PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	QUALITY OF LIFE IN THE LIMELIGHT: A STUDY PROTOCOL OF A SWEDISH REGISTER-BASED COHORT STUDY ON QUALITY OF LIFE AFTER AN INJURY
AUTHORS	Hasselberg, Marie; Rissanen, Ritva

VERSION 1 - REVIEW

REVIEWER	Lovstad, Marianne Norway Sunnaas Rehabilitation Hospital, University of Oslo, Norway
REVIEW RETURNED	11-May-2019

GENERAL COMMENTS	This study protocol described a very interesting prospective register-based study on QoL before and after injuries. I have some minor comments: Abstract: Study description is not clear. What kind of injuries are the authors talking about? What kind of register is it they use? What exactly allows the study to do prospective analysis? Do they have data regarding injuries occurring after inclusion? Introduction: it is stated that improved acute trauma care has resulted in more very severe injuries surviving. This is often stated, but is it a fact? Can the authors show references to e.g. increased survival rates after the most severe injuries? In a study like this, one would also expect that they would predominantly acquire knowledge regarding less severe injuries? It is repeatedly mentioned in the methods section that the study will establish reports of having sustained an injury. The authors should describe this specific item in detail: exactly how is this question phrased? Is it a question of any minimal injury, with or without need of medical attention? Is it injuries that demand hospitalization? Is it only physical/somatic injury? Do they ask for any detailed description of the kind of injury? (mechaims, body parts ect), or kind of treatment received? Also, should be more specific on how pain and insomnia is recorded; numeric rating scales? standardized measures? Mean values over a period of time? Do the authors expect all injuries reported subjectively to be potentially accessible in the patient National Patient register? The data analysis section only mentions SEM and regression analysis, but does not describe all statistical methods planned used. Please extend. There is no power analysis. Where does the

	estimation of 3000 participants come from? Has the register already been searched for the injury variable? If so, please note so. Also, how many do the authors expect will not consent to the online follow-up questionnaire? Psychological consequences of injury is measured by using antidepressant use as a proxy. You will obviously have a lot of injured people showing emotional consequences of an injury who are not on antidepressants. Does a registry with 55 000 participants have no other measures of emotional functioning that can be applied?

REVIEWER	Jocelyn Bowden Post-doctoral Research Fellow University of Sydney, Australia
REVIEW RETURNED	19-May-2019

GENERAL COMMENTS	Dear Study Authors Thank you for the opportunity to read your manuscript. You have presented the protocol for a cohort study examining the changes in quality of life (QoL) of individuals in the Swedish Life-Gene registry who have sustained an injury. Overall I think this is a great opportunity to look at the QoL pre-post injury, and a nice concept for a study. However, at present there is insufficient detail provided on many aspects of the study that are generally required for publication of a protocol paper. The SPIRIT Guidelines for reporting protocols, and the introduction and methods sections of the STROBE guidelines for cohort studies should be used as a basis for your manuscript. Your manuscript as it currently stands does not seem to have all the details required. I have included some specific comments below for consideration, however I suggest you revise your manuscript in accordance with these documents to allow readers to fully understand your study. Major comments 1. You do not seem to have provided a definition of an “injury”, or if there is any timeframe that the injuries have occurred in. The term injury is very broad, and could cover all injuries or a subset (i.e. from a transport accident, sport related etc). Could you please provide a definition of an “injury” for the purposes of this study, and discuss if there are any specific timeframes involved (e.g. any injury after the baseline assessment, only those within 5 years etc). 2. The STROBE guidelines for reporting cohort studies ask you to provide details of the assessment measures to be used, including a description of the measure, if it has been used on this cohort before, why you are using it, the measurement time points of the measure, scoring details, and endpoints etc. Could you please include more details around your measures, and please: a. Please spell out EQ5D at its first use and provide details of what it is. b. Please describe the “ThenTest” questionnaire in more detail. 3. Even though this is a protocol, a flow diagram or schematic of proposed recruitment, timepoints of assessments, and analysis

