

The openVA Toolkit for Verbal Autopsies

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Abstract Verbal autopsy (VA) is a survey-based tool widely used to infer cause of death (COD) in regions without complete-coverage civil registration and vital statistics systems. In such settings, many deaths happen outside of medical facilities and are not officially documented by a medical professional. VA surveys, consisting of signs and symptoms reported by a person close to the decedent, are used to infer the COD for an individual, and to estimate and monitor the COD distribution in the population. Several classification algorithms have been developed and widely used to assign causes of death using VA data. However, the incompatibility between different idiosyncratic model implementations and required data structure makes it difficult to systematically apply and compare different methods. The **openVA** package provides the first standardized framework for analyzing VA data that is compatible with all openly available methods and data structure. It provides an open-source, R implementation of several most widely used VA methods. It supports different data input and output formats, and customizable information about the associations between causes and symptoms. The paper discusses the relevant algorithms, their implementations in R packages under the **openVA** suite, and demonstrates the pipeline of model fitting, summary, comparison, and visualization in the R environment.

Introduction

Verbal autopsy (VA) is a well-established approach to ascertaining the cause of death (COD) when medical certification and full autopsies are not feasible or practical (Garenne, 2014; Taylor et al., 1983). After a death is identified, a specially-trained fieldworker interviews the caregivers (usually family members) of the decedent. A typical VA interview includes a set of structured questions with categorical or quantitative responses and a narrative section that records the “story” of the death from the respondent’s point of view (World Health Organization, 2012). Currently, there are multiple commonly used questionnaires with overlapping, but not identical questions. VAs are routinely used both by researchers in health and demographic surveillance systems (Sankoh and Byass, 2012; Maher et al., 2010) and multi-country research projects (Nkengasong et al., 2020; Breiman et al., 2021), and in national-scale surveys in many low- and middle-income countries (LMICs). For a more comprehensive overview of the current use of VA, we refer readers to Chandramohan et al. (2021).

The process of inferring a cause from VA data consists of two components. First, there must be some external information about the relationship between causes and symptoms. In supervised learning problems, the external information is typically derived from training datasets with known labels. In the context of VA, a common practice is to obtain training data using clinically trained, experienced physicians who read a fraction of the interviews and determine causes. To address the fact that physicians frequently do not agree on causes, VA interviews are often read by two physicians, and sometimes three, and the final causes are determined through a consensus mechanism (e.g., Kahn et al., 2012). This process can be extremely time- and resource-intensive. Another means of obtaining this information is directly through expert opinion. For example, one can ask groups of physicians to rate the likelihood of a symptoms occurring, given a particular COD, which can be converted into a set of probabilities of observing a symptom given a particular cause. Such expert knowledge can be highly useful in analyzing VA data when training datasets do not exist.

Secondly, an algorithmic or statistical model is needed to assign the causes of death by extrapolating the relationship between symptoms and causes to the target population. The cause-of-death assignment model is conceptually a separate construct from the symptom-cause information. The current state of the VA literature, however, often does not distinguish between the two. This is in part due to popular VA software that combines a source of symptom-cause information (e.g., a certain training data or a database of expert knowledge) with a specific algorithm, and requires a specific type of survey instrument to be used. This restriction prevents robust comparison between methods and contexts. A health agency in one region may, for example, want to analyze VA data using the same VA algorithm as a neighboring region to ensure estimates are comparable. Unless the agencies used the same survey format, however, this is not possible with existing tools.

The **openVA** package (Li et al., 2022b) addresses this issue through an open-source toolkit. The **openVA** suite comprises a collection of R packages for the analysis of verbal autopsy data. The goal of this package is to provide researchers with an open-source tool that supports flexible data input formats and allows easier data manipulation and model fitting. The **openVA** suite consists of four core packages that are on CRAN, **InterVA4** (Li et al., 2019), **InterVA5** (Thomas et al., 2021b), **InSilicoVA** (Li et al., 2022a), and **Tariff** (Li et al., 2018), and an optional package **nbc4va** (Wen et al., 2022). Each of these packages implements one coding algorithm. For three of these algorithms – namely, **InterVA-4**,

InterVA-5 and Tariff – there are also compiled software programs distributed by the original authors.

The main focus of this paper is to provide a general introduction to the implementation details of the included algorithms both in terms of the underlying methodology, and through case studies. The **openVA** package has four major contributions:

1. It provides a standardized and user-friendly interface for analysts to fit and evaluate each method on different types of data input using standard syntax. Previously, most of the methods were designed to be used specifically with their own input formats and are usually incompatible with others. The **openVA** package closes this gap by allowing easier and fair model comparison of multiple algorithms on the same data. This significantly facilitates further research on VA algorithms.
2. It provides a series of functionalities to summarize and visualize results from multiple algorithms, which is helpful for analysts not familiar with data manipulation and visualization in R.
3. It does not directly implement any algorithms for coding VA data, so that it is possible for a research group to maintain their own algorithm implementations callable from the **openVA** package, while also making it available to general users as a standalone piece of software. For example, the **nbv4va** was developed and maintained independently by researchers at the Center for Global Health Research in Toronto, but is designed so that it can be seamlessly integrated into the **openVA** package.
4. It is fully open source, and can be run on multiple platforms. The open-source nature of **openVA** significantly expands its potential for methodological research and its suitability for integration within a larger data analysis pipeline. Compared to the alternative implementations, the InterVA-4 and InterVA-5 software are distributed as compiled software that can only be run on Windows system. They provide the source codes as an additional code script, which are difficult to modify and re-compile. Tariff, as implemented through the SmartVA-Analyze application (Serina et al., 2015), was also primarily distributed as a compiled application that can only be run on Windows system (Institute for Health Metrics and Evaluation, 2021b). However, their source codes were recently made available under the open source MIT License on GitHub (Institute for Health Metrics and Evaluation, 2021a).

