PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The impact of endometriosis on women’s life decisions and goal attainment: a cross-sectional survey of members of an online patient community
AUTHORS	Missmer, Stacey A.; Fitzpatrick, Katherine; Tu, Frank; Soliman, Ahmed M.; Chiuve, Stephanie; Cross, Sarah; Eichner, Samantha; Antunez Flores, Oscar; Horne, Andrew; Schneider, Beth; As-Sanie, Sawsan

VERSION 1 – REVIEW

REVIEWER	Facchin, Federica Catholic University of Milan, Psychology
REVIEW RETURNED	28-Jun-2021

GENERAL COMMENTS	I really enjoyed reading such an interesting study on a timely and important topic: the impact of endometriosis on women’s daily activities and major life decisions and goal attainment. Endometriosis is indeed a disabling condition, especially when symptomatic, and there is need for studies like this. The evidence provided by this body of research may help clarify the needs of the women affected by the condition and inform not only clinical practice, but also social policy development and implementation. The manuscript is clear and well written. I am pleased to share with the authors some comments and suggestions, I hope they will find them useful. Introduction The Introduction is informative and provides a clear rationale for conducting such a study. However, the final part of this section highlights the strengths of the study and its importance in the context of endometriosis research and clinical practice (pp. 7, lines 29-56). This material should be moved to the Discussion. The authors may consider the possibility of including additional information to summarize the available evidence on women’s subjective experience of endometriosis (the body of literature cited on p. 6, lines 45-49), especially focusing on the social impact of the condition. As reported by the authors, this body of literature is composed of studies with small sample sizes and qualitative designs. I would not consider the qualitative nature of a research as an intrinsic limitation. Qualitative studies are important to address new research questions informed by women’s own words. The data analyzed in the study were collected in 2018 (before the pandemic), but as a reader I would like to be informed about the challenges derived from the current scenario (see for example the

work of Matthew Leonardi on endometriosis and Covid-19). In fact, I think the pandemic has been exacerbating pre-existing social inequalities, especially for women (not to mention those with a chronic disease).

At the end of the Introduction, the research question should be further clarified (the current research question reported in the manuscript is quite vague).

Methods

P. 9: “This portion of the survey was modeled after a validated instrument created to measure life-course impact of disease in patients with psoriasis”: please, clarify. The two diseases are totally different, and the use of an instrument created in the context of psoriasis to assess the life-course impact of endometriosis sounds counterintuitive.

Given that an online survey was conducted, what platform/software was used (e.g., Qualtrics, Survey Monkey …)?

The questionnaire was available from October 3 to October 3 to October 25. Were specific criteria used to decide when to stop data collection, such as a minimum number of participants?

Statistical analyses: the authors should clarify how missing data were treated. Missing data are very common in online surveys.

Results

Sometimes the information reported is too general. For instance: “most women”, “many women” … without number and percentages. Considering that the whole data analysis strategy is based on descriptive statistics, the authors should always report the exact number of participants (including percentages).

The authors performed additional analyses to examine the characteristics of women who believed their future and life potential were negatively impacted by endometriosis. That is interesting, but it would have been even more interesting to see the findings of a systematic comparison between this group and the group of women who did not feel their life was impacted by the disease. I think it would be useful not only to understand women’s endometriosis-related difficulties, but also their resources: why do some women perceive their lives as more impacted by endometriosis than other women? Do the authors have any ideas based on their findings? Moreover, in this section the authors reported that – for instance – “Overall, women who believed they were LPAF or had NRFP reported more negative experiences compared with the fewer respondents who did not indicate they were LPAF (non-LPAF, 21%; n=154) or had NRFP (non-NRFP, 25%; n=187)”. These are descriptive data. Without a statistical test (e.g., chi square) and a level of significance (P value), the information reported regarding each dimension (for instance, that one group had more negative experiences than the other group) is a speculation derived from a mere observation.

Discussion

	In this section, the authors should clarify what endometriosis-related factors – besides pain symptoms – are associated with a greater perceived negative impact of the disease on women's life course in terms of choices and self-fulfillment. The fact that women cannot follow their career preferences due to endometriosis is terrible, and I think the authors should emphasize the importance of investigating this aspect and the pervasive impact it may have on women's lives and psychological health, for instance with regards to self-esteem and depression. Please, expand the discussion of the wider implications of this study findings in terms of suggestions for future research and clinical practice. Moreover, and equally important: how could these findings inform the development and implementation of social policies? This type of studies is very useful for all women with endometriosis, and especially for the important work of patient associations: the volunteers may present this body of evidence to politicians and authorities, to further demonstrate that women with endometriosis do need attention and support. Endometriosis is a cause of social inequalities, as indicated by the results of this study, combined with other research reporting data about the economic burden of the disease (see the work of Soliman, for example). The study limitations should be reported, including the risk of self-selection bias (the women who chose to participate in the study may have been those most affected by the condition and suffering from severe pelvic pain).

REVIEWER	Cromeens, Martha Grace University of North Carolina at Chapel Hill Graduate School, School of Nursing
REVIEW RETURNED	30-Jun-2021

GENERAL COMMENTS	Review for BMJ Open "The Impact of endometriosis on women's life decisions and goal attainment" Stacey A Missmer, Frank F Tu, Ahmed M Soliman, Stephanie E Chiuve, Sarah Cross, Samantha Eichner, Oscar Antunez Flores, Andrew W Horne, Beth Schneider, Sawsan As- Sanie Comments to the authors: The authors describe a study into the impact of endometriosis on life decisions and goal attainment across the life course. The authors highlight the lack of research focused on the influence of endometriosis on goal attainment in work and education. The work in this submission contributes to a gap in endometriosis research. The authors present a descriptive quantitative study of a cross-sectional survey. The manuscript is well written and includes helpful supplementary materials. The following points are recommendations, observations, or questions for the authors: 1. Abstract: The methods only describe the survey, recruitment, and inclusion criteria, but does mention the analysis, sub-analysis, subsample, or any other helpful information.

