CLINICAL PRACTICE ARTICLE

A Malawi guideline for research study participant remuneration

[version 1; referees: 2 approved with reservations]

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Abstract

Background: Research participant remuneration has been variable and inconsistent world-wide for many years owing to uncertainty regarding best practice and a lack of written guidelines for investigators and research ethics committees. Recent recommendations are that researchers and regulators should develop regionally appropriate written guidelines to define reasonable remuneration based on expense reimbursement, compensation for time and burden associated with participation. Incentives to motivate participation are acceptable in specific circumstances.

Methods: We wished to develop regionally informed, precise and applicable guidelines in Malawi that might also be generally useful for African researchers and review committees. We therefore reviewed the current literature and developed widely applicable and specific remuneration tables using acceptable and evidence-based payment rationales.

Results: There were good international guidelines and limited published regional guidelines. There were published examples of best practice and sufficient material to suggest a structured remuneration table. The rationale and method for the table were discussed at an inter-disciplinary workshop resulting in a reimbursement and compensation model with fixed rates. Payment is recommended pro rata and equally across a study.

Conclusions: Transparent, fair remuneration of research participants is recommended by researchers and regulators in Malawi. The means to achieve this are now presented in the Malawi research participant remuneration table.

Keywords

Health research, remuneration, ethics, compensation, Malawi.
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Competing interests: Stephen Gordon: As a member of the research community in Malawi, I have an interest that best practice is followed and that was the motivation to organize the workshop. Having organised the workshop, I wanted the findings to be as widely available and discussed as possible.

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Introduction

Remuneration of participants in research by researchers is accepted practice\(^1\). Further, the lack of any remuneration, particularly when research is conducted among vulnerable populations, is considered potentially exploitative and hence unethical\(^2\). Regarding payments, clear statements from the Council for International Organisations of Medical Sciences (CIOMS)\(^3\) as well as country-specific regulators such as the Office for Human Research Protection (OHRRP) and the Federal Drug Administration (FDA) of the USA describe a code of practice where remuneration should not be sufficiently large to cause “coercion” or “undue influence” of participants\(^4\). Discussion of the means to determine appropriate remuneration in Africa without undue influence is the subject of this paper. There are currently no specific regional guidelines for Malawi.

Methods

Literature review

To inform this discussion, we carried out a broad literature review. Using the search terms “(volunteer or participant or patient) AND (remuneration or reimbursement or payment) AND (research)”, restricted to English published work in the period 1934–2018, we searched MEDLINE Complete, CINAHL Complete, Global Health and EBSCO host e-book collection. We found 24,605 hits and using the Relevance key, screened titles and brief summaries of the most relevant 200 hits. Then, we refined the search above by adding “AND (Africa)”. We found 424 hits and reviewed them all, citing only those specifically relevant to the discussion of research participant remuneration.

We produced a summary document to define the appropriate contexts in which remuneration might occur and then framed the parameters for a Malawi remuneration table. We discussed in detail the need for transparent guidelines such that researchers could use a framework, and regulators could evaluate the rationale underpinning researcher protocols for remuneration\(^1\).

Malawi remuneration table development

Using the acceptable parameters obtained from the literature review, we determined a range of values for each parameter and then developed tables of values for each parameter. We then determined, in a public discussion, if these value estimates seemed reasonable to a participant group of researchers and regulators. Finally, we stated current exchange rates to allow comparison in other settings and after exchange rate changes. In this way, we produced a table that can be used by researchers and regulators alike to determine appropriate remuneration values.

Results and discussion

Literature review

*The development of current international practice*. In 1998, research participant remuneration in the USA was shown to be inconsistent between different sites in multi-site studies, between studies at the same site and between procedures in the same study\(^5\). This inconsistency was caused by anxiety about inducement and a lack of written guidelines for researchers and Research Ethics Committees (REC; also known as Institutional Review Boards (IRB), but REC will be used in this paper). Several studies indicated, however, that researchers were generally in favour of reimbursement both in clinical trials\(^6\) and in the social sciences\(^7\). The fact that remuneration might bias increased recruitment from impoverished subjects was considered less of a problem than alternatives such as no remuneration, compulsory participation or means-tested remuneration\(^8\). Furthermore, studies indicate that payments did not cause volunteers to ignore risk\(^9\), and that remunerated research participants considered a complex variety of factors before participation\(^10\). Phase 1 trial participants, for example, were less likely to participate in trials of psychotropic drugs than other drug studies, and in trials with painful biopsy sampling compared to those with no pain involved\(^11\). Further, adolescent patients made good judgments, tending to be altruistic compared to their parents\(^12\). A study attempting to increase elderly patient participation in research showed that financial remuneration had little effect\(^13\). Motivating factors reported by research participants often include community benefit, the advancement of science, personal interest and seeking additional health professional contact\(^14\). A Viewpoint paper in the *Lancet* in 2005 concurred that good regulator boards (REC) were critical in determining risk benefit ratio in research, and were more important in ensuring ethical research than the nature or scale of participant benefits\(^15\). In modern day practice, the offer of payments to participate in studies causing harm (a definition of “coercion”) has been outlawed by the appropriate processes of REC\(^16\).