The rest of this paper is organized as follows: We first briefly introduce the main component packages and the underlying algorithms. We then demonstrate standard data structures and model fitting steps with the **openVA** package and functionalities to summarize results. We then discuss how additional information can be incorporated into modeling VA data, and we briefly survey additional packages and software developments built around the **openVA** package. We end with a discussion of remaining issues and limitations of the existing automated VA algorithms and propose new functionalities to be included in **openVA** package.

Structure of the openVA package

The **openVA** suite of packages currently consists of four standalone packages that are available on CRAN and one optional package hosted on GitHub. In this section, we first provide a brief introduction to these five packages, and we discuss the mathematical details behind each algorithm in the next subsection.

- **InterVA4** (Li et al., 2014, 2019) is an R package that implements the InterVA-4 model (Byass et al., 2012). It provides replication of the widely used InterVA software (Byass, 2015). The standard input of **InterVA4** is in the form of a pre-defined set of indicators, based on the 2012 World Health Organization (WHO) VA instrument (World Health Organization, 2012). The default InterVA-4 algorithm cannot be applied to other data input formats because its internal built-in prior information is specific to a fixed set of indicators and causes. The same restriction is also maintained in the **InterVA4** package. However, the mathematical formulation of the InterVA-4 model is completely generalizable to other binary input formats, as described in later sections, and is also implemented in the **openVA** package.
- **InterVA5** (Thomas et al., 2021b) is an R package that implements the InterVA-5 model (Byass et al., 2019). The InterVA-5 model updates the previous version in several ways. First, the input data must adhere to the format of the 2016 WHO VA instrument (D'Ambruso et al., 2017). Second, changes have been made to the data processing steps. It is also worth noting that the model outputs have been expanded by the inclusion of the most likely Circumstances Of Mortality CATegory, or COMCAT, among the results – the categories include: culture, emergency, health systems, inevitable, knowledge, resources, or an indeterminant combination of multiple factors (for more details, see D'Ambruso et al., 2017). Despite these changes, the mathematical formulation of InterVA-5 is identical to that of InterVA-4.

- **InSilicoVA** (Li et al., 2022a) is an R package that implements the InSilicoVA algorithm, a Bayesian hierarchical framework for cause-of-death assignment and cause-specific mortality fraction estimation proposed in McCormick et al. (2016). It is originally designed to work with the WHO VA instrument, i.e., the same input data used by the InterVA software, but is also generalizable to other data input formats. It is a fully probabilistic algorithm and can incorporate multiple sources of information, such as known sub-populations in the dataset, and physician coding when such data are available. The Markov Chain Monte Carlo (MCMC) sampler is implemented in Java for improved speed.
- **Tariff** (Li et al., 2018) is an R package that implements the Tariff algorithm (James et al., 2011). It most closely reflects the description of the Tariff 2.0 method (Serina et al., 2015). The Tariff algorithm is developed by the Institute for Health Metrics and Evaluation (IHME) and is officially implemented in the SmartVA-Analyze software (Institute for Health Metrics and Evaluation, 2021b). However, as the developers of this R package are not affiliated with the authors of the original algorithm, there are some discrepancies in implementation. The source code of the two versions of Tariff was not publicly available at the time when the **Tariff** package was created, so the package was developed based solely on the descriptions in the published work. Despite the difference in implementation, **Tariff** is able to achieve comparable results as the published work as demonstrated in McCormick et al. (2016). More detailed descriptions of the **Tariff** implementations are also discussed in the supplement of McCormick et al. (2016). The later released Python source codes of SmartVA-Analyze have been incorporated in the web application extension of the **openVA** package.
- **nbc4va** (Wen et al., 2022) is an R package that implements the Naive Bayes Classifier for VA encoding (Miasnikof et al., 2015). It calculates the conditional probabilities of symptoms given causes of death from a training dataset, instead of using physician-provided values. **nbc4va** is developed and maintained by researchers at the Center for Global Health Research in Toronto, but is designed so that it can be seamlessly integrated into **openVA**. Currently, the **nbc4va** package is hosted on GitHub and is an optional package that users can choose to load separately.

We note that there are additional methods and implementations to assign causes of death using VA data that are not included in the **openVA** implementation (e.g., Flaxman et al., 2011; Jeblee et al., 2019). These methods are not widely adopted by VA practitioners and most of these implementations are either not publicly available or require data processing steps that are specific to certain datasets, making them impractical for routine use in general. In addition, while the cause-of-death assignment process is closely related to the generic multi-class classification problem, naive application of off-the-shelf classification algorithms has been shown to perform poorly in the context of VA (Murray et al., 2014). Therefore, we focus on the methods that are currently adopted by practitioners. We briefly survey some more recent developments and their implementations at the end of this paper.