	steps etc would help the reader. (See both sets of guidelines). Also how are the data linkages related to the other timepoints? 4. Some more details on your expected population (those in the registry) would be useful to the reader. At present the parameters of the prospective cohort are very vague. 5. P9 line 12 – you have stated that variables in the analysis are selected based on their predictive value as reported by previous studies. What are these previous studies? Please reference these. 6. Marriage (or being in a long term relationship) is often considered a protective factor in QoL and mood studies. Are you including this as a confounder or moderator in your analysis? 7. Consents for data linkages. Do you need consent from the dataset owners to have all these data linkages in Sweden? Can you please describe if you needed to undertake a separate approval process for the linkages, or it this is automatic under Swedish law. 8. Data analysis: Will missing data be a problem? Please describe how you will deal with missing data, or if you are only collecting data from people with full datasets. Administrative information (See SPIRIT Guidelines) 9. Please include the following information if applicable. What is approved protocol version? Please state if you registered your protocol, and if so the registry number, name and WHO Trial registration. 10. Please give some details around the sponsor of the trial, and the proposed roles and responsibilities of the protocol contributors (or other contributors) with regards to conducting the actual trial? E.g. who is doing the data collection, analysis etc for trial. 11. Who is undertaking the data collection (retrieval) from the registry? Are they the same as the people doing the analysis (is anyone blinded)? Are the data de-identified or re-identifiable? What are your data management strategies? What are your planned dates for data retrieval from the different databases (e.g. July 2010 to July 2019)? Minor comments 12. You have been inconsistent in the spelling of LifeGene (Life-Gene), EQ5D, and other acronyms throughout the manuscript. You may wish to revise these. 13. Page 12 line14 Please spell it out “HRQoL”, I don’t believe you have used this acronym previously. 14. Reference 22 – Please provide a translation of this reference. It is currently only in Swedish.

	15. Reference 19 – I'm not sure what this is a reference to, or how to find it. Can you please add more details for this reference. Is it a website, report etc?

VERSION 1 – AUTHOR RESPONSE

Reviewer #1	
Abstract: Study description is not clear. What kind of injuries are the authors talking about? What kind of register is it they use? What exactly allows the study to do prospective analysis? Do they have data regarding injuries occurring after inclusion?	The abstract has been revised and details about the register and type of data has been added, p. 2.
Introduction: it is stated that improved acute trauma care has resulted in more very severe injuries surviving. This is often stated, but is it a fact? Can the authors show references to e.g. increased survival rates after the most severe injuries? In a study like this, one would also expect that they would predominantly acquire knowledge regarding less severe injuries?	We have changed the wording indicating that road safety measures had led to a higher rate of survival following injury. We do not have a reference for the increase survival of those with the most severe injuries, as this has not been stated in the manuscript. Only that survival has increased following injury, a reference for this statement has been added, p. 5. We agree with the reviewer that this study has the potential to acquire knowledge regarding the less severe injuries, which is also stated on p. 6 second paragraph and p. 14 second paragraph.
It is repeatedly mentioned in the methods section that the study will establish reports of having sustained an injury. The authors should describe this specific item in detail: exactly how is this question phrased? Is it a question of any minimal injury, with or without need of medical attention? Is it injuries that demand hospitalization? Is it only physical/somatic injury? Do they ask for any detailed description of the kind of injury? (mechaims, body parts ect), or kind of treatment received? Also, should be more specific on how pain and insomnia is recorded; numeric rating scales? standardized measures? Mean values over a period of time?	A description of the injury question and the pain and insomnia questions has been added to p. 8-9, subheading LifeGene data and Online questionnaire.

Do the authors expect all injuries reported subjectively to be potentially accessible in the patient National Patient register?	A statement has been added to the manuscript, p 10.
The data analysis section only mentions SEM and regression analysis, but does not describe all statistical methods planned used. Please extend.	The regression analysis to be used is defined as a step wise regression as stated on p. 11.
There is no power analysis.	Power analysis has been added to page 8.
Where does the estimation of 3000 participants come from? Has the register already been searched for the injury variable? If so, please note so.	Details about a preliminary search has been added to the manuscript, p.7.
Also, how many do the authors expect will not consent to the online follow-up questionnaire?	The expected participation rate has been included p. 8.
Psychological consequences of injury is measured by using antidepressant use as a proxy. You will obviously have a lot of injured people showing emotional consequences of an injury who are not on antidepressants. Does a registry with 55 000 participants have no other measures of emotional functioning that can be applied?	Thank you for your comment. There are several different variables that can be included in studies. For example, we are planning to include other variables that are included in the description on p. 8, under subheading LifeGene data.
Reviewer #2	
at present there is insufficient detail provided on many aspects of the study that are generally required for publication of a protocol paper. The SPIRIT Guidelines for reporting protocols, and the introduction and methods sections of the STROBE guidelines for cohort studies should be used as a basis for your manuscript. Your manuscript as it currently stands does not seem to have all the details required. I have included some specific comments below for consideration, however I suggest you revise your manuscript in accordance with these documents to allow readers to fully understand your study.	Thank you for this comment. We have tried to follow the available guidelines but as the study is register-based not all items are applicable. Please see below for revision of the manuscript.