A 2018 framework to guide the ethical payment of research participants published in the *New England Journal of Medicine*\(^1\), consistent with CIOMS guidelines\(^1\), distinguished three rationales for remuneration which were:

- reimbursement of out-of-pocket expenses such as travel expenses,
- compensation for time lost at a rate approximately equal to unskilled labour, and
- some incentive to participation, calculated to improve the likelihood of study recruitment and completion\(^1\).

Current practice is therefore that a minimum reimbursement is almost always expected, calculated as reimbursement for expenses and compensation for time lost. The same guideline indicates that research participant remuneration should be prorated (paid per activity and not dependent on study completion), and clearly documented in both the REC protocol and patient information sheet. Recent detailed enquiry among investigators and REC Chairs in the USA, however, showed that only 19% of protocols included time-based compensation and only 12% of protocols included procedure-based estimation of burden\(^18\). Incentives in the form of study completion bonus (9% of protocols) or increased attendance allowance (10% of protocols) were seldom recorded. There was, however, good documentation of remuneration in the patient information sheet (94% of protocols) and this was usually prorated (73% protocols). Problems still remain, however, as early career researchers particularly struggle to define appropriate patient
involvement in research\textsuperscript{19}, and there is some evidence that payments are not adequate in some studies\textsuperscript{20}. We therefore concluded that transparent guidelines would be useful and applicable in Malawi, where the economic context of a low- or middle-income country (LMIC) drives particular concern about remuneration in research.

**The development of guidelines for remuneration in Africa.** The underlying principles for remuneration in LMIC are identical to those elsewhere, but there are contextual considerations including culture that must be included in planning remuneration\textsuperscript{11}, and a relative lack of literature to guide researchers. A recent review has concluded that there is an urgent need for basic descriptive work in India (Marathe, 2018) and the KEMRI Wellcome group in Kenya have worked for several years to define types of volunteer remuneration and good ethical practice in Africa\textsuperscript{22,23}. The KEMRI group have particularly pointed out that individual remuneration, including that offered to patients, is best served by financial compensation, but community recognition is best achieved with in-kind contributions to health facilities and community projects\textsuperscript{23}. Further, researchers should avoid the potential for remuneration to produce family discord. There is a need for transparency in patient information sheets\textsuperscript{24} and in actual practice\textsuperscript{26} but nevertheless, guidelines can be developed in complex situations, including among patients with malnutrition\textsuperscript{18}, and among people living with HIV/AIDS (PLWHA). Among PLWHA, research participant remuneration has even been shown to increase patient’s well-being and self-worth\textsuperscript{17} to the point where remuneration post-trial has been considered\textsuperscript{25}. It has been proposed that participant remuneration results in both individual and community good\textsuperscript{26}, and indeed that defining the remuneration only in terms of opportunity cost, matched to work, is to reduce the opportunity for community good.

In 2002 in South Africa, flat rates for research participation were suggested by the Medical Control Council but did not meet with community approval\textsuperscript{8,21}. The South African NHREC (2012) guidelines for “Payment of Trial Participants in South Africa: Ethical Considerations for REC” note that a recommendation for a flat rate was made at a time when NHREC was not formally constituted, and the guidelines suggest that participants should be compensated for time, inconvenience and expenses\textsuperscript{22}. A recent Malawi recommendation of minimum rates for reimbursement when subjects attend facilities for research led to some confusion among researchers and REC, requiring discussion to understand the nuance and exceptions stated in the recommendation. In a study where the actual amount of reimbursement was discussed in Kenya, zero payments were reimbursed in studies but the practical means to do this is clumsy as receipts are often not issued and the administrative duty to make specific payments are often delegated to clinic staff. Further, *ad hominem* payments do not provide a basis for planning grant budgets and so the Malawi tables are constructed using reasonable predictive data. Travel was determined in three bands of <5 km, 5–10 km, and 10–15 km using standard minibus fares, but we recommend that a single rate be paid in any one study based on the radius of recruitment. At the workshop, participants contributed examples in region where variable travel reimbursement has led to confusion and frustration in the community from whom participants are recruited therefore this was noted and a recommendation included in the resulting table (Table 1). Food was calculated using street restaurant food costs for mid-day meals and accommodation at rates charged by lodges with walled secure compounds. Overnight accommodation is very unusual in research studies, as is travel of more than 15 km.