The **openVA** package is hosted on CRAN and can be installed with the following commands. Since posterior inference is carried out using MCMC in the InSilicoVA algorithm, we set the seed for the random number generator to make the paper reproducible. For the analysis in this paper, we also install the **nbc4va** package separately from GitHub. The versions of the supporting packages can be checked in R using the `openVA_status()` function.

```
set.seed(12345)
library(openVA)
remotes::install_github("rrwen/nbc4va")
library(nbc4va)
openVA_status()
```

Overview of VA cause-of-death assignment methods

The common modeling framework for VA data consists of first converting the survey responses into a series of binary variables, and then assigning a COD to each death based on the binary input variables. Typically, the target of inference consists of two parts: the individual cause-of-death assignment, and the population-level cause-specific mortality fractions (CSMF), i.e., the fraction of deaths due to each cause. In this section, we formally compare the modeling approaches utilized by each algorithm for these two targets. We adopt the following notations. Consider N deaths, each with S binary indicators of symptoms. Let s_{ij} denote the indicator for the presence of j -th symptom in the i -th death, which can take values 0, 1, or NA (for missing data). We consider a pre-defined set of causes of size C . For the i -th death, denote the COD by $y_i \in \{1, \dots, C\}$ and the probability of dying from cause k is denoted by p_{ik} . For the population, the CSMF of cause k is denoted as π_k , with $\sum_{k=1}^C \pi_k = 1$.

- **InterVA4** (Byass et al., 2012) and **InterVA5** (Byass et al., 2019) algorithms calculate the probability

of each COD given the observed symptoms using the following formula,

$$P_{ik} = \frac{\pi_k^{(0)} \prod_{j=1}^S P(s_{ij} = 1 | y_i = k) \mathbf{1}_{s_{ij}=1}}{\sum_{k'=1}^C \pi_{k'}^{(0)} \prod_{j=1}^S P(s_{ij} = 1 | y_i = k') \mathbf{1}_{s_{ij}=1}}$$

where both the prior distribution of each of the causes, $\pi_k^{(0)}$ and the conditional probabilities $P(s_{ij} = 1 | y_i = k)$ are fixed values provided in the InterVA software. It is worth noting that the formula does not follow the standard Bayes' rule as it omits the probability that any symptom is absent. A detailed discussion of this modeling choice can be found in [McCormick et al. \(2016\)](#). The conditional probabilities, $P(s_{ij} = 1 | y_i = k)$, used in InterVA algorithms are represented as rankings with letter grades instead of numerical values ([Byass et al., 2012](#)). For example, $P(s_{ij} = 1 | y_i = k) = A+$ is translated into $P(s_{ij} = 1 | y_i = k) = 0.8$, etc. The standard InterVA software only supports the fixed set of symptoms and causes where such prior information is provided. For a different data input format, this formulation can be easily generalized if training data are available. We include in the [openVA](#) package an extension of the algorithm that calculates $\hat{P}(s_{ij} = 1 | y_i = k)$ from the empirical distribution in the training data and then maps to letter grades with different truncation rules. Details of the extended InterVA algorithm can be found in [McCormick et al. \(2016\)](#).

After the individual COD distributions are calculated, InterVA-4 utilizes a series of pre-defined rules to identify up to the top three most likely COD assignments, and truncates the probabilities for the rest of the CODs to 0 and adds an 'undetermined' category so that the probabilities sum up to 1 (See the user guide of [Byass \(2015\)](#)). Then the population-level CSMFs are calculated as the aggregation of individual COD distributions, such that

$$\pi_k = \sum_{i=1}^N P_{ik}^*$$

where P_{ik}^* denotes the individual COD distribution after introducing the undetermined category.

- **Naive Bayes Classifier** ([Miasnikof et al., 2015](#)) is very similar to the InterVA algorithm with two major differences. First, instead of considering only symptoms that present, the NBC algorithm also considers symptoms that are absent. Second, the conditional probabilities of symptoms given causes are calculated from training data instead of given by physicians, which is similar to our extension of InterVA discussed above. Similar to InterVA, the NBC method can be written as

$$P_{ik} = \frac{\pi_k^{(0)} \prod_{j=1}^S (P(s_{ij} = 1 | y_i = k) \mathbf{1}_{s_{ij}=1} + P(s_{ij} \neq 1 | y_i = k) \mathbf{1}_{s_{ij} \neq 1})}{\sum_{k'=1}^C \pi_{k'}^{(0)} \prod_{j=1}^S (P(s_{ij} = 1 | y_i = k') \mathbf{1}_{s_{ij}=1} + P(s_{ij} \neq 1 | y_i = k') \mathbf{1}_{s_{ij} \neq 1})}$$

and the CSMFs are calculated by $\pi_k = \sum_{i=1}^N P_{ik}$.

