Neurological disease is a major cause of mortality worldwide. The upcoming publication of the Global Burden of Disease analysis depends on accurate and adequate reporting of the cause distribution of deaths internationally. Cerebrovascular disease has traditionally ranked as the third most common cause of death worldwide and accounts for \( \sim 5.5 \) million of the 55 million deaths that occur each year.\(^1\) Other neurological disorders, including epilepsy and dementia, are highly prevalent, but data on the incidence and prevalence of neurological diseases are lacking from many regions. Available information is at best an extrapolation from incomplete civil registration systems. Only one-third of countries globally certify the causes of all deaths. In the Southeast Asia region, less than half of the countries have vital registration. No country in the Africa region has complete data and only six African countries (13\%) have any form of vital registration whatsoever.\(^2\)

**The verbal autopsy method.** Verbal autopsy is the most commonly used method to determine cause of death in places lacking adequate civil registration, where the majority of deaths occur outside of medical care. The method typically involves asking a respondent knowledgeable of the deceased’s fatal illness a series of questions on the signs and symptoms that preceded death (e.g., “During the last 3 months of pregnancy, did she suffer from a convulsion?” or “During the illness that led to death, was he paralyzed on one side?”) combined with an open-ended narrative of the illness-related events.\(^3\) The respondent must 1) be a close family member or caregiver of the decedent, 2) have been present during the illness leading to death, and 3) be able to recount and provide details of the decedent’s health information. The interviewers usually have a secondary school-level education but no medical qualifications and complete intensive short-term training in the study techniques. Ultimate diagnosis is most commonly made by physicians who review the completed surveys.

Validity, which is the accuracy of the verbal autopsy diagnoses compared with an external reference standard, is the most important measurement of the verbal autopsy instrument. Validation studies may best be accomplished in a hospital setting where objective reference standard diagnoses can be developed based on clinical history, examination, laboratory results, and imaging findings. Reviews of the completed verbal autopsy surveys by an individual or a panel of physicians or, alternatively, diagnoses derived from objective algorithms (combinations of verbal autopsy signs and symptoms) predetermined by an expert panel are compared with the reference standard diagnoses to determine the accuracy of the verbal autopsy diagnoses. Such validation studies have established various levels of sensitivity and specificity for verbal autopsy diagnoses of major causes of death.\(^4\) New statistical methods for analyzing verbal autopsy data hold promise for more accurate identification of the cause distribution of deaths and more rapid, computerized processing of high-volume verbal autopsy data.\(^5\)

**Existing use of verbal autopsy for neurological disease.** The World Health Organization (WHO) recognizes three major goals of verbal autopsy: 1) research and longitudinal analysis measures, 2) assessment of the cross-sectional prevalence or burden of disease, and 3) evaluation of disease-focused treatment programs and interventions.\(^6\) Although the use of verbal autopsy methods began as early as the 1930s, there has been little research on neurological causes of death, particularly in adulthood. Early studies that included neurological conditions focused on childhood-predominant diseases including neonatal tetanus, cerebral malaria, and meningitis. In recent years, however, increasing attention has been paid to adult causes of neurological death (Table 1). For example, in a study of 48,000 adult deaths in Chennai, India, the death rate from stroke was found to reach 1308.5/100,000 in people over 75 years of age.\(^7\) Compared with death certificates alone, verbal autopsy yielded fewer unspecified causes of death. In China, a validation study identified more stroke deaths by questionnaire analysis than by medical diagnosis (i.e., verbal autopsy led to false positive diagnoses), with sensitivity of 82\% and specificity of 94\% for the verbal autopsy diagnoses.\(^8\) There have been no validation studies of verbal autopsy for deaths caused by epilepsy, traumatic brain and spinal cord injury, or human immunodeficiency virus (HIV) dementia to date.

**Estimating sample size for verbal autopsy.** Of importance, the numbers needed to understand neurological deaths in large populations may not be exceptionally high. For example, hypothesizing that ischemic stroke is the most common neurological cause of death and accounts for \( \sim 10\% \) of all adult deaths, an annual cluster sample of 1,200 deaths of people 18 years of age and above selected with a design effect of 1.4 could estimate the true cause proportion with precision \( \pm 2\% \) and \( \alpha = 0.05 \) (\( z = 1.96 \)). Using a fixed cohort and the assumption that adult mortality is 2\% per year, achieving this estimate would require monitoring about 30,000 households. Estimating less common neurological diseases that may lead to death—meningitis, cerebral malaria, or epilepsy, for example—will require different numbers depending on the prevalence...
of the disease, its case fatality rate, and the age structure of the population.

Costs and benefits of verbal autopsy. Civil registration for the African continent may cost as little as 10 cents per person (total 80 million US$ annually) but has not achieved sufficient funding to be a quickly realizable goal. The cost of obtaining verbal autopsy data above and beyond that of identifying the deaths was found to be US$4 per death (8 cents per individual monitored in the verbal autopsy program), including physician review and data analysis. The cost likely would be less using automated techniques without physician involvement.

Verbal autopsy can provide baseline data to assess the prevalence of death caused by neurological and other chronic diseases. Data on preventable and modifiable causes of death can ideally identify new health priorities, lead to more appropriate allocation of sparse resources, and assist in the evaluation of health programs. Such data may be of high value to both policy makers and clinicians. Modules added to the verbal autopsy can determine the prevalence of important risk factors and health-related behaviors in the deceased persons. Expected results could include targeted vaccination and risk factor reduction campaigns and the strengthening of health systems in a locally meaningful way. Reliability of medical diagnoses among physician coders over time has recently been reported to be high.

Limitations to verbal autopsy. Verbal autopsy is an interim solution. Because most sites that conduct verbal autopsy cover limited areas within countries, they are most useful for assessing local health needs and contribute less to nationwide or global estimates. Few verbal autopsy instruments have been validated for adult neurological diseases. In general, more work is needed on the comparison between verbal autopsy findings and traditional necropsy, which has been reported only rarely.

Verbal autopsy data can be subject to inaccuracies in recall by the interviewed respondent. When verbal autopsy is delayed, as occurs in many reported studies, the recall period of the respondent may stretch into the months or years after the death. The accuracy of the calculations of incidence and prevalence of neurological disease may be compromised by misclassification error and poor sensitivity of the verbal autopsy instrument. For example, assessment of adult meningitis deaths in Tanzania, Ethiopia, and Ghana found a diagnostic sensitivity of 40–64%. If data are inaccurate, findings can misinform public health policy formulation. The underlying cause and subtypes of many neurological diseases may remain unclear (e.g., hemorrhagic versus ischemic stroke in incidence studies of stroke), leading to the need for further and more in-depth studies.

Opportunities. In the coming years, until civil registration and death certification systems are strengthened, verbal autopsy methods can provide information for some of the world’s poorest regions where little to nothing is reported on neurological causes of death. Resource-poor regions remain of high importance because of the excess neurological disease and resultant premature deaths that can occur. Embedding verbal autopsy studies in periodic population surveys or existing surveillance systems may be an initial step to strengthen the use of verbal autopsy within existing infrastructure. The ongoing prospective study of one million deaths in India is one example of population-based data that can be used to conceptualize neurological disease rates in the adult population. Although a study of this scale may not be easily set up in other resource poor regions, its feasibility in India suggests that other low-income countries may similarly improve their monitoring of community-level deaths through verbal autopsy in sample registration systems. Despite multiple limitations to the verbal autopsy method, engagement of the growing group of community health workers, researchers, and health professionals can lead to meaningful refinements and valuable epidemiological data based on the verbal autopsy approach.

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