 in the discussion section (page 9, line 15), but the introduction may be a better place for it to frame this research.

	4. Both the abstract and the introduction clearly state that the authors are interested in assessing the causal relationship between socioeconomic disadvantage and multimorbidity. Yet in the methods section (page 5, line 6), the authors indicate that they are interested in the association between the two variables. The empirical strategies to identify association and causality are different. The authors mention mediation analysis at the end of the introduction. But I think at least two or three sentences presenting the main methods to explore causality between two variables should be included in the introduction. Otherwise, I think the authors should just use association throughout. 5. The article search is a bit outdates (11 December 2019), I wonder if the authors could check whether further studies have been published since then. 6. There are two study inclusion criteria that deserve further rationale or acknowledgement as possible limitations: including participants from any age group and studies conducted in any country (low, middle and high income). Multimorbidity among children often involves very different diseases and progression than among adults. Also, the construct of socioeconomic status among this young population probably requires separate treatment. The heterogeneity of countries may limit the ability to draw meaningful study conclusions. The definition of socioeconomic status may widely vary between a low-income country and a high-income country. 7. Some evaluation of the quality of the included studies is missing. The authors may want to consider using one (or more depending on study design) of the existing checklists to assess the quality of the studies and, thus, maybe give more weight to results coming from high-quality studies. For example, the authors may want to consider assessing risk of bias through the National Institutes of Health's National Heart, Lung, and Blood Institute quality assessment tools for observational cohort and cross-sectional studies. 8. The results section of the abstract is hard to follow if the reader is not familiar with these theories. To solve this, for example, the authors may state what the behavioral theory means in terms of socioeconomic status and multimorbidity. 9. The strengths and limitations section after the abstract could be improved. In the first bullet point, the authors should add multimorbidity as only socioeconomic position is mentioned. I find the limitation about non-English articles less important than for example, including children or a really heterogenous pool of countries. 10. Page 8, line 51. The conclusion "Supportive evidence was found for the role of these theories" doesn't seem to follow from the paragraphs above the discussion section on the same page with "partial mediator effect" (lines 15, 16) and "explained a small proportion of observed income-related inequalities" (lines 25, 26). What do the findings from empirical studies indicate about the direction and magnitude of the relationship between socioeconomic status and multimorbidity? A clear statement about this piece seems to be missing. Minor points: 1. The social capital theory seems to only apply to this work if the authors want to focus on inequalities, not just socioeconomic status. This point is related to clarifying the socioeconomic concept that the authors want to focus on (major comment number 2).

	2. The authors may want to clarify why the distinction between directly mentioned theories versus inferred is important. Otherwise, this piece could be deleted. 3. Page 7, line 25, please clarify what a “sense of coherence” means. 4. Page 7, line 30. The conclusion about the psychosocial theory being the most referred one doesn’t seem to follow from previous sentences. Did the authors mean to say behavioral theory instead? 5. Page 9, line 32. Please clarify what you mean by “contemporary approaches to causal inference”. This relates to my main comment number 4 on the importance of listing common methodology used for causal inference. 6. Page 9, line 37 “more comprehensive examination of these and other pathways”: the authors could indicate some examples of “other pathways”. 7. Couldn’t Table 2 and 3 be combined into one by only presenting the essential pieces of information to the study aim? In Table 3, what does the column “context of use” mean? For Johnston et al. 2019, the whole abstract seems to be included, which probably is not needed. 8. The Flowchart illustrating the search process lacks a title (at least in my version). Also, the stage on duplicates excluded I think should be presented in a horizontal arrow towards the right to indicate studies that were disregarded.