**Compensation for time and burden.** Particularly in healthy volunteer studies involving a procedure, compensation for both time and the burden of the study are paid. In the Malawi tables,
Table 1. The Malawi research remuneration table.

<table>
<thead>
<tr>
<th>MALAWI RESEARCH PARTICIPANT REMUNERATION</th>
<th>Rate in MK</th>
<th>Number of events</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimburse Expenses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Transport</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Subsistence (one meal)</td>
<td>15000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Accommodation (one night)</td>
<td>15000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compensation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Time - see Note B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total time in hours travelling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total time in hours at facility</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time in days (day = 8hrs)</td>
<td>1000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Burden - see Note C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure A</td>
<td>2000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure B</td>
<td>6000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure C</td>
<td>10000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL for study - see Note D</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVERAGE per visit*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note A: Transport rates. Use the same for all participants in the study, based on furthest travel (5km = 300MK; 10km = 600MK; 15km = 900MK). Note B: Time. Use total time including travel, waiting, consultation, tests, waiting for results and treatment. Note C: Burden Categories. (A) mild discomfort: venesection <60ml, lung function testing, Xray = 2000MK. (B) Moderate discomfort: venesection >60ml, bone marrow, lumbar puncture = 6000MK. (C) Long or complex: bronchoscopy or GI endoscopy and biopsy/BAL = 10000MK. Note D: Minimum remuneration. Recommendation is that this should not be less than 7000 for studies attending facilities. *Divide Total by transport events (C3) to determine Average per visit (MK exchange rate at the time of writing 960 MK to 1 GBP; 700 MK to 1 USD).

the opportunity cost sustained by a volunteer has been calculated using the total time incurred in the study, to include travel to-and-from, waiting at the facility, direct involvement in the project and any time delayed after the process. Time used in completing follow-up diaries or on follow-up phone calls was also included. Time may be reimbursed as a time equivalent in minimum wage labour, but this may under-report the opportunity cost. We consider that the minimum wage provides a reasonable remuneration provided that time is adequately evaluated. In the case of patients receiving a treatment or diagnostic test of proven value that might be outside the normal service, this would not constitute a burden.

The burden of participations in a study, including discomfort, anxiety or embarrassment was included in three bands of procedure discomfort. Risk per se should be minimised by study design and was not specifically reimbursed (this constitutes coercion); we took the view that any harm sustained should be covered by insurance and not participant remuneration. There are examples of good practice regarding research participant’s discomfort burden in Malawi. For example, for bronchoscopy studies, a consultative exercise including participants, research team and health care providers determined participant remuneration. Subsequently, participant interviews determined that most participants were content with the remuneration offered, and that the remuneration was not the reason for participation.

In Kenya, reasons for participation included improve medical care, as published elsewhere. In a study requiring residential monitoring, participants cited saving for various projects (business, housing, school-fees) as a motivation to participate, and lack of family support as a disincentive.

Incentives to participation. In Malawi, there is currently no equivalent of The Over-volunteering Prevention System (TOPS) found in other centres. Studies must therefore screen carefully and avoid the problem of over-recruitment by participant enquiry. One survey of nasopharyngeal carriage, offering a bottle of Coca-Cola as remuneration, observed a problem of over-recruitment (volunteers attempting to participate twice) and had to re-structure consent and sampling processes.
Given that a risk of over-volunteering therefore already exists in Malawi, and that there is no surveillance system in place, caution is advised on offering incentives to participation.

In the tables, we noted that remuneration of participants should be pro-rated (in the sense of pro rata, in that completion is not necessary) because of fairness needed when participants are required to withdraw from a study (e.g. owing to side effects in a drug trial). Participants might fail to disclose adverse side effects if this would sustain a reimbursement penalty. Completion bonuses run a risk of participant coercion. Increased payments for repeat procedures that become tedious and burdensome were discussed as an option but there was no consensus of support for this approach.