	2. Abstract: the results do not mention results for the LPAF or NRFP groups. 3. Background (P. 7, Ln 43-52): The purpose of providing the examples in the fourth paragraph of the Background is not clear. Aren’t the examples provided elements of a multidisciplinary team treating endometriosis (per the citation) regardless of further understanding of the burden and impact of endometriosis across the life course. 4. Background (P. 7, Ln 54): Why is infertility singled out in the last sentence of the fourth paragraph versus any other endometriosis symptom? 5. Background: The article references the life course (e.g., “Life-course impairment”) but this term/concept was not defined or explained. 6. Background/Purpose: There is no background that leads the reader to understand the rationale or foundation for analyzing and reporting the participants identifying as LPAF or NRFP separately. 7. Methods (P. 9, Ln 33): Please provide more information about the pilot—quantity and source of participants. 8. Survey Response and demographics: Please provide more information about the number of respondents who started the survey and respondents who were excluded. Also, more information is needed about sample size and descriptors of the subsamples of participants who identified as LPAF and NRFP. It would be ideal if these groups are reported in comparison to the larger sample on Table 1. 9. Sample/Table 1: a. Diversity of samples in endometriosis research is concerning, especially across race and ethnicity. Please report race/ethnicity of the participants if that data was collected. If not, the diversity and socioeconomic status of the sample should be addressed. b. The authors should address sampling bias. The sample appears to be highly educated with access to care and is sampled from an online support group/social network (potentially indicating resources). This appears to sample a narrow group in the population. This is particularly concerning in light of the results surrounding goal attainment in work and education. Those who might be most impacted by the symptom burden of endometriosis might not have been sampled, or those sampled might have resources to mitigate the burden (e.g., 46% reported missing work due to endometriosis, but that might be a privilege of an affluent sample). c. Why did the study exclude Puerto Rico (“United States (excluding Puerto Rico)”)? 10. Results: The study presents a sample across multiple countries. It would be helpful to see the survey results reported for participants from each country, especially considering goal attainment at work. 11. Overall: The value of performing a sub-analysis of those identifying as LPAF and NRFP is unclear. This aspect of the study needs to be fleshed out from the background through the methods, results, and discussion with more detail and explanation. More information is needed to better understand this sample (Table 1). Analysis comparing the LPAF and NRFP groups to the larger sample would be helpful.

VERSION 1 – AUTHOR RESPONSE

Response to Reviewers' Comments:
Reviewer 1: Dr. Federica Facchin, Catholic University of Milan: I really enjoyed reading such an interesting study on a timely and important topic: the impact of endometriosis on women's daily activities and major life decisions and goal attainment. Endometriosis is indeed a disabling condition, especially when symptomatic, and there is need for studies like this. The evidence provided by this body of research may help clarify the needs of the women affected by the condition and inform not only clinical practice, but also social policy development and implementation. The manuscript is clear and well written. I am pleased to share with the authors some comments and suggestions, I hope they will find them useful.

1. Introduction: The Introduction is informative and provides a clear rationale for conducting such a study. However, the final part of this section highlights the strengths of the study and its importance in the context of endometriosis research and clinical practice (pp. 7, lines 29-56). This material should be moved to the Discussion.

Author response: Thank you for your review. This paragraph has been moved to the Discussion.

1. Introduction: The authors may consider the possibility of including additional information to summarize the available evidence on women's subjective experience of endometriosis (the body of literature cited on p. 6, lines 45-49), especially focusing on the social impact of the condition. As reported by the authors, this body of literature is composed of studies with small sample sizes and qualitative designs. I would not consider the qualitative nature of a research as an intrinsic limitation. Qualitative studies are important to address new research questions informed by women's own words.

Author response: The summary of evidence on women's subjective experiences of endometriosis has been further described in the Introduction. The revised sentence now reads: "The few existing studies have small sample sizes or are qualitative, relying on informational interviews to ascertain the life-course impact of the disease, but highlight the substantial impacts that endometriosis can have on social activities, intimate relationships, education, work productivity, and psychological well-being."

1. Introduction: The data analyzed in the study were collected in 2018 (before the pandemic), but as a reader I would like to be informed about the challenges derived from the current scenario (see for example the work of Matthew Leonardi on endometriosis and Covid-19). In fact, I think the pandemic has been exacerbating pre-existing social inequalities, especially for women (not to mention those with a chronic disease).

Author response: Thank you for the suggestion. We have added a statement to the Introduction to describe recent challenges, which reads: "These issues have been further exacerbated by the COVID-19 pandemic, which has led to reduced access to medical care, delayed treatments, increased stress, and mandated self-isolation (Leonardi M, et al. Front Reprod Health. 2020;2; Leonardi M, et al. Hum Reprod Open. 2020;2020:hoaa028)."

1. Introduction: At the end of the Introduction, the research question should be further clarified (the current research question reported in the manuscript is quite vague).