REVIEWER	Ingram, Elizabeth UCL, Department of Applied Health Research
REVIEW RETURNED	10-Sep-2021

GENERAL COMMENTS	This review addresses the pertinent issue of theoretical explanations through which socioeconomic disadvantage leads to multimorbidity. I would be happy to recommend this for publication if a number of additional areas are addressed. My first main comment is that the paper would be considerably improved if the main results were presented in a more digestible way (currently the results of most interest are in writing in Table 3). For example, the Singh et al., (2016) paper cited by the authors uses a deductive, structured approach that classifies each study according to their type and extent of theory use and presents their results in their Table 2. This review could take a similar approach. This would give a more comprehensive and easy to digest summary of the use of theory across this body of literature. My second main comment is that there could be some clarity around certain aspects of the paper. For example, it would be helpful to better understand what the authors mean by “theory” (clarity on the distinction between frameworks and models, implicit theory and explicitly mentioned theory would be helpful). In addition, an understanding of why they excluded qualitative research could strengthen the paper given that we might expect this field of research to contribute to the knowledge the authors are seeking. My third comment is that there could be more information on each study included in the results. For example, whilst included in Table 2, I think it could strengthen the paper by including a subsection in the results that describes how the included studies differ in their measurement of social disadvantage. It would also be helpful to

	know how the authors themselves are defining socio-economic disadvantage. Have they consulted relevant frameworks e.g., the WHO CSDH or the Dahlgren and Whitehead Rainbow? In addition, there is considerable variation in how multimorbidity is defined across studies (number and type of conditions selected and cut-off used). It would be helpful to include more information in the text or table that captures how definitions of multimorbidity differ across the included literature (this could just be added to column 5 of Table 2, for example). Finally, I think it would strengthen the paper if the discussion section included a specific subsection that gave a more comprehensive discussion of the review findings, their comparisons to previous literature, and their implications for policy. At present, this subsection seems to be weaved into the strengths and limitations subsection (paragraph starting line 13 page 9). The limitations of the paper could also be developed further. For example, the authors state that they have excluded the term comorbidity from the search strategy and why, yet haven't listed this as a limitation (which I would consider it to be given that the terms 'multimorbidity' and 'comorbidity' are used interchangeably). In addition, there has not been an assessment of study quality. I think that this should be listed as a limitation and an area where further research is needed as I suspect that the type and extent of theories used may differ by study quality. A more general point is that there are a handful of grammatical errors – I have spotted some in the first, third and fourth bullet points of the strengths and limitations box, and in line 26 of page 3.

REVIEWER	Hardman, Ruth La Trobe University, School of Rural Health
REVIEW RETURNED	17-Sep-2021

GENERAL COMMENTS	This is a well-written paper about an important topic. I only had a couple of issues: first, on the exclusion criteria. One of the papers excluded for comorbidity (Barnett et al) does in fact focus on non-disease specific multimorbidity so potentially should have been included, although it remains neutral as to the theoretical basis for the relationship between SE disadvantage and multimorbidity. Second, I would have liked to see some more expansion in the discussion around whether the current explanatory theories linking social disadvantage and (single) chronic health conditions are useful or could be used to provide research direction when exploring the relationship between multimorbidity and social disadvantage.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

Major points

Comment 1: The paper doesn't conceptually treat multimorbidity any different than a single condition in terms of how it may be affected by socioeconomic disadvantage. The theories listed in the introduction "are proposed to explain associations between social inequalities and health" (line 31,

