PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	An international qualitative study exploring patients' experiences of cutaneous leishmaniasis: Study set-up and protocol
AUTHORS	Erber, Astrid; Arana, Byron; Bennis, Issam; Ben Salah, Afif; Boukthir, Aicha; Castro Noriega, Maria del Mar; Cissé, Mamoudou; Cota, Gláucia; Handjani, Farhad; Kebede, Mairie Guizaw; Lang, Trudie; López Carvajal, Liliana; Marsh, Kevin; Martinez Medina, Dalila; Plugge, Emma; Olliaro, Piero

VERSION 1 – REVIEW

REVIEWER	Luigi Gradoni Istituto Superiore di Sanità, Roma, Italy
REVIEW RETURNED	04-Feb-2018

GENERAL COMMENTS	Major comments This ms consists of a well-written description of the set-up of a collaborative study and protocol, without providing verification of its performance by a preliminary pilot study. It is up to the BMJ Open's Editor to decide about suitability for publication of a protocol. P10 L.36 "We planned for ten interviews in each of the eight sites. The sample size was determined by the available resources": in the face of over one million cases of CL estimated to occur each year globally, two funding institutions involved, and the complex and costly organization of the study implementation described in P7, I find it incredible that only 10 interviews by country/endemic site have been planned. Minor comments P4 L31: non-specialist readers might be curious to know what the other 2 forms are. Specialist readers might be interested to know why MCL was not considered along with CL in this study (since the mucosal sequelae appear after typical CL manifestations), and why PKDL has been ignored in this protocol. P6 L11: [3,6] is repeated twice P6 L20: "Domecq et al noted"

REVIEWER	Julio Heras-Mosteiro University of King Juan Carlos, Spain
REVIEW RETURNED	17-Mar-2018

GENERAL COMMENTS	- I think this protocol is pertinent and really important. There is a lack of evidence in patients' view in Leishmaniasis and this work would be a relevant work both for researchers and patients. - Nevertheless, I have some comments regarding to the methodological section: 1.- I consider researchers could introduce any participant with the experience of Leishmanisis in children (i.e a mother which is also a patient and takes care of a child with leishmania). This would be very interesting. 2.- I am the opinion that the interviews should be conducted preferabily outside the healthcare facility, optimally in the patient's home. This scenary would be more neutral for the interviews. 3.- I have one big concern about the data analysis. In the paper authors anticipated it when they named the contextual and cultural connotations or colloquial expressions. I do not agree with the solution that the researchers described. This transcultural research is really interesting but the perception of illness or quality of life (aim of the study) is undoubtfully mediated by cultural factors and it is risky trying to mix all this cultural experiences. How would the research afford this huge heterogenety in a sole new paper? 4.- The strategy of analysis for objective 2 is not clear: will the trained researcher coordinate a bigger team or he/she will refine the analyses? 5.- Authors must describe as limitation of the study that "researchers will not have witnessed any of the interviews" because, as they write, this is not usual in qualitative research.

VERSION 1 – AUTHOR RESPONSE

Reviewers' Reports:

Reviewer: 1
Reviewer Name: Luigi Gradoni
Institution and Country: Istituto Superiore di Sanità, Roma, Italy
Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below
Major comments

This ms consists of a well-written description of the set-up of a collaborative study and protocol, without providing verification of its performance by a preliminary pilot study. It is up to the BMJ Open’s Editor to decide about suitability for publication of a protocol.

P10 L.36 “We planned for ten interviews in each of the eight sites. The sample size was determined by the available resources”: in the face of over one million cases of CL estimated to occur each year globally, two funding institutions involved, and the complex and costly organization of the study implementation described in P7, I find it incredible that only 10 interviews by country/endemic site have been planned.

Within the scope of this study and the time and resources available, this sample size was deemed realistic by the team. This information has been added:
'The sample size of 80 patients for the entire study was determined by the available resources and the given timeframe, in the light of the expected complexity of analysis, in particular with regards to the different languages and cultural contexts.' (p. 9)

Minor comments

P4 L31: non-specialist readers might be curious to know what the other 2 forms are. Specialist readers might be interested to know why MCL was not considered along with CL in this study (since the mucosal sequelae appear after typical CL manifestations), and why PKDL has been ignored in this protocol.

Thank you for pointing this out! This additional information has been incorporated into the introduction for clarification, and an explanation as to why MCL and PKDL had to be excluded has been added: 'Cutaneous leishmaniasis (CL) is the most common of the forms of diseases caused by protozoan parasites belonging to the genus Leishmania, which include also visceral leishmaniasis (VL) or kala-azar (with post-kala azar dermal leishmaniasis (PKDL)) and muco-cutaneous leishmaniasis (MCL).' (p.4)

'We aim at the majority of interviewed patients reflecting a clinical trial population, since the study focusses on informing clinical trial and product design. Patients with severe comorbidities, MCL or PKDL are excluded.' (p.10)

P6 L11: [3,6] is repeated twice

One instance has been removed, and references have been updated.

P6 L20: “Domecq et al noted”

Thank you for picking this up.