Malawi remuneration tables
In order that the challenge of presenting clear, specific guidelines that would allow transparency in reviewing protocols at REC, the Malawi research remuneration tables were developed as shown in Table 1 and Table 2. Table 1 shows the table for calculation, with Table 2 completed for a simple study and Table 3 for a more complex study. Some degree of international comparison may be achieved using the dollar exchange rate provided. This does not, however, take any account of purchasing power or local wages therefore appropriate regional and international comparison will be made by replacing the values for round-trip travel (5, 10 and 15km) and for a day’s wages at the local minimum wage. A working example of the remuneration Table is given in Supplementary File 1.

Conclusion
International guidelines and current best practice both indicate that structured remuneration of research participants is ethical and appropriate in Malawi. From a review of the literature, we provide an underpinning rationale for remuneration based on reimbursement of expenses and compensation for time and burden, but not incentive to participate. We then provide specific tables to guide researchers and regulators in the amount

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**Table 2. Worked example for a simple study.** Volunteers attend for collection of a complex data set in which the process of travel and study completion takes 4 hours including a blood test. They re-attend for results on a second occasion taking one hour. This example using the Malawi table shows the remuneration for a participant who travelled 15km round trip (900MK), was provided lunch (1500MK) in a day that involved 6 hours of attendance and one large blood sample and was then followed up on a second visit which only required 2 hrs time in travel and at the facility (hence 8 hours total) and a small blood sample. Remuneration was MK12800. The US dollar exchange rate was 719 MK to the dollar.

<table>
<thead>
<tr>
<th>MALAWI RESEARCH PARTICIPANT REMUNERATION</th>
<th>Rate in MK</th>
<th>Number of events</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reimburse Expenses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Transport - see Note A</td>
<td>900</td>
<td>2</td>
<td>1800</td>
</tr>
<tr>
<td>b) Subsistence (one meal)</td>
<td>1500</td>
<td>1</td>
<td>1500</td>
</tr>
<tr>
<td>c) Accommodation (one night)</td>
<td>15000</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Compensation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Time - see Note B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total time in hours travelling</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total time in hours at facility</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time in days (day = 8hrs)</td>
<td>1000</td>
<td>1.5</td>
<td>1500</td>
</tr>
<tr>
<td>b) Burden - see Note C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure A</td>
<td>2000</td>
<td>1</td>
<td>2000</td>
</tr>
<tr>
<td>Procedure B</td>
<td>6000</td>
<td>1</td>
<td>6000</td>
</tr>
<tr>
<td>Procedure C</td>
<td>10000</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTAL for study - see Note D</strong></td>
<td></td>
<td></td>
<td>12800</td>
</tr>
<tr>
<td><strong>AVERAGE per visit</strong></td>
<td></td>
<td></td>
<td>6400</td>
</tr>
</tbody>
</table>
Table 3. Worked example for a complex study. Volunteers attend for collection of a complex data set 4 hours and a large blood test. They re-attend 6 further occasions taking one hour and a simple blood test each time. There are 2 additional visits for bronchoscopy (4 hours). This example shows the participant travelled 15km round trip, attended for 4 hrs and had a large blood test, then 6 follow-up visits and 2 visits for bronchoscopy resulting in a total study remuneration of MK 55100.

<table>
<thead>
<tr>
<th>MALAWI RESEARCH PARTICIPANT REMUNERATION</th>
<th>Rate in MK</th>
<th>Number of events</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimburse Expenses</td>
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<td></td>
</tr>
<tr>
<td>a) Transport - see Note A</td>
<td>900</td>
<td>9</td>
<td>8100</td>
</tr>
<tr>
<td>b) Subsistence (one meal)</td>
<td>1500</td>
<td>3</td>
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<td>c) Accommodation (one night)</td>
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</tr>
<tr>
<td>Compensation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Time - see Note B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total time in hours travelling</td>
<td></td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Total time in hours at facility</td>
<td></td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Time in days (day = 8hrs)</td>
<td>1000</td>
<td>4.5</td>
<td>4500</td>
</tr>
<tr>
<td>b) Burden - see Note C</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Procedure A</td>
<td>2000</td>
<td>6</td>
<td>12000</td>
</tr>
<tr>
<td>Procedure B</td>
<td>6000</td>
<td>1</td>
<td>6000</td>
</tr>
<tr>
<td>Procedure C</td>
<td>10000</td>
<td>2</td>
<td>20000</td>
</tr>
<tr>
<td>TOTAL for study - see Note D</td>
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<td></td>
<td>55100</td>
</tr>
<tr>
<td>AVERAGE per visit*</td>
<td></td>
<td></td>
<td>6122</td>
</tr>
</tbody>
</table>

to remunerate. We publish these in Wellcome Open Research in order that revised versions can be updated and available as required.