Author response: The end of the Introduction section has been revised to clarify the study objectives and now reads: "The objective of this multinational survey was to gain a better understanding of patient perspectives on how endometriosis impacts their daily activities and identify how the disease may influence women's major life decisions and attainment of their goals. In addition, we sought to understand endometriosis-related life-course impacts specifically in women who reported low optimism or low goal attainment. Insights into a patient's complete experience with endometriosis are needed to develop and provide access to effective treatments to reduce the negative impacts of endometriosis on a woman's life course. Greater awareness of the potential negative life-course impacts of endometriosis is important for helping physicians to identify and understand patients' needs and improve the long-term management of endometriosis."

1. Methods, P. 9: "This portion of the survey was modelled after a validated instrument created to measure life-course impact of disease in patients with psoriasis": please, clarify. The two diseases are totally different, and the use of an instrument created in the context of psoriasis to assess the life-course impact of endometriosis sounds counterintuitive.

Author response: We chose to begin our endometriosis-focused survey development modelling from the instrument developed for patients with psoriasis, because it has been validated, used clinically, and published in the scientific literature. While psoriasis and endometriosis are physically very different diseases, they are both chronic diseases with excess psychological and psychosocial burden. Our focus was on the methodologic approach, and we therefore started from this validated tool that has been successfully implemented for a condition that has at least a portion of life course impacts similar to endometriosis.

1. Methods: Given that an online survey was conducted, what platform/software was used (e.g., Qualtrics, Survey Monkey…)?

Author response: The online survey was created by MyHealthTeams, a company that creates social networks for communities of individuals living with chronic conditions to foster discussion and provide support among people facing similar circumstances, in collaboration with AbbVie. The survey was programmed and administered through Qualtrics and posted on the social media network website MyEndometriosisTeam.com. The Methods section has been revised to clarify how the survey was conducted and now reads: "The survey was programmed and administered through Qualtrics, an online survey tool that allows users to capture survey responses in an anonymized manner. The survey was provided in English and available online on the social media network website MyEndometriosisTeam.com from October 3 through October 25, 2018." and "Invitations posted on the public Facebook page for MyEndometriosisTeam recruited additional women to participate in the survey, which was live on the MyEndometriosisTeam.com website from October 3 to October 25, 2018."

1. Methods: The questionnaire was available from October 3 to October 25. Were specific criteria used to decide when to stop data collection, such as a minimum number of participants?

Author response: The first survey invitation was sent out to all members who met the survey qualifications. A reminder email was sent out to members who did not open the first email two weeks after the initial send. The survey was left open for an additional week to allow the last few responses to come in. This approach balances getting a robust sample with creating a good experience for members of our social networks, including MyEndometriosisTeam, and has been our standard practice.

1. Statistical analyses: the authors should clarify how missing data were treated. Missing data are very common in online surveys.

Author response: Responses were required for all closed-ended questions; therefore, no imputations for missing data were required. We have added this information to the paragraph on survey development in the Methods section.

1. Results: Sometimes the information reported is too general. For instance: "most women", "many women" … without number and percentages. Considering that the whole data analysis strategy is based on descriptive statistics, the authors should always report the exact number of participants (including percentages).

Author response: Thank you for the suggestion. We have added the numbers and percentages to the Abstract and Results sections.

1. Results: The authors performed additional analyses to examine the characteristics of women who believed their future and life potential were negatively impacted by endometriosis. That is interesting, but it would have been even more interesting to see the findings of a systematic comparison between this group and the group of women who did not feel their life was impacted by the disease. I think it would be useful not only to understand women's

endometriosis-related difficulties, but also their resources: why do some women perceive their lives as more impacted by endometriosis than other women? Do the authors have any ideas based on their findings?

Author response: Thank you for the suggestion. We agree that this is an important question and are planning a future publication to focus on this topic.

1. Results: Moreover, in this section the authors reported that – for instance – “Overall, women who believed they were LPAF or had NRFP reported more negative experiences compared with the fewer respondents who did not indicate they were LPAF (non-LPAF, 21%; n=154) or had NRFP (non-NRFP, 25%; n=187)”. These are descriptive data. Without a statistical test (e.g., chi square) and a level of significance (P value), the information reported regarding each dimension (for instance, that one group had more negative experiences than the other group) is a speculation derived from a mere observation.

Author response: Thank you for your feedback. We have added text to the limitations section to clarify that these are observational findings only and hypothesis testing was not an aim of the study and was not conducted. To clarify that this statement refers to results from this study and is not meant to generalize that all women who believe they are LPAF or have NRFP have more negative experiences than those who do not, this sentence has been revised to read: “Overall, the observational data in this study suggested women who believed they were LPAF or had NRFP generally reported more negative experiences than the fewer respondents who did not indicate they were LPAF (non-LPAF, 21%; n=154) or had NRFP (non-NRFP, 25%; n=187).”

1. Discussion: In this section, the authors should clarify what endometriosis-related factors – besides pain symptoms – are associated with a greater perceived negative impact of the disease on women’s life course in terms of choices and self-fulfillment. The fact that women cannot follow their career preferences due to endometriosis is terrible, and I think the authors should emphasize the importance of investigating this aspect and the pervasive impact it may have on women’s lives and psychological health, for instance with regards to self-esteem and depression.