Reviewer: 2
Reviewer Name: Julio Heras-Mosteiro
Institution and Country: University of King Juan Carlos, Spain
Competing Interests: None declared

- I think this protocol is pertinent and really important. There is a lack of evidence in patients' view in Leishmaniasis and this work would be a relevant work both for researchers and patients.
- Nevertheless, I have some comments regarding to the methodological section:
1.- I consider researchers could introduce any participant with the experience of Leishmanisis in children (i.e a mother which is also a patient and takes care of a child with leishmania). This would be very interesting.

We agree that this would be interesting, and several patients who as parents talk about their children who have CL have been interviewed are included, and detailed in the manuscript:
'The study will however include the perspectives of some children with CL as told by their parents, when being interviewed about their own disease experiences.' (p. 10)

2.- I am the opinion that the interviews should be conducted preferably outside the healthcare facility, optimally in the patient's home. This scenary would be more neutral for the interviews.

Thank you, this was also deemed a challenge during discussions, where the local PIs pointed out that family members could potentially disturb the interviews, and prevent the patient being interviewed from speaking freely. If this is anticipated, the interview will take place in the healthcare facility. An explanation has been added to the manuscript:

'The setting will be chosen balancing its neutrality with giving the patients the opportunity to speak freely and comfortably about sensitive topics without disturbances by e.g. family members.' (p. 10)

3.- I have one big concern about the data analysis. In the paper authors anticipated it when they named the contextual and cultural connotations or colloquial expressions. I do not agree with the solution that the researchers described. This transcultural research is really interesting but the perception of illness or quality of life (aim of the study) is undoubtfully mediated by cultural factors and it is risky trying to mix all this cultural experiences. How would the research afford this huge heterogenety in a sole new paper?

Thank you for highlighting this important challenge in our research. We agree that perceptions of illness and health are culturally mediated. Data from individuals in each country will be analysed separately. We will then look for commonalities across countries but also differences between countries. We will carefully document these and ensure they are fully reported with appropriate illustrative quotes. We will therefore capture the (possibly considerable) heterogeneity but we will not lose themes that are shared across these diverse countries and cultures. In particular with regards to QoL-related outcomes, great heterogeneity is anticipated. Our approach will use an established and internationally validated outcome measurement instrument (e.g. the Dermatology Life Quality Index (DLQI)) in combination with research approaches for linking outcome measures to established instruments (e.g. the International Classification of Functioning, Disability and Health (ICF) Linking Rules). This approach has been added on p. 11f in the manuscript:

'In particular with regards to QoL-related outcomes, great heterogeneity corresponding to the cultural context is anticipated. For analysis we plan to use an established and internationally validated outcome measurement instrument such as the Dermatology Life Quality Index (DLQI) [36,37] as a frame of reference in combination with research approaches for linking outcome measures to established instruments, e.g. the International Classification of Functioning, Disability and Health (ICF) Linking Rules [38].' (p. 11)

4.- The strategy of analysis for objective 2 is not clear: will the trained researcher coordinate a bigger team or he/she will refine the analyses?

Thank you for pointing this out. The workflow has now been clarified to indicate how both, the trained and the experienced researcher, collaborate for analysis of the interviews:
'Analysis of the pooled interviews for objective (2) will be done centrally by a trained researcher, to ensure consistency of analysis across all sites, with feedback from the PIs. An experienced qualitative researcher will provide supervision, and, in order to ensure data quality, methodological consistency and transparency, will analyse around 20% of the interview transcripts in parallel. Discrepancies will be resolved by discussion.' (p. 11)

5.- Authors must describe as limitation of the study that "researchers will not have witnessed any of the interviews" because, as they write, this is not usual in qualitative research.

This has been added as a separate point to the study limitations:
'Due to the multicentre nature of this study, the analysis of all interviews for outcomes and eligibility criteria will be conducted by two researchers who have not been involved in the interviews, which is unusual in qualitative research. However, feedback will be sought from the local PIs in order to validate the preliminary individual site results, and on the overall results.' (p. 4)

FORMATTING AMENDMENTS (if any)
Required amendments will be listed here; please include these changes in your revised version:
1. Supplementary File Format

- Please re-upload your supplementary files in PDF format.
They have been uploaded as .pdf.

Upon request by the Editorial Office, a sub-heading 'Patient and public involvement' has been added: 'Patients were not involved in the study design, recruitment and conduct, but their experiences and preferences will inform the development of the research questions for analysis as described in objective (3). A lay summary containing the main study results will be provided to the local PIs for dissemination to participants and their communities.' (p. 12)

Please note that, in addition, the following changes have been made:
- A secondary affiliation for the first author AE ('Authors and affiliations', p. 1) and one more source of funding (a doctoral fellowship held by the first author, 'Funding statement', p. 14) have been added.
- The subspecies designation 'V.' (Viannia) has been added to the relevant Leishmania species in Supplementary file 2, in order to be consistent with the main manuscript.
- References have been updated (articles that were in in press have been published since).
- All CL patients that have contributed so far were thanked in the Acknowledgements (p. 14).