PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<u>see an example</u>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	The long-term psychological consequences of symptomatic
	pulmonary embolism: a qualitative study.
AUTHORS	Noble, Simon; Lewis, Rhian; Whithers, Jodie; Lewis, Sarah; Bennett,
	Paul

VERSION 1 - REVIEW

REVIEWER	Beth Waldron
	University of North Carolina at Chapel Hill
	Chapel Hill, North Carolina, United States
REVIEW RETURNED	21-Feb-2014

GENERAL COMMENTS	The psychological impact of VTE is an understudied, yet clinically important area. As a first examination of the subject, this qualitative study provides a much needed starting place for additional discussion and investigation into this area. While there are limitations in this study, they reflect that lack of previous adequate groundwork done in this field and are therefore understandable.
	The psychological themes uncovered in this study are fully consistent with anecdotal reports I receive from patients. VTE is a potentially life threatening condition and its psychological impact is evident. It is surprising so little past study has occurred.
	Regarding methods, it would be nice to know more about the demographics of the participants so as to provide additional context to themes so they can be expanded upon for future study. For example, was it the younger patients in the survey who were more likely to view PE as a life altering event than the older? A 20 year old female with a contraceptive associated VTE considering how the VTE experience may impact future decisions on pregnancy planning/prophylaxis, implications of a potential genetic thormbophilia, etc may experience a different psychological dynamic than a 70 year old male with a surgery associated VTE. Treatment was touched upon, but would be nice to know a little more so as to understand if those on long-term anticoagulation were more apt to be traumatized than those on short-term treatmentie is it the PE experience itself or the long-term treatment that causes anxiety/depression or perhaps a combination of both. Are those for whom a clear VTE trigger cannot be identified more apt to have anxiety, PTSD, than those with a clearly provoked VTE? Are those with a known thrombophilia more likely to experience additional psychological burden? Are those with severe post thrombotic complications more likely to have PTSD? There are many additional avenues for exploration and while it is beyond the scope of this study to report, providing a little more reporting of demographic profile might help guide which directions would be most productive
	for future researchers to explore.

In general, this is an excellent topic. Good approach of design for a qualitative study in an area for which there is little past work to build upon. The analysis is insightful and opens the door to an exploration of both clinical and peer support structure for patients with VTE. I
look forward to seeing this work made widely available and welcome
its contribution.

REVIEWER	Roland von Känel Bern University Hospital, Switzerland
REVIEW RETURNED	23-Feb-2014

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GENERAL COMMENTS	An interesting, well written and important qualitative study on the psychological impact of symptomatic pulmonary embolism – this clearly is an underexplored area in clinical research. My specific comments are as follows: 1) Strengths of this study, p. 3: I do not agree with the authors' statement that this is the first study to explore the psychological consequences of a common medical condition. Think for instance about the large fields of psychooncology and behavioral cardiology both reporting on PTSD attributable to these illnesses. 2) Introduction, p.4: Also, it is not true that no previous studies have investigated the impact of VTE on everyday life. Particularly, disease-specific and disease non-specific quality of life (including mental quality of life) have previously been assessed, although not with qualitative methods; cf. for instance: van Korlaar et al, Thromb Haemost 2003 &Thromb Res 2004; Kahn et al, J Thromb Haemost 2008; Lukas et al, Thromb Haemost 2009 3) Therefore, the authors may want to highlight the novelty of their study. It seems to me this is their qualitative assessment of PTSD symptomatology in VTE patients. 4) It would be interesting to learn whether previous qualitative studies on other life-threatening diseases yielded similar major themes. As there is no control group (with another disease), the observed major themes might only partially be specific for pulmonary embolism patients. 5) Results, p. 16: the finding that providing the patients with information (i.e., patient education) was perceived as positive should be emphasized in the Discussion: Education, as opposed to PTSD treatment, is something that could easily be provided by hematologists. 6) Discussion, p. 18: the study is the first to describe PTSD symptomatology in VTE patients, but in a strict sense, the authors did not make a formal clinical diagnosis of PTSD with a structured clinical interview.
	7) Minor: p. 6: should be "field", not "filed"; p. 15: sentence "This
	form of information gathering" is odd and should be rephrased.

REVIEWER	Marc Carrier
	Ottawa Hospital Research Institute
REVIEW RETURNED	27-Feb-2014

GENERAL COMMENTS	This is a qualitative review assessing the psychological
	consequences of experiencing PE. The study is novel, interesting
	and clinically important. Psychological consequences of coronary
	artery disease have been previously evaluated but this is the first

report assessing the consequence in patients with PE. The manuscript is well written. The methodology is rigorous and the Interpretative Phenomenological Analysis (IPA) is well known and validated. The limitations are well acknowledged. The manuscript
might be a interesting way to introduce and initiate this type of
research to the readers of BMJ open.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

Regarding methods, it would be nice to know more about the demographics of the participants so as to provide additional context to themes so they can be expanded upon for future study. Treatment was touched upon, but would be nice to know a little more so as to understand if those on long-term anticoagulation were more apt to be traumatized than those on short-term treatment--ie is it the PE experience itself or the long-term treatment that causes anxiety/depression or perhaps a combination of both. Are those for whom a clear VTE trigger cannot be identified more apt to have anxiety, PTSD, than those with a clearly provoked VTE?