Author response: We have revised the Discussion to explain endometriosis-related factors that were reported by women to have the most negative impacts on their life potential. The additional text reads: “In addition to pain, women reported that the endometriosis-related experiences that most impacted their lives in a negative way included depression or anxiety (80%), heavy menstrual bleeding (71%), the need to take prescription treatments (57%) or undergo multiple surgeries (49%), or infertility (46%). In other studies, women have reported not feeling “normal” or feminine, experiencing a range of negative emotions (eg, anger, depression, hopelessness, disappointment, and exhaustion), having limited physical or sexual activity, struggling to find appropriate treatments, feeling guilt over disrupted relationships, and suffering in silence due to endometriosis-related symptoms (Cole JM, et al. Feminism & Psychology. 2021;31:171–91; Moradi M, et al. BMC Womens Health. 2014;14:123.”

1. Discussion: Please, expand the discussion of the wider implications of this study findings in terms of suggestions for future research and clinical practice. Moreover, and equally important: how could these findings inform the development and implementation of social policies? This type of study is very useful for all women with endometriosis, and especially for the important work of patient associations: the volunteers may present this body of evidence to politicians and authorities, to further demonstrate that women with endometriosis do need attention and support. Endometriosis is a cause of social inequalities, as indicated by the results of this study, combined with other research reporting data about the economic burden of the disease (see the work of Soliman, for example).

Author response: We have added a paragraph to the Discussion to explain the implications of our study’s findings for clinical practice. The revised paragraph reads: “Examining the cumulative life-course impact of endometriosis may influence a physician’s ability to understand a woman’s complete experience with the disease, help identify patients who are most vulnerable to its impacts, and inform options for management. A fuller understanding of the life-course impact of endometriosis may also elucidate patterns of patient needs and identify which forms of supportive multidisciplinary care are necessary, including the need for early referral to specialists and other professionals who provide complementary healthcare. These needs are likely to change over time, during the different phases of each patient's life. For example, teams that include gynecologists and pain specialists may help patients manage endometriosis-associated pain symptoms; reproductive endocrinologists may help manage infertility, if this occurs; sexual health counselors may collaborate with patients who have dyspareunia; and counselors/psychologists may assist with chronic stress and mental health issues. Physicians who are responsive to patients' individual needs and values can positively support overall quality of life in those patients whexperience infertility and other negative symptoms of endometriosis, such as chronic abdominal pain, dysmenorrhea, and dyspareunia. Endometriosis may also contribute to social inequalities; further research is needed to explore this topic and develop social policies to address these inequalities." This publication aims to increase awareness of the burden of endometriosis with evidence-based information, which is an important first step towards informing future social policies.

1. Discussion: The study limitations should be reported, including the risk of self-selection bias (the women who chose to participate in the study may have been those most affected by the condition and suffering from severe pelvic pain).

Author response: The risk of self-selection bias has been added to the "Strengths and limitations" section following the Abstract, and the study limitations have been added to the Discussion. The new paragraph reads: "Limitations of this study include the selection of participants from an online community with voluntary participation, no targeted sampling, and no way to calculate a response rate. The participants were generally well educated, had access to health care, and participated in an online social network. Data on race, ethnicity, or socioeconomic status were not collected. Patients who experienced the most significant psychosocial impacts of endometriosis or lacked the resources to access the online community may not have been represented in the sample population, whereas the patients who were most affected by severe pelvic pain may have been more likely to participate in the study. These factors may have led to self-selection bias; therefore, the results of this study may not be fully representative of the overall population of patients with endometriosis."

Reviewer 2: Ms. Martha Grace Cromeens, University of North Carolina at Chapel Hill Graduate School: The authors describe a study into the impact of endometriosis on life decisions and goal attainment across the life course. The authors highlight the lack of research focused on the influence of endometriosis on goal attainment in work and education. The work in this submission contributes to a gap in endometriosis research. The authors present a descriptive quantitative study of a cross-sectional survey. The manuscript is well written and includes helpful supplementary materials. The following points are recommendations, observations, or questions for the authors:

1. Abstract: The methods only describe the survey, recruitment, and inclusion criteria, but does mention the analysis, sub-analysis, subsample, or any other helpful information.

Author response: Thank you for your review. The Abstract has been revised to include more details on the methods and now reads: "Design: An anonymous online survey was distributed in October 2018 through the social media network MyEndometriosisTeam.com. Participants: Women aged 19 years and older living in several English-speaking countries who self-identified as having endometriosis. Outcome measures: Patients' perspectives on how endometriosis has affected their work, education, relationships, overall life decisions, and attainment of goals. Subanalyses were performed for women who identified as "less positive about the future" (LPAF) or "had not reached their full potential" (NRFP) due to endometriosis."

1. Abstract: the results do not mention results for the LPAF or NRFP groups.

Author response: We have added a statement to the Results section of the Abstract that reads: "Women who identified as LPAF or NRFP generally reported more negative experiences than those who were non-LPAF or non-NRFP."

1. Background (P. 7, Ln 43-52): The purpose of providing the examples in the fourth paragraph of the Background is not clear. Aren't the examples provided elements of a multidisciplinary team treating endometriosis (per the citation) regardless of further understanding of the burden and impact of endometriosis across the life course?

Author response: This paragraph has been moved to the Discussion section per Reviewer #1's comments, as it helps clarify the importance of physician awareness of the life-course impact of endometriosis and the importance of our study's findings in the context of clinical practice.

1. Background (P. 7, Ln 54): Why is infertility singled out in the last sentence of the fourth paragraph versus any other endometriosis symptom?

Author response: This paragraph has been moved to the discussion based on comments from Reviewer #1. The last sentence has been revised to include other endometriosis symptoms and now reads: "Physicians who are responsive to patients' individual needs and values can positively support overall quality of life in those patients who experience infertility and other negative symptoms of endometriosis, such as chronic abdominal pain, dysmenorrhoea, and dyspareunia."