- **InSilicoVA** algorithm ([McCormick et al., 2016](#)) assumes a generative model that characterizes both the CSMF at the population level, and the COD distributions at the individual level. In short, the core generative process assumes

$$s_{ij} | y_i = k \propto \text{Bernoulli}(P(s_{ij} | y_i = k)) \quad (1)$$

$$y_i | \pi_1, \dots, \pi_C \propto \text{Categorical}(\pi_1, \dots, \pi_C) \quad (2)$$

$$\pi_k = \exp \theta_k / \sum_{k=1}^C \exp \theta_k \quad (3)$$

$$\theta_k \propto \text{Normal}(\mu, \sigma^2) \quad (4)$$

and hyperpriors are also placed on $P(s_{ij} | y_i = k)$, μ , and σ^2 . The priors for $P(s_{ij} | y_i = k)$ are set by the rankings used in InterVA-4 if the data are prepared into InterVA format, otherwise they are learned from training data. The priors on μ and σ^2 are diffuse uniform priors. Parameter estimation is performed using MCMC, so that a sample of posterior distributions of π_k can be obtained after the sampler converges.

- **Tariff** algorithm ([James et al., 2011](#)) differs from the other three methods in that it does not calculate an explicit probability distribution of the COD for each death. Instead, for each death i , a Tariff score is calculated for each COD k so that

$$\text{Score}_{ik} = \sum_{j=1}^S \text{Tariff}_{kj} \mathbf{1}_{s_{ij}=1}$$

where the symptom-specific Tariff score Tariff_{kj} is defined as

$$\text{Tariff}_{kj} = \frac{n_{kj} - \text{median}(n_{1j}, n_{2j}, \dots, n_{Cj})}{\text{IQR}(n_{1j}, n_{2j}, \dots, n_{Cj})}$$

where n_{kj} is the count of how many deaths from cause k contain symptom j in the training data. The Tariff scores are then turned into rankings by comparing them to a reference distribution of scores calculated from re-sampling the training dataset to obtain a uniform COD distribution. It is worth noting that the Tariff algorithm produces the COD distribution for each death in terms of their rankings instead of the probability distributions. And thus the CSMF for each cause k is calculated by the fraction of deaths with cause k being the highest ranked cause, i.e.,

$$\pi_k = \frac{\sum_{i=1}^N \mathbf{1}_{y_i=k}}{N}$$

In addition to the different model specifications underlying each algorithm, there is also a major conceptual difference in handling missing symptoms across the algorithms. Missing symptoms could arise from different stages of the data collection process. For example, the respondent may not know whether certain symptoms existed or may refuse to answer a question. From a statistical point of view, knowing that a symptom does not exist provides some information to the possible cause assignment, while a missing symptom does not. Although in theory, most of the VA algorithms could benefit from distinguishing ‘missing’ from ‘absence’, InSilicoVA is the only algorithm that has been implemented to acknowledge missing data. Missing indicators are assumed to be equivalent to ‘absence’ in InterVA, NBC, and Tariff.

Data preparation

In the **openVA** package, we consider two main types of standardized questionnaire: the WHO instrument and the IHME questionnaire. In this section, we focus on describing these two data formats and tools to clean and convert data. Pre-processing the raw data collected from the survey instrument (usually with Open Data Toolkit) is usually performed with additional packages and software outside of the analysis pipeline in R. We briefly mention software for data pre-processing towards the end of this paper.

The WHO standard format

For users familiar with InterVA software and the associated data processing steps, the standard input format from the WHO 2012 and 2016 instruments is usually well understood. For the 2012 instrument, the data expected by the InterVA-4 software are organized into a data frame where each row represents one death and the corresponding VA information is contained in 246 fields, starting from the first item being the ID of the death. The 245 items following the ID each represent one binary variable of symptom/indicator, where ‘presence’ is coded by ‘Y’, and ‘absence’ is coded by an empty cell.

To accommodate updates for the WHO 2016 instrument (D’Ambruoso et al., 2017), the InterVA-5 software accepts a data frame with 354 columns that include 353 columns of symptom/indicators followed by an additional column for the record ID. It should be noted that the R package **InterVA5** retains the format with the record ID residing in the first column. Another important update with InterVA-5 is that it acknowledges the difference between “Yes” and “No” (or “Y/y” and “N/n”, which is different from the coding scheme in InterVA-4), both of which are processed as relevant responses, while all other responses are treated as missing values and ignored. With respect to the list of causes of death, InterVA-5 utilizes the WHO 2016 COD categories, which is nearly identical to the WHO 2012 COD categories (used by InterVA-4) except that hemorrhagic fever and dengue fever are two separate categories in the 2016 COD categories.

The same input format is inherited by the **openVA** package, except for one modification. We further distinguish ‘missing’ and ‘absence’ in the input data frame explicitly. We highly recommend that users pre-process all the raw data so that a ‘missing’ value in the data spreadsheet is coded as a ‘.’ (following the Stata practice familiar to many VA practitioners), and an ‘absence’ value is indicated by an empty cell, as in the standard InterVA-4 software. For WHO 2016 data, both ‘.’ and ‘-’ (following the default coding scheme of InterVA-5 software) are interpreted as missing values. For methods other than InSilicoVA, ‘missing’ and ‘absence’ will be considered the same internally and thus will not introduce a compatibility problem.