We are grateful for the reviewer's constructive comments. We have expanded the discussion to expand upon the interesting issues raised. We have been wary of introducing too many other variables within the demographics summary since we knew the numbers would be too small to identify any associated factors. We feel it would be more important in this first paper to keep the demographics as they are and highlight issues that need to be considered in future studies (which are underway)

Are those with a known thrombophilia more likely to experience additional psychological burden? Are those with severe post thrombotic complications more likely to have PTSD? There are many additional avenues for exploration and while it is beyond the scope of this study to report, providing a little more reporting of demographic profile might help guide which directions would be most productive for future researchers to explore.

We agree there are many other avenues for exploration and hope to pursue these in the future.

Reviewer Name Roland von Känel

An interesting, well written and important qualitative study on the psychological impact of symptomatic pulmonary embolism - this clearly is an underexplored area in clinical research. My specific comments are as follows:

Strengths of this study, p. 3: I do not agree with the authors' statement that this is the first study to explore the psychological consequences of a common medical condition. Think for instance about the large fields of psychooncology and behavioral cardiology both reporting on PTSD attributable to these illnesses.

We agree with the reviewer and are grateful for this being pointed out. Fortunately this error was only occurred in the summary of strengths of the topic and the manuscript refers to the data on patients post myocardial infarction and breast cancer. We are happy to clarify the sentence by changing it to:

"This is the first time the psychological consequences of symptomatic pulmonary embolism have been explored."

Introduction, p.4: Also, it is not true that no previous studies have investigated the impact of VTE on everyday life. Particularly, disease-specific and disease non-specific quality of life (including mental quality of life) have previously been assessed, although not with qualitative methods; cf. for instance: van Korlaar et al, Thromb Haemost 2003 &Thromb Res 2004; Kahn et al, J Thromb Haemost 2008; Lukas et al, Thromb Haemost 2009

The original manuscript has referred to two of Kahn's papers including the one cited by the reviewer since they do make mention of psychological impact of venous thrombotic disease (not pulmonary embolism). We are familiar with the other references provided which use questionnaires to evaluate HRQoL. These too focused on long-term consequences of venous thrombosis (not pulmonary emboli) and the development of post thrombotic syndrome. For completeness we shall include them in the introduction with some clarifying sentences as follows.

"Whilst the physical consequences of VTE have been extensively reported, the possible impact of VTE on patients' psychological and emotional well-being has received little attention. Other common and potentially life-threatening conditions such as cancer and myocardial infarction have been researched extensively with clear evidence that such illnesses can result in significant psychological morbidity. To date, no studies have investigated the impact of VTE on everyday life."

"Whilst the physical consequences of VTE have been extensively reported, the possible impact of VTE on patients' psychological and emotional well-being has received less attention. Such work has involved the use of validated QoL tools and has focused on the chronic consequences of deep vein thrombosis and less so on pulmonary emboli(15-17). Other common and potentially life-threatening conditions such as cancer and myocardial infarction have been researched extensively with clear evidence that such illnesses can result in significant psychological morbidity. To date, no qualitative studies have investigated the impact of VTE on everyday life."

Therefore, the authors may want to highlight the novelty of their study. It seems to me this is their qualitative assessment of PTSD symptomatology in VTE patients.

Whilst this study has identified PTSD as a consequence of pulmonary emboli, the aim of the study was to explore the psychological impact of symptomatic PEs overall. The high association with PTSD was an interesting conclusion but not the primary aim of the study.

We would therefore respectfully request to leave the focus of the study and how we present it as per the original protocol and methods.

It would be interesting to learn whether previous qualitative studies on other life-threatening diseases yielded similar major themes. As there is no control group (with another disease), the observed major themes might only partially be specific for pulmonary embolism patients.

We agree with the reviewer's observations and would hope future research may answer this interesting observation.

Results, p. 16: the finding that providing the patients with information (i.e., patient education) was perceived as positive should be emphasized in the Discussion: Education, as opposed to PTSD treatment, is something that could easily be provided by hematologists.

We have expanded the final paragraph accordingly, which now reads:

"Finally this study highlights several areas of opportunity for healthcare professionals to deliver support to patients post VTE. Participants reported the need for support, be it through information

giving, empathy or identifying psychological distress early on. Several of these needs particularly information giving could easily be provided by members of the multiprofessional team. Further research in underway to explore whether the introduction of a simple cost effective intervention may reduce the development of long-term psychological distress and the ongoing challenges it brings."

Discussion, p. 18: the study is the first to describe PTSD symptomatology in VTE patients, but in a strict sense, the authors did not make a formal clinical diagnosis of PTSD with a structured clinical interview.

We have rephrased the sentence as follows "the study is the first to describe symptomatology suggestive of PTSD in VTE patients"

Minor: p. 6: should be "field", not "filed";

This has been corrected

p. 15: sentence "This form of information gathering." is odd and should be rephrased. This has been rephrased