1. Background: The article references the life course (e.g., "Life-course impairment") but this term/concept was not defined or explained.

Author response: The definition of life-course impairment has been clarified in the third paragraph of the Introduction. The revised sentence now reads: "In contrast, few studies have examined the impact of endometriosis on a woman's life course based on how symptoms and experiences resulting from the disease influence major life events and decisions (such as whether to pursue educational opportunities, choose a career path, establish intimate relationships, and plan for a family) and the overall ability of patients to attain their life goals".

1. Background/Purpose: There is no background that leads the reader to understand the rationale or foundation for analyzing and reporting the participants identifying as LPAF or NRFP separately.

Author response: These 2 attributes were included in the study to gauge the total negative impact of endometriosis on women's lives and not just the impact on specific aspects of life, such as employment, education, or relationships. For the bulk of the analysis, results are reported for all survey respondents, not just those who indicated that they were LPAF or NRFP.

1. Methods (P. 9, Ln 33): Please provide more information about the pilot—quantity and source of participants.

Author response: Thank you for your query. We have revised the wording here and removed the text about the pilot.

1. Survey Response and demographics: Please provide more information about the number of respondents who started the survey and respondents who were excluded. Also, more information is needed about sample size and descriptors of the subsamples of participants who identified as LPAF and NRFP. It would be ideal if these groups are reported in comparison to the larger sample on Table 1.

Author response: 942 respondents opened the survey, 900 of whom met the screening criteria. In total, 743 respondents completed the survey (82.5% completion rate). The breakdown of LPAF and NRFP was based on the percent of women who answered strongly agree/somewhat agree on 2 attributes: "how much do you agree or disagree that because of endometriosis you are less positive about the future" and 'how much do you agree or disagree that because of endometriosis you have not reached your full potential." The goal of asking these questions was to understand the total negative impact of endometriosis on women's lives. We have added baseline demographics for women who identified as LPAF or NRFP to Table 1.

1. Sample/Table 1: Diversity of samples in endometriosis research is concerning, especially across race and ethnicity. Please report race/ethnicity of the participants if that data was collected. If not, the diversity and socioeconomic status of the sample should be addressed.

Author response: Data on race, ethnicity, or socioeconomic status were not collected in this survey. This limitation has been added to the Discussion section.

1. Sample/Table 1: The authors should address sampling bias. The sample appears to be highly educated with access to care and is sampled from an online support group/social network (potentially indicating resources). This appears to sample a narrow group in the population. This is particularly concerning in light of the results surrounding goal attainment in work and education. Those who might be most impacted by the symptom burden of endometriosis might not have been sampled, or those sampled might have resources to mitigate the burden (e.g., 46% reported missing work due to endometriosis, but that might be a privilege of an affluent sample).

Author response: The risk of self-selection bias has been added to the "Strengths and limitations" section following the Abstract, and the study limitations have been added to the Discussion. The new paragraph reads: "Limitations of this study include the selection of participants from an online community with voluntary participation, no targeted sampling, and no way to calculate a response rate. The participants were generally well educated, had access to health care, and participated in an online social network. Data on race, ethnicity, or socioeconomic status were not collected. Patients who experienced the most significant psychosocial impacts of endometriosis or lacked the resources to access the online community may not have been represented in the sample population, whereas the patients who were most affected by severe pelvic pain may have been more likely to participate in the study. These factors may have led to self-selection bias; therefore, the results of this study may not be fully representative of the overall population of patients with endometriosis."

1. Sample/Table 1: Why did the study exclude Puerto Rico ("United States (excluding Puerto Rico)")?

Author response: Patients from Puerto Rico were separated from the United States population into the "other" category due to IRB exemption qualifications that were different for residents of Puerto Rico versus residents of the 50 states of the United States. This statement has been added to the footnote of Table 1.

1. Results: The study presents a sample across multiple countries. It would be helpful to see the survey results reported for participants from each country, especially considering goal attainment at work.

Author response: The majority of participants were from the United States, and an analysis of survey results by individual countries would be based on very small n's for some countries. We have performed a comparison of survey results for participants from the US vs non-US for the impact of endometriosis on education and employment, which demonstrates similar findings in the US compared with the rest of the world. These data have been added to the manuscript as Supporting Information Figure 1 and we have added a statement to the Results section which reads: "These findings were consistent among patients in the United States compared with the rest of the world (supporting information figure 1)."

1. Overall: The value of performing a sub-analysis of those identifying as LPAF and NRFP is unclear. This aspect of the study needs to be fleshed out from the background through the methods, results, and discussion with more detail and explanation. More information is needed to better understand this sample (Table 1). Analysis comparing the LPAF and NRFP groups to the larger sample would be helpful.

Author response: Analyses comparing the LPAF and NRFP responses to the overall study population are presented in Supporting Information Table 1. We have also revised the manuscript text to more clearly explain the rationale for performing a subanalysis of patients identifying as LPAF and NRFP. For example, the study objective, in the end of the background section, has been revised to read: "The objective of this multinational survey was to gain a better understanding of patient perspectives on how endometriosis impacts their daily activities and identify how the disease may influence women's major life decisions and attainment of their goals. In addition, we sought to understand endometriosis-related life-course impacts specifically in women who reported low optimism or low goal attainment."