The PHMRC format

The Population Health Metrics Research Consortium (PHMRC) gold standard VA data (Murray et al., 2011) consist of three datasets corresponding to adult, child, and neonatal deaths, respectively. All deaths occurred in health facilities and gold-standard causes are determined based on laboratory, pathology and medical imaging findings. These datasets can be downloaded directly using the link returned by the function `getPHMRC_url()`. For example, we can read the adult VA dataset using the following command.

```
PHMRC_adult <- read.csv(getPHMRC_url("adult"))
```

Although the data are publicly accessible, a major practical challenge for studies involving the PHMRC gold standard dataset is that the pre-processing steps described from the relevant publications are not clear enough nor easy to implement. The **openVA** package internally cleans up the PHMRC gold standard data when calling the `codeVA()` function on the PHMRC data. The procedure follows the steps described in the supplement material of McCormick et al. (2016). Notice that the original PHMRC data are useful for comparing and validating new methods, as well as for using as training data, but the cleaning functions only require that the columns are exactly the same as the PHMRC gold standard datasets, so they could also be used for new data that are pre-processed into the same format.

Customized format

In addition to the two standard questionnaires discussed previously, researchers might also be interested in including customized dichotomous symptoms in their analysis. The **openVA** package also supports customized inputs as long as they are dichotomous. In such case, neither the built-in conditional probability matrix of InterVA nor the PHMRC gold standard dataset could be used to learn the relationship between training and testing data, thus different training data with known causes of death are necessary for all three algorithms. The `ConvertData()` function can be used to convert data with customized coding schemes into the format recognized by the **openVA** package.

Finally, we note that the **openVA** package currently does not reformat data from one standardized questionnaire to another. This is because mapping the symptoms collected from one questionnaire to those collected by another questionnaire inevitably creates loss of information. Such mapping tasks can be useful for some applications. For example, a full mapping of a PHMRC dataset into the WHO format enables the use of physician provided conditional probabilities included in the InterVA software on data collected by PHMRC questionnaires. This remains as an important feature to be added to the package in the future.

Fitting VA cause-of-death assignment models

In this section, we demonstrate the model fitting process in the **openVA** package using two datasets: (1) a random sample of 1,000 deaths from the ALPHA network without cause-of-death labels collected with the WHO 2012 instrument, and (2) the adult VA records in the PHMRC gold standard data, with the 1,554 records from Andhra Pradesh, India used as a testing set and the rest used as a training dataset. In the first case without gold standard training data, only InterVA and InSilicoVA can be fitted. All four methods can be fitted in the second case.

Modeling data collected with WHO 2012 questionnaire

The randomly sampled VA records from the ALPHA network sites are already included in the **openVA** package as a dataset `RandomVA1` and can be loaded directly.

```
data(RandomVA1)
dim(RandomVA1)

#> [1] 1000 246

head(RandomVA1[, 1:10])

#>   ID elder midage adult child under5 infant neonate male female
#> 1 d1      Y                      Y
#> 2 d2      Y                      Y
#> 3 d3      Y                      Y
```

```
#> 4 d4          Y          Y
#> 5 d5          Y          Y
#> 6 d6          Y          Y
```

The `codeVA()` function provides a standardized syntax to fit different VA models. Internally, the `codeVA()` function organizes the input data according to the specified data type, checks for incompatibility of the data and specified model, and calls the corresponding model fitting functions. It returns a classed object of the specified model class. In this example, we use version 4.03 of the InterVA software, which is the latest release of the original software compatible with the WHO 2012 instrument. Any additional model-specific parameters can be passed through the arguments of `codeVA()`. Here we specify the HIV and malaria prevalence levels required by the InterVA model to be 'high'. Guidelines on how to set these parameters can be found in [Byass et al. \(2012\)](#).

```
fit_inter_who <- codeVA(data = RandomVA1, data.type = "WHO2012",
                      model = "InterVA", version = "4.03",
                      HIV = "h", Malaria = "h")
```

```
summary(fit_inter_who)
```

```
#> InterVA-4 fitted on 1000 deaths
#> CSMF calculated using reported causes by InterVA-4 only
#> The remaining probabilities are assigned to 'Undetermined'
#>
#> Top 5 CSMFs:
#>   cause                      likelihood
#> Undetermined                 0.154
#> HIV/AIDS related death      0.122
#> Stroke                      0.072
#> Reproductive neoplasms MF  0.058
#> Pulmonary tuberculosis     0.055
```

We can implement InSilicoVA method with similar syntax. We use the default parameters and run the MCMC for 10,000 iterations. Setting the `auto.length` argument to `FALSE` specifies that the algorithm does not automatically increase the length of the chain when convergence failed. In practice, we recommend setting this argument to `TRUE` if the algorithm displays warnings concerning MCMC convergence. The InSilicoVA algorithm is implemented using a Metropolis-Hastings within Gibbs sampler. The acceptance rate is printed as part of the message as the model samples from the posterior distribution.

```
fit_ins_who <- codeVA(RandomVA1, data.type = "WHO2012", model = "InSilicoVA",
                    Nsim = 10000, auto.length = FALSE)
```

```
summary(fit_ins_who)
```

```
#> InSilicoVA Call:
#> 1000 death processed
#> 10000 iterations performed, with first 5000 iterations discarded
#> 250 iterations saved after thinning
#> Fitted with re-estimated conditional probability level table
#> Data consistency check performed as in InterVA4
#>
#> Top 10 CSMFs:
#>   Mean Std.Error Lower Median Upper
#> Other and unspecified infect dis 0.266 0.0168 0.235 0.265 0.301
#> HIV/AIDS related death          0.102 0.0091 0.085 0.102 0.119
#> Renal failure                   0.101 0.0108 0.084 0.101 0.123
#> Other and unspecified neoplasms 0.062 0.0089 0.046 0.061 0.080
#> Other and unspecified cardiac dis 0.058 0.0076 0.044 0.058 0.075
#> Digestive neoplasms             0.050 0.0077 0.033 0.050 0.065
#> Acute resp infect incl pneumonia 0.048 0.0073 0.034 0.049 0.063
#> Pulmonary tuberculosis          0.039 0.0068 0.025 0.039 0.054
#> Stroke                         0.038 0.0061 0.027 0.038 0.052
#> Other and unspecified NCD       0.034 0.0089 0.018 0.034 0.052
```