page 3). The authors in my opinion should indicate how each theory may be relevant to multimorbidity specifically.
Response 1: Thank you for this comment. Many of these theoretical pathways are not specific for one chronic condition. In fact, behavioural factors such as smoking and alcohol misuse are risk factors for metabolic and cardiovascular diseases, highlighting the potential of explaining the presence of multiple conditions in individuals living in socioeconomic disadvantage. We have added text to each theory suggesting how they may apply to multimorbidity:
Behavioural:
"Behavioural theory can be extended to apply to multimorbidity from a common risk factor approach, as a behavioural risk factor can cause multiple diseases (for example, smoking can cause cancer, asthma, cardiovascular diseases (1, 2))."
Psychosocial
"The perceived lack of control and psychosocial stress may lead to adverse health behaviours and may activate neuro-endocrine mechanisms, and in doing so, may affect multiple body systems and lead to multimorbidity."
Materialist
"Lack of material resources such as inadequate housing for example, can lead to multimorbidity by causing depression as well as respiratory illnesses such as asthma."
Social support
"Social support is considered to be a distal determinant of health that may influence health through multiple mechanisms, for example by reducing stress and providing access to local resources, and in doing so, may prevent both mental and physical multimorbidities."
Social capital
"Similar to social support, high social capital is likely to boost health and prevent multiple chronic conditions by reducing stressors and increasing access to shared resources."
Comment 2: The authors use inconsistent terminology to refer to socioeconomic disadvantage, including socioeconomic inequalities, socioeconomic position, social inequalities, social disadvantage. I think the authors should pick one term and use it consistently throughout the text. Also, a paragraph in the introduction explicitly providing a description for this term along with measurement approaches would be very useful.
Response 2: Thank you for this comment. We have applied the term socioeconomic position/status and socioeconomic disadvantage throughout the paper when appropriate we have used socioeconomic inequalities. Here is the amended text in the paper to define each of these terms:
"Socioeconomic condition or status indicates the position in which an individual or a group is located within the social structure. It can be measured using educational attainment, income, occupation, wealth and area level measures (deprivation, socio-economic scores). We use the term socioeconomic inequalities in health to indicate the differences in rates of disease between individuals living in different socioeconomic conditions. Socioeconomic disadvantage refers to those who have the lowest socioeconomic conditions (3, 4)."
Comment 3: The introduction should be more focused on the goal of the paper (socioeconomic inequalities and multimorbidity). Only a very general sentence is provided (lines 17 and 18). Some actual statistics would be useful to understand the magnitude of the problem. The authors mention reference 4 in the discussion section (page 9, line 15), but the introduction may be a better place for it to frame this research.
Thanks for this suggestion. The following paragraph was added in response:
"A meta-analysis of 24 cross-sectional studies reported that low education compared to high education was associated with 64% higher odds of multimorbidity (5). Another systematic review with 41 studies from North America, Europe and Australasia reported that people with the lowest level of income had 4.4 times higher odds of multimorbidity than those with the highest level of income, while those in most deprived areas had 1.42 times higher odds of multimorbidity than those in the least deprived areas (6). A clear causal relationship between socioeconomic conditions and multimorbidity

has also been argued based on empirical evidence (7), however, pathways through which socioeconomic disadvantage leads to multimorbidity are not well studied (8)."

Comment 4: Both the abstract and the introduction clearly state that the authors are interested in assessing the causal relationship between socioeconomic disadvantage and multimorbidity. Yet in the methods section (page 5, line 6), the authors indicate that they are interested in the association between the two variables. The empirical strategies to identify association and causality are different. The authors mention mediation analysis at the end of the introduction. But I think at least two or three sentences presenting the main methods to explore causality between two variables should be included in the introduction. Otherwise, I think the authors should just use association throughout.

Thank you for this suggestion. We removed the term "causal" where applicable and changed it to association throughout.

Comment 5: The article search is a bit outdates (11 December 2019), I wonder if the authors could check whether further studies have been published since then.

Thanks for this comment. We have updated the search on 28/09/2021 as suggested and added 27 additional papers into our review.

Comment 6: There are two study inclusion criteria that deserve further rationale or acknowledgement as possible limitations: including participants from any age group and studies conducted in any country (low, middle and high income). Multimorbidity among children often involves very different diseases and progression than among adults. Also, the construct of socioeconomic status among this young population probably requires separate treatment. The heterogeneity of countries may limit the ability to draw meaningful study conclusions. The definition of socioeconomic status may widely vary between a low-income country and a high-income country.

We were interested in documenting the use of theories applied to understand multi-morbidity. At this stage we are not examining effect modification or differences on application of theories by age or context. We note this in the discussion:

"It is also worth noting that given the variations in the relationship of interest by country level of income and age group, future studies should examine the relevance of theories across different contexts and ages."

