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"Probabilistic Cause-of-death Assignment using Verbal Autopsies"

The Importance of Cause-of-death Assignment

While cause-of-death assignment may appear to be a given in western contexts, understood within a global scale, such certainties recede into the background. Specifically, research has shown that fewer than one-third of global deaths have a medically certified cause. In light of such somber statistics, it is unsurprising that those countries with the most critical needs have the least amount of information as many deaths occur outside of hospitals without documented medical care. Under such dire conditions, Dr. Tyler McCormick and his team creatively employ statistical methods in order to provide cause-of-death assignment to these areas.

Overview of Verbal Autopsies (VA)

In areas without widespread hospital care, verbal autopsies (VA) have become a common strategy to obtain cause-of-death. Typically, VA entails asking a relative or community member of the decedent about the circumstances of death. Within this interview, caregivers are commonly asked a mix of binary, category, or free response questions that center around pre-existing medical conditions, conditions leading up to the death, as well as any information about healthcare.

Based upon a standard World Health Organization (WHO) questionnaire that has been improved over time, the VA survey, for the purposes of Dr. McCormick and his colleagues' study, only apply to adult deaths even though the 2016 WHO VA instrument can be applied to all age groups. While the VA procedure appears straightforward, in practice, many cultural aspects have to be accounted for. In particular, given the sensitive nature of these interviews, enumerators oftentimes converse with respondents first in order to establish a rapport prior to reading the questions to them.

In the roll out of their project, Dr. McCormick and his team partner with research groups employing a variety of methods including ethnography, allowing them to gain insight into the exact conditions of these areas. Through such collaborations, they have found great heterogeneity in their geographically specified research areas, showing degrees of cultural independence often in close proximity.

What are some of the limitations and challenges experienced in VA? How can we overcome these limitations?

While a variety of methods have been proposed to assign cause-of-death through VA data, they all rely upon a "gold standard," which is a database of a large number of deaths that have been confirmed and certified by medical professionals. Not only expensive and difficult to create, gold standard databases include mostly in-hospital deaths which are incomparable to the deaths in places that need VA. Thus, it is not possible to impose a universal

gold standard on labeling deaths. As a result, cause-of-death can be ambiguous even in the best circumstances.

After examining the initial findings from VA, they found that the link between symptoms and cause-of-death assignment are often context-dependent. Specifically, medical professionals from different societies and cultures perceive similar symptoms to be associated with different causes. As a result, even physician coding varies across different locations. Therefore, in order to establish a true gold standard, it is necessary to train a model across geographies and time. Because creating such a gold standard database is impossible, Dr. McCormick and his team focus their energies upon developing a method that does not depend upon it.

What are the current methods for assigning cause-of-death and their limitations?

Endorsed by the WHO and used extensively at Health and Demographic Surveillance System (HDSS) sites, a method developed by Peter Byass called InterVA does not employ gold standard deaths as the basis to infer the relationship between symptoms and causes-of-death. Instead, InterVA uses a ranked list of symptoms associated with each cause to infer cause-of-death.

Dr. McCormick identifies three primary problems of the InterVA approach: (1) it does not account for uncertainty; (2) it ignores no-cause cases; and (3) it uses an arbitrary base for ranking. The essence of the InterVA problem is that it is not a real Bayesian method.

How does Dr. McCormick and his team improve upon the existing approaches to VA?

Dr. McCormick and his team improves upon InterVA by using an innovative statistical method to more realistically classify cause-of-death from the information obtained from VA. Unlike InterVA, their method allows for uncertainty in both the cause-of-death assignments of specific individuals and the distribution of death by cause across the population. Using a hierarchical Bayesian framework, they develop a new statistical tool called InSilicoVA, which assigns a likely cause-of-death for a certain individual and also estimates a population distribution by that same cause. A key feature is the use of information between inferred individual cause and population cause distributions.

How Does InSilicoVA Perform?

In order to test the effectiveness of InSilicoVA, they compare their method first to alternatives using a dataset of gold standard deaths and second, using data from two sites where no gold standard deaths are available. In the first case, InSilicoVA more accurately gauges cause of death than either InterVA or Tariff (which uses gold standard training data) across six sites within four countries.

In the second case, they compare the performance of InSilicoVA to that of InterVA (its closest comparator because neither rely upon gold standard databases) in Agincourt (South Africa) and Karonga (Malawi). From the results at both sites, InSilicoVA was more conservative and used confidence intervals in its results whereas InterVA did not. More importantly, InSilicoVA assigned a larger portion of the deaths to causes labeled “other,” demonstrating the uncertainty in assigning highly accurate cause-of-death using VA data. Because InSilicoVA errs on the side of caution, it produces more “honest” results rather than ones that are “artificially precise.”