Modeling the PHMRC data

In the second example, we consider a prediction task using the PHMRC adult dataset. We first load the complete PHMRC adult dataset from its on-line repository, and organize it into training and test datasets. We treat all deaths from Andhra Pradesh, India as the test dataset.

```
PHMRC_adult <- read.csv(getPHMRC_url("adult"))
is.test <- which(PHMRC_adult$site == "AP")
test <- PHMRC_adult[is.test, ]
train <- PHMRC_adult[-is.test, ]
dim(test)

#> [1] 1554  946

dim(train)

#> [1] 6287  946
```

In order to fit the models on the PHMRC data, we specify `data.type = "PHMRC"` and `phmrc.type = "adult"` to indicate the data input is collected using the PHMRC adult questionnaire. We also specify the column of the causes-of-death label in the training data. The rest of the syntax is similar to the previous example.

When the input consists of both training and testing data, the InterVA and InSilicoVA algorithms estimate the conditional probabilities of symptoms using the training data, instead of using the built-in values. In such case, the `version` argument for the InterVA algorithm is suppressed. There are several ways to map the conditional probabilities of symptoms given causes in the training dataset to a letter grade system, specified by the `convert.type` argument. The `convert.type = "quantile"` performs the mapping so that the percentile of each rank stays the same as the original $P_{s|c}$ matrix in InterVA software. Alternatively we can also use the original fixed values of translation, and assign letter grades closest to each entry in $\hat{P}_{s|c}$. This conversion is specified by `convert.type = "fixed"`, and is more closely aligned to the original InterVA and InSilicoVA setting. Finally, we can also directly use the values in the $\hat{P}_{s|c}$ without converting them to ranks and re-estimating the values associated with each rank. This can be specified by `convert.type = "empirical"`. In this demonstration, we assume the fixed value conversion.

```
fit_inter <- codeVA(data = test, data.type = "PHMRC", model = "InterVA",
  data.train = train, causes.train = "gs_text34",
  phmrc.type = "adult", convert.type = "fixed")

fit_ins <- codeVA(data = test, data.type = "PHMRC", model = "InSilicoVA",
  data.train = train, causes.train = "gs_text34",
  phmrc.type = "adult", convert.type = "fixed",
  Nsim=10000, auto.length = FALSE)
```

The NBC and Tariff method can be fit using similar syntax.

```
fit_nbc <- codeVA(data = test, data.type = "PHMRC", model = "NBC",
  data.train = train, causes.train = "gs_text34",
  phmrc.type = "adult")

fit_tariff <- codeVA(data = test, data.type = "PHMRC", model = "Tariff",
  data.train = train, causes.train = "gs_text34",
  phmrc.type = "adult")
```

Notice that we do not need to transform the PHMRC data manually. Data transformations are performed automatically within the `codeVA()` function.

Summarizing results

In this section we demonstrate how to summarize results, extract output, and visualize and compare fitted results. All the fitted object returned by `codeVA()` are S3 objects, for which a readable summary of model results can be obtained with the `summary()` function as shown in the previous section. In addition, several other metrics are commonly used to evaluate and compare VA algorithms at either the population or individual levels. In the rest of this section, we show how to easily calculate and visualize some of these metrics with the [openVA](#) package.

CSMF Accuracy

We can extract the CSMFs directly using the `getCSMF()` function. The function returns a vector of the point estimates of the CSMFs, or a matrix of posterior summaries of the CSMF for the InSilicoVA algorithm.

```
csmf_inter <- getCSMF(fit_inter)
csmf_ins <- getCSMF(fit_ins)
csmf_nbc <- getCSMF(fit_nbc)
csmf_tariff <- getCSMF(fit_tariff)
```

One commonly used metric to evaluate the CSMF estimates is the so-called CSMF accuracy, defined as

$$CSMF_{acc} = 1 - \frac{\sum_j^C CSMF_i - CSMF_j^{(true)}}{2(1 - \min CSMF^{(true)})}$$

The CSMF accuracy can be readily computed using functions in **openVA** as the codes below shows.

```
csmf_true <- table(c(test$gs_text34, unique(PHRC_adult$gs_text34))) - 1
csmf_true <- csmf_true / sum(csmf_true)
c(getCSMF_accuracy(csmf_inter, csmf_true, undet = "Undetermined"),
  getCSMF_accuracy(csmf_ins[, "Mean"], csmf_true),
  getCSMF_accuracy(csmf_nbc, csmf_true),
  getCSMF_accuracy(csmf_tariff, csmf_true))

#> [1] 0.53 0.74 0.77 0.68
```

We use the empirical distribution in the test data to calculate the true CSMF distribution, i.e., $CSMF_j^{(true)} = \frac{1}{n} \sum_{i=1}^n \mathbf{1}_{y_i=j}$. Then we evaluate the CSMF accuracy using the `getCSMF_accuracy()` function. As discussed previously, the default CSMF calculation is slightly different for different methods. For example, the InterVA algorithm creates the additional category of Undetermined by default, which is not in the true CSMF categories and needs to be specified. The creation of the undetermined category can also be suppressed by `interVA.rule = FALSE` in the `getCSMF()` function call. For the InSilicoVA algorithm, we use the posterior mean to calculate the point estimates of the CSMF accuracy.

