Development of a post-mortem procedure to reduce the uncertainty regarding causes of death in developing countries

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A major failure of our global society in the 21st century is that many people in developing countries are not only born and live without any official record of their existence—a flagrant deprivation of an essential human right—but also die without having been seen by medically qualified personnel. The resultant uncertainty about the real burden of specific causes of death is being increasingly recognised by international health and funding agencies as a crucial limitation in the prioritisation of effective public health programmes and assessment of their effect.[1] Recently published estimates of the main causes of global and cause-specific mortality[2,3] have stirred a profound debate about the validity and adequacy of existing methods used to estimate cause of death.[4]

Complete diagnostic autopsies, indisputably the gold-standard method to estimate cause of death in developed countries,[5] are undertaken infrequently in resource-poor settings. Reasons for this include the large proportion of deaths that occur outside the health system, insufficient facilities or trained human resources,[6] cultural or religious apprehension about the practice of post-mortem procedures from the community perspective,[7] and decreasing consent rates in such regions. To bypass such problems, WHO now recommends the use of non-invasive indirect methods such as the verbal autopsy,[8] a protocolised procedure that allows the classification of causes of death through analysis of data derived from structured interviews with family, friends, and caregivers. However, the Achilles' heel of the verbal autopsy is its accuracy, which depends largely on the quality of the diagnostic criteria, the type of diseases involved, the location of death, and the delay between death and verbal autopsy. Deaths associated with non-specific signs and symptoms are the most problematic,[5] and are an especially common issue for perinatal and neonatal deaths. Despite these key limitations, verbal autopsies are the only source of data for cause of death in many settings, and their practice and improvement should therefore be encouraged. Assessment of the cause of in-hospital deaths is generally based on the clinician's diagnosis of the disease(s) that led to the fatal outcome. However, such estimations are also prone to frequent misclassification errors. Indeed, when clinical diagnoses have been contrasted with post-mortem findings, rates of major clinical–pathological discrepancies have ranged from 10% to above 30%,[9,10] especially in the diagnosis of infectious diseases.

Thus, because the feasibility of routinely doing complete diagnostic autopsies is problematic, and indirect methods such as the verbal autopsy or clinical diagnosis are suboptimal, the development of feasible and more straightforward direct methods to ascertain the cause of death seems to be a priority. In recent years, the concept of minimally invasive autopsy as an alternative to classic complete diagnostic autopsy has been proposed. Minimally invasive autopsy includes the use of imaging techniques, such as MRI or CT scan, coupled with targeted small diagnostic biopsies (by needle puncture) of key organs. Although little experience has been gained with such techniques so far, they have been shown to produce reliable and comparable results to the complete diagnostic autopsy[11–13] in developed countries. A further advantage of the method is the chance to improve our understanding of the pathogenesis of diseases that need human samples to be studied fully.

However, in its present form, minimally invasive autopsy is not a feasible technique in resource-poor settings. Thus, procedures to make minimally invasive autopsy feasible and acceptable in developing countries need to be defined and standardised. These include the use of low-cost and portable imaging devices, the number of organs that need to be sampled, the preferred routes to obtain contamination-free tissue, and the specific pathology and microbiology procedures that can provide relevant information related to the cause that underlies death. A consortium of African, American, Asian, and European institutions with expertise in clinical and socioanthropological research in low-income or middle-income settings has been created with the aim to develop such a method. A validation exercise is being undertaken to compare the diagnostic reliability of a methodically predefined minimally invasive autopsy device against the gold standard of complete diagnostic autopsy in two tertiary hospitals (in Maputo, Mozambique, and Manaus, Amazonas, Brazil), and to explore the potential use of classic and advanced microbiology techniques to further

investigate infectious causes of death in patients of any age. Such a minimally invasive autopsy device would need to balance out the best possible practices with the challenges of working in resource-poor settings, and also consider its future global applicability. In this respect, uncertainties related to the communities' perception and acceptability of such a method, and the feasibility of actually implementing it in basic clinics or even in the community, needs to be explored rigorously. Social sciences research to complement the validation exercise has started in rural and urban areas in five countries (Mozambique, Gabon, Kenya, Mali, and Pakistan) and should provide the necessary answers and approaches for the future implementation of this method in resource-poor settings.

Confirmation that minimally invasive autopsy is a feasible, valid, and reliable method to inform about the cause of death could allow the introduction of such simplified techniques as an alternative to complete diagnostic autopsies or as a complement to verbal autopsy and clinical diagnosis. It would also strengthen the validity of contemporary and future models and cross-disease burden estimates, which are presently hampered by insufficient inputs of raw data. Such a method could conceivably shed a clarifying light on one of the most fundamental, puzzling, and unresolved epidemiological questions: what do people die from in developing countries?

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