Response to Editors' Comments:

1. In agreement with overlapping comments from the reviewers, the editors feel that the main limitation of the study is the selection of participants – because (i) patients were selected from among an online community (already a self-selecting population) and (ii) because participation was voluntary, with open participation and no targeted sampling or way to calculate a response rate, there is a second-phase of participant self-selection. Both of these will result in bias, making the population unrepresentative of overall population with endometriosis. To address this, the editors would like to request: (i) that this limitation is discussed explicitly in the abstract, "Strengths and limitations" section (after the abstract), and main text Discussion, including discussing *how* (see reviewer comments) this might have impacted the findings; (ii) that the authors focus less on the quantitative findings, given that the lack of representativeness makes these less meaningful, and focus more on the qualitative findings of the study; and (iii) ensure that appropriate caveats are mentioned for claims made with respect to the conclusions and interpretation of your findings (particularly any quantitative findings, but also with respect to the representatives/generalizability of the qualitative findings).

Author response: Thank you for your review. The risk of self-selection bias has been added to the "Strengths and limitations" section following the Abstract, and the study limitations have been added to the Discussion. The new paragraph reads: "Limitations of this study include the selection of participants from an online community with voluntary participation, no targeted sampling, and no way to calculate a response rate. The participants were generally well educated, had access to health care, and participatein an online social network. Data on race, ethnicity, or socioeconomic status were not collected. Patients who experienced the most significant psychosocial impacts of endometriosis or lacked the resources to access the online community may not have been represented in the sample population, whereas the patients who were most affected by severe pelvic pain may have been more likely to participate in the study. These factors may have led to self-selection bias; therefore, the results of this study may not be fully representative of the overall population of patients with endometriosis."

We included quantitative data based on the limited information in the published scientific literature related to the various negative impacts that endometriosis can have on a woman's life course, which is a gap in endometriosis research, as noted by Reviewer 2. We believe that these data are important because they can inform physicians about patient needs and inform future research and social policies. Additionally, we have added additional quantitative details to the Abstract and Results sections based on comment #9 from Reviewer 1. However, we understand that qualitative data may not be generalizable to all women with endometriosis due to the inherent limitations of survey data, and we have added this limitation to the Discussion section.

1. Please revise the title of your manuscript to include the research question, study design and setting. This is the preferred format of the journal. For the study design and setting, a possible description could be "a cross-sectional survey of members of an online patient community" (or similar). Please also ensure that the same study description terminology is used in the abstract and in the Methods section of the main text.

Author response: The title has been revised to: "The impact of endometriosis on women's life decisions and goal attainment measured in a cross-sectional survey of members of an online patient community". The Abstract has also been revised to reflect this description and now reads: "Design: An anonymous online survey was distributed in October 2018 through the social media network MyEndometriosisTeam.com. Participants: Women aged 19 years and older living in several English-speaking countries who self-identified as having endometriosis. Oucome measures: Patients' perspectives on how endometriosis has affected their work, education, relationships, overall life decisions, and attainment of goals. Subanalyses were performed for women who identified as "less positive about the future" (LPAF) or "had not reached their full potential" (NRFP) due to endometriosis." These descriptions are also used throughout the Methods section.

1. Please ensure that your abstract is formatted according to our Instructions for Authors (http://bmjopen.bmj.com/pages/authors/#research), including all relevant subheadings.

Author response: The abstract has been revised to include relevant subheadings.

1. Please revise the ‘Strengths and limitations’ section of your manuscript (after the abstract). This section should contain up to five short bullet points, no longer than one sentence each, that relate specifically to the methods. The results of the study should not be summarized here.

Author response: The “Strengths and limitations” section has been revised and now reads:

- “Strength: Quantitative survey with a meaningful sample size and sample population that spanned multiple countries
- Strength: Targeted research questions developed based on existing conversations on a social network platform
- Strength: Use of social network familiar to patients, facilitating honesty in responses to sensitive topics
- Limitation: Possible self-selection bias due to voluntary participation in an online community and no targeted sampling
- Limitation: Self-reported patient responses that were not confirmed by medical records or other complementary data”

1. Please ensure that you have fully described the methodological limitations of the study in the ‘Strengths and limitations’ section and (in greater detail) in the main text Discussion section.

Author response: The study limitations have been clarified in the “Strengths and limitations” section following the Abstract and further described in the Discussion. The new paragraph reads: “Limitations of this study include the selection of participants from an online community with voluntary participation, no targeted sampling, and no way to calculate a response rate. The participants were generally well educated, had access to health care, and participated in an online social network. Data on race, ethnicity, or socioeconomic status were not collected. Patients who experienced the most significant psychosocial impacts of endometriosis or lacked the resources to access the online community may not have been represented in the sample population, whereas the patients who were most affected by severe pelvic pain may have been more likely to participate in the study. These factors may have led to self-selection bias; therefore, the results of this study may not be fully representative of the overall population of patients with endometriosis.”

1. The information about informed consent is confusing – you state that informed consent was not obtained, but then you state that participants did consent to the survey. Was this just not ‘informed’ consent? Please amend to clarify. Please also clarify if the ethics approval also determined that informed consent would not be required.

Author response: The ethics approval section of the Methods has been revised for clarification and now reads “The Advarra Institutional Review Board (Columbia, MD, USA) reviewed the cross-sectional survey for participants in the United States and determined that informed consent was not required (exempt determination #Pro00029982, 26 September 2018). However, participants did consent to participate in a survey and email invitations were provided to people who opted to receive communications.”

1. Along with your revised manuscript, please include a copy of the STROBE checklist indicating the page/line numbers of your manuscript where the relevant information can be found (https://strobe-statement.org/index.php?id=strobe-home). Please ensure that you revise the manuscript wherever needed to ensure all STROBE reporting requirements are adhered to.