Individual COD summary

At the individual level, we can extract the most likely cause-of-death assignment from the fitted object using the `getTopCOD()` function.

```
cod_inter <- getTopCOD(fit_inter)
cod_ins <- getTopCOD(fit_ins)
cod_nbc <- getTopCOD(fit_nbc)
cod_tariff <- getTopCOD(fit_tariff)
```

With the most likely COD assignment, other types of metrics based on individual COD assignment accuracy can be similarly constructed by users. The summary methods can also be called for each death ID. For example, using the Tariff method, we can extract the fitted rankings of causes for the death with ID 6288 by

```
summary(fit_inter, id = "6288")

#> InterVA-4 fitted top 5 causes for death ID: 6288
#>
#> Cause                Likelihood
#> Stroke                0.509
#> Pneumonia             0.318
#> COPD                  0.081
#> Other Infectious Diseases 0.064
#> Renal Failure         0.013
```

The `summary()` function for InSilcoVA does not provide uncertainty estimates for individual COD assignments by default. This is because, in practice, the calculation of individual posterior probabilities of COD distribution can be memory-intensive when the dataset is large. To obtain individual-level uncertainty measurements, we can either run the MCMC chain with the additional argument `indiv.CI = 0.95` when calling `codeVA()`, or update the fitted object directly with the saved posterior draws.

```

fit_ins <- updateIndiv(fit_ins, CI = 0.95)
summary(fit_ins, id = "6288")

#> InSilicoVA fitted top causes for death ID: 6288
#> Credible intervals shown: 95%
#>
#>      Mean Lower Median Upper
#> Stroke      0.5043 0.3485 0.5083 0.6361
#> Pneumonia    0.4116 0.2615 0.4083 0.5834
#> Other Infectious Diseases 0.0660 0.0411 0.0642 0.0966
#> Epilepsy     0.0099 0.0064 0.0097 0.0142
#> COPD         0.0053 0.0031 0.0052 0.0079
#> Malaria      0.0007 0.0005 0.0007 0.0011
#> Diabetes     0.0005 0.0003 0.0005 0.0009
#> Acute Myocardial Infarction 0.0004 0.0003 0.0004 0.0006
#> Falls        0.0004 0.0001 0.0004 0.0013
#> Renal Failure 0.0004 0.0002 0.0003 0.0005

```

For N deaths, C causes, the posterior mean of individual COD distributions returned by the InSilicoVA model, along with median and with credible intervals can be represented by a $(N \times C \times 4)$ -dimensional array. The function `getIndivProb()` extracts this summary in the form of a list of 4 matrices of dimension N by C , which can then be saved to other formats to facilitate further analysis. For other methods, the point estimates of individual COD distribution are returned as the N by C matrix.

```

fit_prob <- getIndivProb(fit_inter)
dim(fit_prob)

#> [1] 1554 34

```

Visualization

The previous sections discuss how results could be extracted and examined in R. In this subsection, we show some visualization tools provided in the [openVA](#) package for presenting these results. The fitted CSMFs for the top causes can be easily visualized by the `plotVA()` function. The default graph components are specific to each algorithm and individual package implementations, with options for further customization. For example, Figure 1 shows the estimated CSMF from the InterVA algorithm in the PHMRC data example.

```
plotVA(fit_inter, title = "InterVA")
```

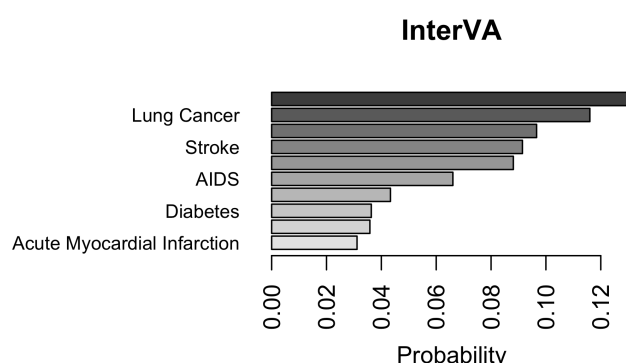


Figure 1: Top 10 CSMFs estimated by InterVA.