Comment 7: some evaluation of the quality of the included studies is missing. The authors may want to consider using one (or more depending on study design) of the existing checklists to assess the quality of the studies and, thus, maybe give more weight to results coming from high-quality studies. For example, the authors may want to consider assessing risk of bias through the National Institutes of Health's National Heart, Lung, and Blood Institute quality assessment tools for observational cohort and cross-sectional studies.

Thank you for this comment. The objective of this review was to map the use of socio-epidemiological theories explaining the relationship between socioeconomic disadvantage and multimorbidity. We were not focused on quantifying the effect of socioeconomic disadvantaged on the onset of multiple chronic conditions or in quantifying the proportion of association mediated through material, behavioural or psychosocial pathways. We therefore chose to conduct a scoping over a systematic review as these are the most appropriate design to map the existing evidence. As opposed to systematic reviews, scoping reviews do not require a quality assessment of the evidence (9). We have now clarified this in our methods section:

"Because the objective of this review is to offer a snapshot of the available evidence of theories explaining socioeconomic inequalities in multimorbidity and not on assessing the effect of socioeconomic disadvantage on multimorbidity development, we did not assess the quality of included papers in accordance with the guidelines for conducing scoping reviews (10)."

This is also acknowledged as a limitation in our discussion:

"Moreover, we did not use any tool to assess the quality of the included studies. This information is already provided by existing reviews (5, 6)."

Comment 8: The results section of the abstract is hard to follow if the reader is not familiar with these theories. To solve this, for example, the authors may state what the behavioral theory means in terms of socioeconomic status and multimorbidity.

Thanks for this suggestion. We addressed this by adding a brief note within parenthesis for each of the theories mentioned in the abstract. The following text was added:
"Behavioural theories (health behaviours) were the most frequently used, followed by materialist (access to health resources) and psychosocial (stress pathways) theories."
Comment 9: The strengths and limitations section after the abstract could be improved. In the first bullet point, the authors should add multimorbidity as only socioeconomic position is mentioned. I find the limitation about non-English articles less important than for example, including children or a really heterogenous pool of countries.
Thank you. The decision of including articles from any country and age groups aligns with our aim of examining the application of epidemiologic theories to explain the association between socioeconomic disadvantage and multimorbidity. Given that this review is only focused on the relationship between socioeconomic disadvantage and multimorbidity in the general population differences by specific population characteristics such as age and country of residence is beyond the scope of this review. We also acknowledge that these differences are worthy of further exploration. We noted this in the discussion section (please see response to comment 6)
Comment 10: Page 8, line 51. The conclusion "Supportive evidence was found for the role of these theories" doesn't seem to follow from the paragraphs above the discussion section on the same page with "partial mediator effect" (lines 15, 16) and "explained a small proportion of observed income-related inequalities" (lines 25, 26). What do the findings from empirical studies indicate about the direction and magnitude of the relationship between socioeconomic status and multimorbidity? A clear statement about this piece seems to be missing.
Thanks for this comment. The text was modified to reflect the extent to which the evidence supports the explanatory epidemiological theories identified in this review. The sentence now reads:
"Existing evidence partially supports these theories. All studies that tested mediation found an effect of socioeconomic disadvantage on multimorbidity, while only three found evidence that this effect is transmitted through social support, behavioural factors and socioeconomic changes across the life course (7, 11-14)."
Minor points
Comment 1: The social capital theory seems to only apply to this work if the authors want to focus on inequalities, not just socioeconomic status. This point is related to clarifying the socioeconomic concept that the authors want to focus on (major comment number 2).
Yes, we are interested in socioeconomic disadvantage as well as the inequalities on multimorbidity arising from socioeconomic differences. Please see our response to comment 2 above.
Comment 2: The authors may want to clarify why the distinction between directly mentioned theories versus inferred is important. Otherwise, this piece could be deleted.
A directly mentioned theory implies that the authors have considered a specific theoretical pathway for the effect of socioeconomic disadvantage on multimorbidity. Otherwise, readers need to interpret which theory was used, with the possibility of these being wrongly inferred. For example, behavioural theories can be considered either as a subset of psychosocial theory or a 'behavioural theory'. We modified the methods section to clarify this:
"Use of theory was categorised as inferred by us (reviewers/readers) or explicitly mentioned by the original study authors. It is important to distinguish between the two because the former relies on the reviewers/readers' subjective judgement (which may not be accurate) while the latter accurately reflects the theoretical reasoning of the original authors."
Comment 3: Page 7, line 25, please clarify what a "sense of coherence" means.
Aaron Antonovsky defines sense of coherence as "the extent to which one sees one's world as comprehensible, manageable and meaningful" (15). We added the following sentence in response:
"In addition, three studies applied the 'sense of coherence', which indicates an individual's coping capacity to deal with life and stressful events."
Comment 4: Page 7, line 30. The conclusion about the psychosocial theory being the most referred one doesn't seem to follow from previous sentences. Did the authors mean to say behavioral theory instead?