Author response: We have included the STROBE checklist with the relevant page and line numbers for each item.

VERSION 2 – REVIEW

REVIEWER	Facchin, Federica Catholic University of Milan, Psychology
REVIEW RETURNED	22-Oct-2021

GENERAL COMMENTS	I carefully examined the revised manuscript and the authors' responses to my comments. My concerns were fully addressed, and I am satisfied with the current version of the manuscript. At this point, I only have some minor comments: 1) The authors provided a satisfactory response to my question regarding the reasons for modelling a portion of the survey after a validated instrument focused on psoriasis. The explanation provided in the response letter makes sense and should be incorporated in the manuscript (p. 8). 2) P. 16, lines 9-11: is this sentence correct? 3) The Discussion section is very long, and I think it should be restructured to improve its organization and facilitate reading. For instance, strengths and limitations of the study should be reported at the end of the section, along with suggestions for future research and clinical practice. Please, consider organizing this material in specific subsections with their own titles. 4) Conclusions: there is no need to repeat the main findings of the study. Please, just provide a final key message.

REVIEWER	Cromeens, Martha Grace University of North Carolina at Chapel Hill Graduate School, School of Nursing
REVIEW RETURNED	03-Nov-2021

GENERAL COMMENTS	Review for BMJ Open "The Impact of endometriosis on women's life decisions and goal attainment" Stacey A Missmer, Frank F Tu, Ahmed M Soliman, Stephanie E Chiuve, Sarah Cross, Samantha Eichner, Oscar Antunez Flores, Andrew W Horne, Beth Schneider, Sawsan As- Sanie Comments to the authors: The authors describe a study of the impact of endometriosis on life decisions and goal attainment across the life course. The authors highlight the lack of research focused on the influence of endometriosis on goal attainment in work and education. The work in this submission contributes to a gap in endometriosis research. The authors present a descriptive quantitative study of a cross-sectional survey. The manuscript is well written and includes helpful supplementary materials. The authors made significant changes and improvements to the original manuscript. The following points are recommendations, observations, or questions for the authors: 1. Survey Development: The authors removed information about a pilot study to test the questionnaire. However, the survey was

	modeled after a life-course impact survey for patients with psoriasis. More information is needed about the development of the survey and validation. 2. Results and Discussion: The authors make statements of comparison (or giving the impression of comparison) between the LPAF and NRFP groups and the larger sample. These statements are problematic with descriptive statistics without further statistical analysis. 3. Overall: a. Though the authors provided some explanation about subanalysis for LPAF and NRFP in the Survey Analysis (“These two questions were selected for this subanalysis to focus on the life-course impact attributed to endometriosis as identified by those who reported low optimism or low goal attainment.”) more clarity is needed in the background and methods for why these groups were separately analyzed and the meaning. b. The phrase “life course impairment” is not explained or defined. It is a confusing statement. Is this according to the judgment of the researchers or the participants? Is this a phrase the authors created?

VERSION 2 – AUTHOR RESPONSE

Page 1 of 3

Response to Reviewers' Comments:

Reviewer 1: Dr. Federica Facchin, Catholic University of Milan: I carefully examined the revised manuscript and the authors’ responses to my comments. My concerns were fully addressed, and I am satisfied with the current version of the manuscript. At this point, I only have some minor comments:

1. The authors provided a satisfactory response to my question regarding the reasons for modeling a portion of the survey after a validated instrument focused on psoriasis. The explanation provided in the response letter makes sense and should be incorporated in the manuscript (p8).

Author response: Thank you for your review. This explanation has been incorporated into the Methods section, and the revised sentence on page 8 now reads: “This tool was used as a starting point for model development as it has been validated for another chronic disease with excess psychological and psychosocial burden, has been used clinically, and was published in the scientific literature.”

1. Page 16, lines 9-11: is this sentence correct? “A survey of women with endometriosis who self-reported pronounced symptoms also reported experiences that were perceived by them to negatively impact their views of the future and overall life potential.”

Author response: Yes, this sentence is correct; for clarity, the sentence has been revised as follows: “This survey found that women with endometriosis who self-reported pronounced symptoms reported experiences that negatively impacted their perspective of the future and overall life potential.”

1. The Discussion section is very long, and I think it should be restructured to improve its organization and facilitate reading. For instance, strengths and limitations of the study should

be reported at the end of the section, along with suggestions for future research and clinical practice. Please, consider organizing this material in specific subsections with their own titles.

Author response: Thank you for the suggestion. We have reorganized the Discussion into subsections, with strengths and limitations and future implications sections towards the end.

1. Conclusions: there is no need to repeat the main findings of the study. Please, just provide a final key message.

Author response: We have condensed the Conclusions section to a single sentence. The concluding sentence now reads: “Our international study of the impact of endometriosis on a woman’s life course helps provide a clearer understanding of her complete experience with the disease and shows that most women experience a high burden associated with endometriosis that affects overall life potential in many different ways.”

Reviewer 2: Ms. Martha Grace Cromeens, University of North Carolina at Chapel Hill Graduate School: The authors describe a study of the impact of endometriosis on life decisions and goal attainment across the life course. The authors highlight the lack of research focused on the influence of endometriosis on goal attainment in work and education. The work in this submission contributes to a gap in endometriosis research. The authors present a descriptive quantitative study of a cross-sectional survey. The manuscript is well written and includes helpful supplementary materials. The authors made significant changes and improvements to the original manuscript. The following points are recommendations, observations, or questions for the authors:

1. Survey development: The authors removed information about a pilot study to test the questionnaire. However, the survey was modeled after a life-course impact survey for patients with psoriasis. More information is needed about the development of the survey and validation.