Data availability
All data underlying the results are available as part of the article and no additional source data are required.

Grant information
This study and the workshop was supported by the Wellcome Trust through the MLW Core grant (206545) and an Ethics Workshop Award.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Malawi Research Ethics Workshop 2018 participants
Delegates listed in alphabetical order, grouped by institution also in alphabetical order.

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Supplementary material

Supplementary File 1. Working examples of the remuneration tables shown in Tables 1–3.

Click here to access the data

References


This is a descriptive paper demonstrating the findings from a literature review on renumeration in research specifically targeted on papers from African settings as well as the findings from a research ethics workshop conducted in Malawi.

The paper is an important one as it brings up a discussion in relation to the need for clearer guidelines with regards to remuneration for research which is a particularly difficult subject in low income settings such as Malawi where there are often concerns about coercion. It opens up a discussion which is really important and provides a pragmatic approach to addressing it.

The results of the review were interesting but it was not always clear whether the results were specifically of those articles found from African settings or a mixture of articles that were found and felt to be relevant. There was not much critical appraisal of these articles but maybe not that necessary for this paper. It might have been helpful to have a list of those papers found from Africa in a supplementary file for those who would like to look into this in more detail.

The paper describes the guidelines for remuneration as having been developed mainly from a research ethics workshop conducted in Malawi. Although the list of authors is at the end of the paper, it might have been helpful to have a list of the professions of those persons to understand the backgrounds of those participating. There was no representation from lay persons and the group who were involved were very research-focussed as far as I can gather. It would be important to discuss this in the limitations and to think through how this might be moved forward in the future to ensure that the points of view of research participants, lay persons and communities are considered. It will be helpful to know what the cost is to families or single individuals and whether this varies by gender and profession. I agree that not enough reference is made to consider compensation for those who might be accompanying a minor or a person with major health issues who needs support. This needs to be discussed further or considered in future papers or research.

It is not clear what “burden” means and whether there again should be some future consideration of how this should be classified. Some studies may not take bloods but may do a number of complex investigations or tests which take a large amount of time and require the individual to be motivated and engaged. There was some discussion about the time factor taken but it was not clear to me as to how one would distinguish between someone who might be having a large amount of blood taken but not be there for very long vs someone who might be having complex hearing or vision testing or detailed neuromotor
examinations which might take hours to complete. Maybe this is something that is a limitation and which needs further discussion for future work.

This paper should however be indexed to widen the debate and to put something forward for discussion but with some of these limitations taken into account.

Is the background of the cases’ history and progression described in sufficient detail?
Yes
Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Partly
Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes
Is the conclusion balanced and justified on the basis of the findings?
Yes

Competing Interests: No competing interests were disclosed.

Referee Expertise: Neurodevelopmental paediatrics and International Child Health.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 12 Dec 2018

Stephen Gordon, Malawi Liverpool Wellcome Trust Programme of Clinical Tropical Research, Malawi

We thank Dr Gladstone for thoughtful and helpful comments made on the first version. We have improved the clarity and purpose of this paper by responding to all the points raised (more than 10) but in particular:
1. We thank Dr Gladstone for identifying the usefulness of this work.
2. We have clarified each point where clarification was requested including the composition of the workshop attendee list, decisions around remuneration of expenses (e.g. travelling companions).
3. We have discussed the group experience with working with research participants in this field. We did not have representation at the stakeholder workshop as the governance of remuneration was the focus rather than the financial amount. 6 publications of studies researching participant responses were cited, with authors from 3 of them present at the workshop.
4. We have not provided a list of papers cited/searched but we have checked the method described and found it to be robust on several platforms. We think that a current search is quick and easy and will generate hits in an up-to-date manner.
5. We thank Dr Gladstone for raising the point about neurocognitive and other fatigue burdens in research participation. The issue of “burden” is complex and study-specific. We think that the guideline table allows investigators to work with the concept of a range of burden in research, and to propose acceptable remuneration for discomfort, be it physical, mental or other.

Once again, we thank the reviewers and offer this much improved manuscript for indexing.