Thank you, the text was modified to reflect this:
“Collectively, behavioural theory was the most referred to among studies”
Comment 5: Page 9, line 32. Please clarify what you mean by “contemporary approaches to causal inference”. This relates to my main comment number 4 on the importance of listing common methodology used for causal inference.
Thank you. The following text was added in response:
“However, the use of contemporary approaches to causal inference, using a counterfactual framework to maximise exchangeability between exposed and unexposed participants, was limited (59)”
Comment 6: Page 9, line 37 “more comprehensive examination of these and other pathways”: the authors could indicate some examples of “other pathways”.
Thank you for this comment. The text was modified in response:
“Approaches need to shift towards a more comprehensive examination of pathways to allow policymakers to select interventions with maximum capacity to reduce health inequalities.”
Comment 7: Couldn’t Table 2 and 3 be combined into one by only presenting the essential pieces of information to the study aim? In Table 3, what does the column “context of use” mean? For Johnston et al. 2019, the whole abstract seems to be included, which probably is not needed.
Thank you for this comment. Table 3 was replaced to present the findings in a more comprehensive manner.
Comment 8: The Flowchart illustrating the search process lacks a title (at least in my version). Also, the stage on duplicates excluded I think should be presented in a horizontal arrow towards the right to indicate studies that were disregarded.
Thank you for this comment. The flowchart has now been updated according to the latest version of PRISMA (16).
Reviewer: 2
Comment 1: My first main comment is that the paper would be considerably improved if the main results were presented in a more digestible way (currently the results of most interest are in writing in Table 3). For example, the Singh et al., (2016) paper cited by the authors uses a deductive, structured approach that classifies each study according to their type and extent of theory use and presents their results in their Table 2. This review could take a similar approach. This would give a more comprehensive and easy to digest summary of the use of theory across this body of literature.
Thank you. Table 3 was modified as suggested.
Comment 2: My second main comment is that there could be some clarity around certain aspects of the paper. For example, it would be helpful to better understand what the authors mean by “theory” (clarity on the distinction between frameworks and models, implicit theory and explicitly mentioned theory would be helpful). In addition, an understanding of why they excluded qualitative research could strengthen the paper given that we might expect this field of research to contribute to the knowledge the authors are seeking.
Theories can be tested using empirical data. We excluded qualitative research because we were interested on how the theories were used to explain the relationship between socioeconomic disadvantage and multimorbidity. The following text was added in response:
“Theories are used in epidemiology to understand relationships. Mainly because, as opposed to conceptual frameworks, specific theoretical pathways can be tested using empirical data. These theories provide insight into the mechanism through which an exposure (e.g. socioeconomic position) leads to a health outcome (17). As such, they are particularly helpful to inform intervention designs”
Comment 3: My third comment is that there could be more information on each study included in the results. For example, whilst included in Table 2, I think it could strengthen the paper by including a subsection in the results that describes how the included studies differ in their measurement of social disadvantage. It would also be helpful to know how the authors themselves are defining socio-economic disadvantage. Have they consulted relevant frameworks e.g., the WHO CSDH or the Dahlgren and Whitehead Rainbow? In addition, there is considerable variation in how multimorbidity is defined across studies (number and type of conditions selected and cut-off used). It would be