Author response: Thank you for your review. Reviewer 1 also asked why a portion of the survey was developed using a validated instrument focused on psoriasis. In the previous response letter, we explained that we began our endometriosis-focused survey development modelling from the instrument developed for patients with psoriasis because it has been validated, used clinically, and published in the scientific literature. While psoriasis and endometriosis are physically quite different diseases, they are both chronic diseases with excess psychological and psychosocial burden. Our focus was on the methodologic approach, and we therefore started from this validated tool that has been successfully implemented for a condition that has at least a portion of life-course impacts similar to endometriosis. This explanation has been incorporated into the Methods section, and the revised sentence on page 8 now reads: “This tool was used as a starting point for model development as it has been validated for another chronic disease with excess psychological and psychosocial burden, has been used clinically, and was published in the scientific literature.”

1. Results and Discussion: the authors make statements of comparison (or giving the impression of comparison) between the LPAF or NRFP groups. These statements are problematic with descriptive statistics without further statistical analysis.

Author response: We have removed comparative statements between the LPAF and NRFP groups in the Results and Discussion sections. Additionally, we have added text to the limitations section of the Discussion as follows: “Any between-group comparisons are observational in nature and no definitive conclusions can be made in the absence of formal statistical analysis.”

1. Overall:

. Though the authors provided some explanation about subanalysis for LPAF and NRFP in the Survey Analysis ("These two questions were selected for this subanalysis to focus on the life-course impact attributed to endometriosis as identified by those who reported low optimism or low goal attainment"), more clarity is needed in the background and methods for why these groups were separately analyzed and the meaning.

Author response: The LPAF and NRFP subgroups were created to identify the survey respondents whose lives were most negatively impacted by endometriosis and understand the specific reasons why those respondents felt that way. This approach has been used in other studies that used Likert scales to measure disease burden. The rationale for performing this subanalysis is explained in the last paragraph of the Background section, which has been expanded as follows: "In addition, we sought to understand the endometriosis-related life-course impacts specifically in women who reported low optimism or low goal attainment by investigating the specific reasons for life-course impairment among the subset of women who felt their lives were most negatively impacted by endometriosis."

a. The phrase "life-course impairment" is not explained or defined. It is a confusing statement. Is this according to the judgement of the researchers or the participants? Is this a phrase that the authors created?

Author response: The term "life-course impairment" was first defined by Kimball et al in 2010 as "cumulative life-course impairment", a term to describe the impact of psoriasis on a person's ability to achieve their full life potential with respect to relationships, social activities, work, and psychological well-being. We have revised the third paragraph of the Background section to more clearly introduce and define this term; the revised sentence now reads: "In contrast, few studies have examined the impact of endometriosis on a woman's life course (ie, "life-course impairment") based on how symptoms and experiences resulting from the disease influence major life events and decisions (such as whether to pursue educational opportunities, choose a career path, establish intimate relationships, and plan for a family) and the overall ability of patients to attain their life goals (Bhatti Z, et al. J R Soc Med. 2011;104:241-50; Kimball AB, et al. J Eur Acad Dermatol Venereol. 2010;24:989-1004)."

In this analysis, life-course impairment was defined by the investigators as survey participants who reported low optimism or low goal attainment. We have added this definition to the survey analysis section in the Methods: "For this analysis, life-course impairment was defined as respondents who "somewhat agreed" or "strongly agreed" that endometriosis had negatively impacted their education, employment, relationships, social activities, and physical and emotional well-being."

VERSION 3 – REVIEW

REVIEWER	Facchin, Federica Catholic University of Milan, Psychology
REVIEW RETURNED	10-Feb-2022

GENERAL COMMENTS	The authors did a great job and made their manuscript more enjoyable and clear. The study reported in this paper provides useful evidence on an overlooked aspect of endometriosis, which remains an important cause of health and social inequalities.

REVIEWER	Cromeens, Martha Grace

	University of North Carolina at Chapel Hill Graduate School, School of Nursing
REVIEW RETURNED	19-Feb-2022

GENERAL COMMENTS	The authors describe a study into the impact of endometriosis on life decisions and goal attainment across the life course. The authors highlight the lack of research focused on the influence of endometriosis on goal attainment in work and education. The work in this submission contributes to a gap in endometriosis research. The authors present a descriptive quantitative study of a cross-sectional survey. The manuscript is well written and includes helpful supplementary materials.

VERSION 3 – AUTHOR RESPONSE

Reviewer 1: Dr. Federica Facchin, Catholic University of Milan: The authors did a great job and made their manuscript more enjoyable and clear. The study reported in this paper provides useful evidence on an overlooked aspect of endometriosis, which remains an important cause of health and social inequalities.

Author response: Thank you for your review and positive comments.

Reviewer 2: Ms. Martha Grace Cromeens, University of North Carolina at Chapel Hill Graduate School: The authors describe a study into the impact of endometriosis on life decisions and goal attainment across the life course. The authors highlight the lack of research focused on the influence of endometriosis on goal attainment in work and education. The work in this submission contributes toa gap in endometriosis research. The authors present a descriptive quantitative study of a cross-sectional survey. The manuscript is well written and includes helpful supplementary materials.

Author response: Thank you for your review and positive feedback.