Ethics of health research priority setting

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Need for awareness among funders, grant proposal reviewers, researchers and research ethics committees about ethical priority setting for research

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For confidentiality, specific details of the grant proposal have been changed.

Brief description of the research proposal
A multi-year project to examine the incidence of acute kidney injury (AKI) from snake bites in adults and children admitted to hospital in a low income country (LIC). The incidence and mortality were suggested to be high based on a small study in a neighboring country (same researchers). In addition multiple different novel blood/urine diagnostics for AKI will be evaluated, including point-of-care (POC) devices. Case identification and study enrollment will be conducted mainly by hospital staff, some research staff to be hired. No clinical interventions are planned. Laboratory results will be forwarded to the clinical teams without comment. AKI outcomes will be documented upon discharge/death. Follow-up is not planned. No costing data will be collected. The principle investigator (PI) is junior faculty from a high-income country (HIC). All co-investigators are from the HIC, one local co-investigator will oversee the study, in addition to full time clinical responsibilities and is doing a PhD on another topic.

Background regarding importance of topic of study
Around 13.3 million people may be affected by AKI each year, of whom 1.7 million die (numbers similar to tuberculosis cases/deaths)[1]. Most AKI deaths occur in low- and middle-income countries (LMICs). The true AKI burden is unknown. AKI is often preventable; death is avoidable if diagnosed early. In LMICs, laboratory testing required for diagnosis is not always accessible/affordable. AKI is often missed and can lead to chronic kidney disease. AKI is associated with infections, insect/animal bites, pregnancy etc. Structural risk factors include poverty, unclean water, environmental exposures, often superimposed on inadequate public health measures, poor access to care, use of traditional remedies. Facilities for management, including intensive care and dialysis are often limited in LMICs, especially where patients must pay out of pocket. *AKI is common, carries significant risk of death and/or catastrophic health expenditure, is preventable and treatable, awareness is low and it is globally understudied*[2].

Ethical issues
Is the research topic a priority?
Principles/values: justice, equity, proportionality in research, transparency, solidarity
Considering AKI, the overall research topic is important, but limited focus on the small subset of AKI related to snake bites may not be appropriate given the need for broader understanding of AKI as a whole in the local context. *This raises the questions of who sets the priorities? How research priorities can be set when disease burden priorities are unknown*? The current *status quo* perpetuates the *de facto* relative de-prioritization of understudied topics, even when the topic should be of high priority (but burden unknown) – based on numbers and/or equity criteria.

Should research methodology to be tested be prioritized within studies?
Principles/values: sustainability, reciprocity, transparency
The study of multiple novel diagnostic methodologies for AKI may be of value, but the potential for future implementation and sustainability in the local context is unlikely. Feasibility and acceptability have been presumed, not determined. Sensitivity and specificity could be determined in the HIC. *Is prioritization of feasible/acceptable techniques/interventions justifiable, especially in LMICs where these tests will not soon be available?*

How comprehensively should a priority problem be studied by one research group?
Principles/values: accountability, sustainability, solidarity, potential harm
The proposal will assess diagnosis and incidence of AKI, no treatment or follow-up. *If the clinical burden is proposed to be high, should there be an ethical requirement that when research is deemed important enough to prioritize, that a holistic approach to the problem is required*? Would this be feasible to ask of a single research group? A single funder? Should collaborations be mandated? Should this lead to clear open-ended open calls for projects on the topic?

Responsibility of research funders to fund priority research areas?
Principles/values: autonomy, accountability, clinical/implementation research ethics, transparency
The researchers emphasize that AKI from snake bites has significant morbidity and mortality (elsewhere), but do not put this into perspective of AKI as a whole, which is under-researched in LIC and LMICs. Funders should be informed about priority areas being researched and those needing further research[3]. *Where would they obtain such information? Should national funding agencies be held to different standards than niche philanthropic agencies?* How can donors be motivated to support priority areas rather than niche areas of interest (if not a priority)?

Responsibility of researchers to set/address research priorities?
Principles/values: autonomy, accountability
Identification of relevant and priority research topics should occur in the local context with local experts. A local PI is included in the AKI study, but their contribution will be study coordination (and management of patients if requested by clinical teams). His scientific input does not seem to have been sought. *This overlaps with the issue of decolonizing global health. HIC academic ladder/incentives should incorporate fair sharing of research benefits and opportunities.*

Responsibility of reviewers to question whether research priorities are being addressed?
Principles/values: accountability, justice, equity
Reviewers are often chosen from HICs, without local insight. Funders may rely on expert reviewers to assess the topic priority. *Should expert reviewers (without conflicts of interest) be expected to understand/communicate local research priorities to funders/researchers?*

Who should have oversight and set the research priorities?
Principles/values: accountability, justice, equity, stewardship, sustainability, transparency
Many ethical concerns were not identified by the HIC research ethics committee (REC), minimized by the researchers, and accepted by the funder. The role of local RECs is important. RECs should understand local research priorities (*determined by whom?),* may identify similar or overlapping projects by diverse researchers/funders, may suggest collaboration on priority areas.

Conclusions
Setting priorities for research is an important challenge for global health, but cannot occur in a vacuum. Ideally health priorities in a specific context would be clear and this will facilitate ethical priority setting for research. The true priorities, especially in low-resource settings remain unknown. Reliance on available data will bias towards issues that have been funded/studied already. The gaps must be identified. This may in itself be a priority research agenda[4]. Setting this aside, were priorities known, or with the consultation of local experts who may understand relevant priorities, oversight would be necessary to ensure research is focused on priority areas. Researchers and funders themselves should be mindful of this, but realistically, well informed grant reviewers and (national?) RECs may be in an optimal position to have oversight.

Recommendations (to be developed/led by WHO with others - Nuffield?, CIOMs?**)**:

1. ***Develop training modules for researchers and funders*** to highlight the need to focus on priority research questions, ethical issues supporting this, and optimal practice to "decolonize" global health. Potentially included as part of research ethics certification.
2. ***Develop tools to support reviewers and REC members***
    - Develop training modules for REC members about priority setting in research, what this means, what the relevant ethics issues are. Could be based on ethics issues identified for Health Policy and Systems Research and Implementation Research (examples in refs[5,6])
    - Develop a checklist for Reviewers and RECs to evaluate whether a proposal adheres to ethics of priority setting in research.

References

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