helpful to include more information in the text or table that captures how definitions of multimorbidity differ across the included literature (this could just be added to column 5 of Table 2, for example).
Thank you for this comment. We added the following text to clarify how socioeconomic status was defined:
“For this review socioeconomic status could be measured using the following indicators: occupation, income (household or individual), educational attainment, area level of socioeconomic deprivation, wealth, and social class (16, 31).”
In addition, we modified table 2 to include definitions of socioeconomic disadvantage and multimorbidity as defined by each study.
Comment 4: Finally, I think it would strengthen the paper if the discussion section included a specific subsection that gave a more comprehensive discussion of the review findings, their comparisons to previous literature, and their implications for policy. At present, this subsection seems to be weaved into the strengths and limitations subsection (paragraph starting line 13 page 9). The limitations of the paper could also be developed further. For example, the authors state that they have excluded the term comorbidity from the search strategy and why, yet haven’t listed this as a limitation (which I would consider it to be given that the terms ‘multimorbidity’ and ‘comorbidity’ are used interchangeably). In addition, there has not been an assessment of study quality. I think that this should be listed as a limitation and an area where further research is needed as I suspect that the type and extent of theories used may differ by study quality.
Thanks for this comment. The discussion section has been modified accordingly. In addition, we added the following text to acknowledge the limitations highlighted above:

“Moreover, we did not use any tool to assess the quality of the included studies. Therefore, this review provides limited information about the methodological strengths and weaknesses of the current literature. Lastly, we restricted this review to articles assessing only multimorbidity and excluded those looking at comorbidities. We acknowledge that some authors use both terms interchangeably, therefore papers using the term comorbidity to indicate the presence of multiple independent chronic conditions may be missing from this review”
Comment 5: A more general point is that there are a handful of grammatical errors – I have spotted some in the first, third and fourth bullet points of the strengths and limitations box, and in line 26 of page 3.
Thank you. We have proofread the manuscript and addressed the grammatical errors.
Reviewer 3
Comment 1: first, on the exclusion criteria. One of the papers excluded for comorbidity (Barnett et al) does in fact focus on non-disease specific multimorbidity so potentially should have been included, although it remains neutral as to the theoretical basis for the relationship between SE disadvantage and multimorbidity.
Thank you for this comment. This paper is now added to the review.
Comment 2: Second, I would have liked to see some more expansion in the discussion around whether the current explanatory theories linking social disadvantage and (single) chronic health conditions are useful or could be used to provide research direction when exploring the relationship between multimorbidity and social disadvantage.
Thank you, the text has now been updated as:
“Second, there is a paucity of evidence on pathways (e.g. behavioural, material, psychosocial) between the shared causal factor (exposure to socioeconomic disadvantage) and multiple conditions that co-occur in multimorbidity (8). The lack of evidence precludes policy makers from intervening on causal mechanisms that can prevent, or mitigate observed socioeconomic inequalities in multimorbidity (18)”

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VERSION 2 – REVIEW

REVIEWER	Soley-Bori, Marina King's College London
REVIEW RETURNED	09-Dec-2021

GENERAL COMMENTS	Great revision, no more comments.

REVIEWER	Ingram, Elizabeth UCL, Department of Applied Health Research
REVIEW RETURNED	20-Dec-2021