You do not seem to have provided a definition of an “injury”, or if there is any timeframe that the injuries have occurred in. The term injury is very broad, and could cover all injuries or a subset (i.e. from a transport accident, sport related etc). Could you please provide a definition of an “injury” for the purposes of this study, and discuss if there are any specific timeframes involved (e.g. any injury after the baseline assessment, only those within 5 years etc).	The definition of injury and the timeframe has been added to the manuscript, p. 7.
The STROBE guidelines for reporting cohort studies ask you to provide details of the assessment measures to be used, including a description of the measure, if it has been used on this cohort before, why you are using it, the measurement time points of the measure, scoring details, and endpoints etc. Could you please include more details around your measures,	Manuscript has been revised accordingly, p. 9.
Please spell out EQ5D at its first use and provide details of what it is.	The manuscript has been revised accordingly.
Please describe the “ThenTest” questionnaire in more detail.	A description of the “Then-Test” has been added to the manuscript, p. 9.
Even though this is a protocol, a flow diagram or schematic of proposed recruitment, timepoints of assessments, and analysis steps etc would help the reader. (See both sets of guidelines). Also how are the data linkages related to the other timepoints?	Thank you for the suggestion. As this is a register-based cohort-study a flow chart will not provide additional information as the study population is based on the register information available and a complete-case analysis is undertaken, hence participants will not exit the study at different time point and reasons.
Some more details on your expected population (those in the registry) would be useful to the reader. At present the parameters of the prospective cohort are very vague.	Details of the LifeGene population has been added to the manuscript, .p 7.
P9 line 12 – you have stated that variables in the analysis are selected based on their predictive value as reported by previous studies. What are these previous studies? Please reference these	The manuscript has been revised accordingly, p. 11.
Marriage (or being in a long term relationship) is often considered a protective factor in QoL and mood studies. Are you including this as a confounder or moderator in your analysis?	Relationship status has been added to the cofounders in the analysis, p. 12.

Consents for data linkages. Do you need consent from the dataset owners to have all these data linkages in Sweden? Can you please describe if you needed to undertake a separate approval process for the linkages, or it this is automatic under Swedish law.	All national registers in Sweden are open for data linkage for research, based on an ethical approval with specific research questions and research plan. No separate approval process is needed.
Data analysis: Will missing data be a problem? Please describe how you will deal with missing data, or if you are only collecting data from people with full datasets.	The analysis included only complete-case analysis. A clarifying statement has been added to the manuscript p.8 and p. 11.
Please include the following information if applicable. What is approved protocol version? Please state if you registered your protocol, and if so the registry number, name and WHO Trial registration.	Not applicable.
Please give some details around the sponsor of the trial, and the proposed roles and responsibilities of the protocol contributors (or other contributors) with regards to conducting the actual trial? E.g. who is doing the data collection, analysis etc for trial.	Details regarding the funder's role has been added to the manuscript, p. 16.
Who is undertaking the data collection (retrieval) from the registry? Are they the same as the people doing the analysis (is anyone blinded)? Are the data de-identified or re-identifiable? What are your data management strategies? What are your planned dates for data retrieval from the different databases (e.g. July 2010 to July 2019)?	Details regarding the retrieval have been added to p. 11 and the timeline for the retrieval from data bases has been added to p. 7.
You have been inconsistent in the spelling of LifeGene (Life-Gene), EQ5D, and other acronyms throughout the manuscript. You may wish to revise these.	The manuscript has been revised accordingly.
Page 12 line14 Please spell it out "HRQoL", I don't believe you have used this acronym previously.	The wording of HRQoL has been changed to QoL.
Reference 22 – Please provide a translation of this reference. It is currently only in Swedish.	A translation of the title has been added to the reference.

Reference 19 – I'm not sure what this is a reference to, or how to find it. Can you please add more details for this reference. Is it a website, report etc?	The reference has been revised.

VERSION 2 – REVIEW

REVIEWER	Marianne Løvstad Sunnaas rehabilitation Hospital, University of Oslo
REVIEW RETURNED	16-Jul-2019

GENERAL COMMENTS	I am pleased to have been given the opportunity to read the revised version of this manuscript. I find that the authors have addressed the initial concerns, and recommend publication of this paper.