**Competing Interests:** No competing interests were disclosed.

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**Referee Report 22 November 2018**

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I am not able to answer the clinical practice article-specific questions because this paper does not fit neatly into this category (though it is not obvious where it would fit any better and one should not be deterred from accepting it on that ground alone).

This paper makes a useful addition to the literature. It publishes (for comment/benefit of others in the same position) a method (in the form of a table) of making a transparent calculation of reimbursement for research participants in Malawi. This takes into account immediate out of pocket expenses (such a travel and subsistence), time taken to participate – including travel time (opportunity costs to the participant, calculated on the basis of the minimum wage) and recompense for burden (using three categories with different sums according to severity). The total is then averaged accordingly to the number of participation events. The authors arrived at the table by a combination of literature review and consultation with researchers and regulators.

I have annotated a copy of the paper for the authors, which can be viewed here. What follows is a summary of the main points of concern.

- The paper would be improved if the authors provided a more robust and detailed justification of: their definition of coercion; decision to go with minimum wage; the obligation on RECs to ask how calculations have been arrived at if an explanation is not provided; the categories of burden adopted (e.g. is a large blood test really equal to a lumber puncture?); lack of consensus around repeat payments for multiple tedious visits.
- Include the summary document referred to on page one in the supplementary materials.
- The consultation/discussion/participant group appears not to have included lay people. Why was this? Do the authors consider that this is a significant limitation? Either way this should be discussed. Are there plans to evaluate participants’ reaction to the assumptions and resulting calculations in the table?
- The authors state on page 4 that in Malawi expenses for a companion are also often paid. Why is this and why is this not reflected in the table (how did you decide to exclude this)?
- The decision to average the payments needs greater elaboration and justification. Note, for example, that the average for participation in the first worked example is more than in the second (which is considerably more onerous). Also note that in the second worked example a participant might not seem to have been fairly remunerated (according the amounts proposed by the authors as fair) if she was withdrawn by the researchers after e.g. the first visit and first bronchoscopy.
The calculations in the first worked example don’t make sense to me. On the basis of the notes provided, the total amount of time spent in the study appears to be 9 hours $2 \times 2 = 4$ hours travelling + $1 \times 4$ hour appointment + $1 \times 1$ hour appointment.

In the same table, it was also not clear why any allowance for burden was being made if the patients were being brought back to be given results. The authors previously state on p. 5 that ‘diagnostic test of proven value ... would not constitute a burden’? This needs to be clarified in the notes or changed.

More minor points:

- When describing the literature it may be useful to record where the research was carried out and to distinguish between papers that report empirical findings and more philosophical pieces where authors are arguing for their own positions. Literature seems to be taken at face value with no discussion of validity. Consider whether literature pertaining to one sort of research (e.g. phase I trials) is pertinent to others (e.g. phase III trials).
- Be cautious of over generalizing – e.g. it is not obvious that current practice is to include expenses AND compensation for time lost. Current practice where?
- The pale grey fill on Table 1 is confusing. Consider removing. Consider modifying the presentation of the table so that the headings are in pale grey – in the worked examples alternate lines are pale grey.
- Last sentence first column on page 5 unclear.
- The supplementary file does not add anything and could be deleted.
- Other minor points/comments included in the annotation, including typos where spotted.

**Competing Interests:** No competing interests were disclosed.

**Referee Expertise:** Ethics

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

We thank Professor Draper for thoughtful and helpful comments made on the first version.

We have improved the clarity and purpose of this paper by responding to all the points raised (more than 40) but in particular:

1. We thank Prof Draper for identifying the usefulness of this work.
2. We have clarified each point where clarification was requested including the definition of coercion, the composition of the workshop attendee list, decisions around remuneration of expenses (e.g. travelling companions).
3. We have discussed the group experience with working with research participants in this field. We did not have representation at the stakeholder workshop as the governance of remuneration was the focus rather than the financial amount. 6 publications of studies researching participant responses were cited, with authors from 3 of them present at the workshop.
4. We have corrected the (embarrassing) error in our worked example and the legend. This occurred with a mistake in combining 2 previous examples.
5. We have identified the country of origin of source material where missing, as much of the discussion is context specific.
6. The issue of “burden” is complex and study-specific. We think that the guideline table allows investigators to work with the concept of a range of burden in research, and to propose acceptable remuneration for discomfort, be it physical, mental or other.

Once again, we thank the reviewers and offer this much improved manuscript for indexing.

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