GENERAL COMMENTS	I'm happy that the authors have addressed my comments to date on this paper. I would be happy to recommend this for publication if a handful of additional minor areas are addressed: • I suggest you consider consistently using one term to refer to the concept of multimorbidity. I have noted that you've referred to the following terms in addition to the term multimorbidity: multi-morbidities, multimorbidities, multiple chronic conditions, multiple conditions, multiple independent chronic conditions. • You also use the terms socioeconomic disadvantage, socioeconomic position, socioeconomic status and socioeconomic inequalities interchangeably. Whilst I'm aware that you need to do this to some extent to reflect the terms used by the different papers you include in your review, I suggest that you pick one and stick to it throughout when referring to the concept yourself as (as you have defined) they have slightly different meanings. • In the section of your results "Testing the explanatory potential of theories" perhaps consider quantifying the extent to which the risk factors these 5 papers explore mediated observed associations between socioeconomic position and multimorbidity (as you have done for the Singh paper). I think this would improve your paper. I.e., to what extent did the 5 risk factors explored in the Katikireddi paper mediate the associations between area-level deprivation/household income and multimorbidity? • Consider revising the fourth bullet point on the strengths and limitations of review box at the beginning of the manuscript. The exclusion of non-English literature will have missed papers published in developing countries but will also have missed papers published in countries that are "developed" but that don't speak English as their first language. • P4L21-23 – socioeconomic inequalities occur not only across countries but also within countries. • P4 L28 – our paper included studies from countries outside of North America, Europe, and Australasia. Maybe just say high income countries? • I'm assuming you've excluded other review papers in your review. If so, please add something to reflect that in your inclusion criteria table. • Consider clearly stating that the identification of the 751 unique papers (P9L21) relates to your initial/first screen • There are a handful of places at which I think you need to reference some of your statements/claims. For example, at the following points: P4L45, P4L55, P6L12, P5L39 (statement about accumulation model), P5L44 (statement about neo-liberal framework), P12L14. • I have spotted grammatical errors at these points: P3L50, P3L54, P4L10, P4L24, P9L17, P9L25, P9L30.

	• Consider giving dates in words and not numbers given that for example 28/09/2021 (as wrote in the abstract) can mean different things in different countries. • "by country level of income or age group" P12L22 – consider rewriting this sentence as, as it stands, I don't understand the point being made.

VERSION 2 – AUTHOR RESPONSE

Reviewer 2

Comment 1: I suggest you consider consistently using one term to refer to the concept of multimorbidity. I have noted that you've referred to the following terms in addition to the term multimorbidity: multi-morbidities, multimorbidities, multiple chronic conditions, multiple conditions, multiple independent chronic conditions.

Thanks for this comment. The manuscript was updated to a more consistent use of multimorbidity. Where applicable, all other terms were replaced by multimorbidity.

Comment 2: You also use the terms socioeconomic disadvantage, socioeconomic position, socioeconomic status and socioeconomic inequalities interchangeably. Whilst I'm aware that you need to do this to some extent to reflect the terms used by the different papers you include in your review, I suggest that you pick one and stick to it throughout when referring to the concept yourself as (as you have defined) they have slightly different meanings.

Thanks for this comment. In the last submitted version we had addressed the comment raised by the reviewer. We have further amended the text to clarify this as presented in the revised methods section:

"We use the term socioeconomic position to reflect socioeconomic status of individuals or groups in the population. Socioeconomic status indicates the position in which an individual or a group is located within the social structure. It can be measured using educational attainment, income, occupation, wealth and area level measures (deprivation, socio-economic scores). We use the term socioeconomic inequalities in health to indicate the differences in disease levels between people living with different socioeconomic positions. Socioeconomic disadvantage refers to those who have the low socioeconomic position."

Furthermore, the terms socioeconomic status and socioeconomic condition were updated to socioeconomic position when appropriate. We did not edit the terms socioeconomic inequalities and socioeconomic disadvantage as these are intended to reflect socioeconomic differences in levels of disease and low socioeconomic position respectively.

Comment 3: In the section of your results "Testing the explanatory potential of theories" perhaps consider quantifying the extent to which the risk factors these 5 papers explore mediated observed associations between socioeconomic position and multimorbidity (as you have done for the Singh paper). I think this would improve your paper. I.e., to what extent did the 5 risk factors explored in the Katikireddi paper mediate the associations between area-level deprivation/household income and multimorbidity?

Thanks for this comment. We have added the proportions to reflect the extent of mediation for the explored socioeconomic theories when these were available.

Comment 4: Consider revising the fourth bullet point on the strengths and limitations of review box at the beginning of the manuscript. The exclusion of non-English literature will have missed papers published in developing countries but will also have missed papers published in countries that are "developed" but that don't speak English as their first language.

Thank you. The fourth bullet point was updated to:

"Articles that were not in English were excluded from our review. This could have obstructed the inclusion of papers from countries where English is not the main language, therefore limiting the generalisability of our findings."

Comment 5: P4L21-23 – socioeconomic inequalities occur not only across countries but also within countries.

Thanks for this comment. We have updated the text to reflect that socioeconomic inequalities in multimorbidity exist within countries regardless of their level of economic development.

"Furthermore, abundant empirical evidence shows socioeconomic inequalities in multimorbidity within several countries at different stages of economic development (1-5)."

Comment 6: P4 L28 – our paper included studies from countries outside of North America, Europe, and Australasia. Maybe just say high income countries?

Thanks for this comment. The text was updated as suggested:

"Another systematic review with 41 studies from high income countries reported that people with the lowest level of income had 4.4 times higher odds of multimorbidity than those with the highest level of income, while those in most deprived areas had 1.42 times higher odds of multimorbidity than those in the least deprived areas (6)."

Comment 7: I'm assuming you've excluded other review papers in your review. If so, please add something to reflect that in your inclusion criteria table.

Thank you. In response to this comment, we added the following point to our exclusion criteria:

"Literature reviews, scoping reviews and systematic reviews"

Comment 8: Consider clearly stating that the identification of the 751 unique papers (P9L21) relates to your initial/first screen

We appreciate this comment. The text was updated in response:

"Our initial search led to the identification of 751 unique papers that underwent title and abstract screening."

Comment 9: There are a handful of places at which I think you need to reference some of your statements/claims. For example, at the following points: P4L45, P4L55, P6L12, P5L39 (statement about accumulation model), P5L44 (statement about neo-liberal framework), P12L14.

Thank you for this comment. We added in-text citation at the end of these sentences.

Comment 10: I have spotted grammatical errors at these points: P3L50, P3L54, P4L10, P4L24, P9L17, P9L25, P9L30.

Thanks for this comment. We have revised the manuscript to address the grammatical errors at the following points:

P3 L50:

“Our review has identified critical gaps in the literature that must be addressed if interventions and public policies are to be designed to reduce socioeconomic inequalities in multimorbidity.”

P3L54:

“We applied a comprehensive search strategy to identify relevant articles and applied a peer-reviewed robust methodology to assess theories in studies on socioeconomic inequalities in multimorbidity.”

P4L10:

“Multimorbidity leads to reduced quality of life, high psychological distress, burden of polypharmacy and managing multiple treatment protocols, and an increased risk of premature death in people.”

P4L24:

”Furthermore, multiple studies have reported socioeconomic inequalities in multimorbidity within countries regardless of their level of economic development.”

P9L17:

“No patients were directly involved in this study as this is a review of published studies.”

P9L25:

“In addition, two studies were included for full-text review from other sources. Thirty-six studies proceeded to data charting stage after completion of full-text review. The updated search on 28 September 2021 led to a further screening of 461 titles and abstracts from the 573 newly identified records.”

P9L30:

“After full text screening of 44 studies, 27 new studies were included in the review. A total of 64 studies were included in this review.”

Comment 11: Consider giving dates in words and not numbers given that for example 28/09/2021 (as wrote in the abstract) can mean different things in different countries.

Thanks for this comment. We revised the abstract in response:

“The last search was performed on the 28th of September 2021.”

Comment 12: “by country level of income or age group” P12L22 – consider rewriting this sentence as, as it stands, I don’t understand the point being made.

Thanks for this comment: The text now reads:

“It is also worth noting that given the variations in the relationship of interest according to individual (e.g. age) and contextual characteristics (e.g. country level of income development), future studies should examine the relevance of theories across different contexts and age groups.”

VERSION 3 – REVIEW

REVIEWER	Ingram, Elizabeth UCL, Department of Applied Health Research
REVIEW RETURNED	26-Jan-2022

GENERAL COMMENTS	This is a great revision. I am happy with the authors' responses to my comments, and I have no further comments.