The CSMFs can also be aggregated for easier visualization of groups of causes. For the InterVA-4 cause list, we included an example grouping built into the package, so the aggregated CSMFs can be compared directly. In practice, the grouping of causes of deaths often needs to be determined according to context and the research question of interest. Changing the grouping can be easily achieved by modifying the grouping argument in the `stackplotVA()` function. For example, to facilitate the new category of Undetermined returned by InterVA, we first modify the grouping matrix to include it as a new cause and visualize the aggregated CSMF estimates in Figure 2.

```

data(SampleCategory)
grouping <- SampleCategory
grouping[,1] <- as.character(grouping[,1])
grouping <- rbind(grouping, c("Undetermined", "Undetermined"))
compare <- list(InterVA4 = fit_inter_who,
               InSilicoVA = fit_ins_who)
stackplotVA(compare, xlab = "", angle = 0, grouping = grouping)

```

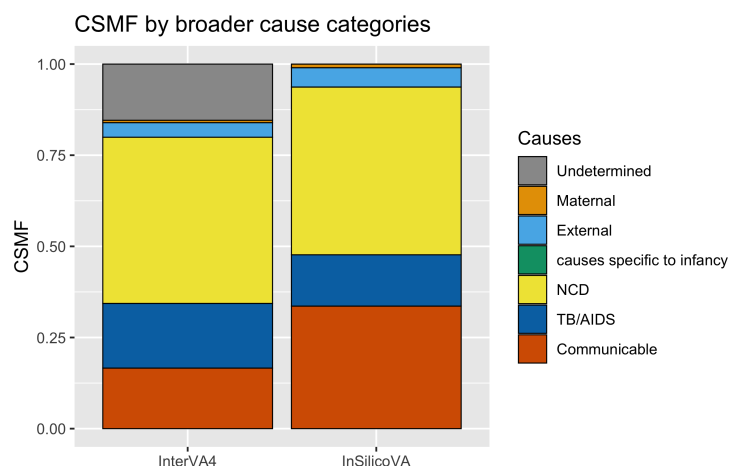


Figure 2: Estimated aggregated CSMFs for InterVA-4 and InSilicoVA, adding undetermined category.

The ordering of the stacked bars can also be changed to reflect the structures within the aggregated causes, as demonstrated in Figure 3.

```

group_order <- c("TB/AIDS", "Communicable", "NCD", "External", "Maternal",
               "causes specific to infancy", "Undetermined")
stackplotVA(compare, xlab = "", angle = 0, grouping = grouping,
            group_order = group_order)

```

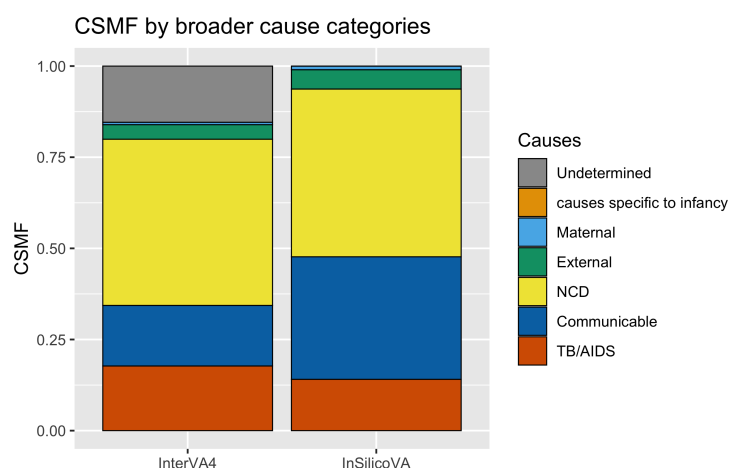


Figure 3: Estimated aggregated CSMFs for InterVA-4 and InSilicoVA, with the causes reordered.

Incorporating additional information

Among the VA methods discussed in this paper, the InSilicoVA algorithm (McCormick et al., 2016) allows for more flexible modifications to the Bayesian hierarchical model structure when additional information is available. In this section, we illustrate two features unique to the InSilicoVA method: jointly estimating CSMFs from multiple populations, and incorporating partial and potentially noisy physician codings into the algorithm.

Sub-population specific CSMFs

In practice researchers may want to estimate and compare CSMFs for different regions, time periods, or demographic groups in the population. Running separate models on subsets of data can be inefficient and does not allow parameter estimation to borrow information across different groups. The generative framework adopted by InSilicoVA allows the specification of sub-populations in analyzing VA data. Consider an input dataset with G different sub-populations. We can estimate different CSMFs $\pi^{(g)}$ for $g = 1, \dots, G$ for each sub-population, while assuming the same conditional probability matrix, $P_{s|c}$ and other hyperpriors. As an example, we show how to estimate different CSMFs for sub-populations specified by sex and age groups, using a randomly sampled ALPHA dataset with additional columns specifying the sub-population each death belongs to.

```
data(RandomVA2)
head(RandomVA2[, 244:248])

#>   stradm smobph scosts   sex age
#> 1      .      .      .  Men 60+
#> 2      .      .      . Women 60-
#> 3      .      .      . Women 60-
#> 4      .      .      . Women 60+
#> 5      .      .      . Women 60-
#> 6      .      .      . Women 60-
```

Then we can fit the model with one or multiple additional columns specifying sub-population membership for each observation.

```
fit_sub <- codeVA(RandomVA2, model = "InSilicoVA",
  subpop = list("sex", "age"), indiv.CI = 0.95,
  Nsim = 10000, auto.length = FALSE)
```

Functions discussed in the previous sections work in the same way for the fitted object with multiple sub-populations. Additional visualization tools are also available. Figure 4 plots the CSMFs for two sub-populations on the same plot by specify `type = "compare"`.

```
plotVA(fit_sub, type = "compare", title = "Comparing CSMFs", top = 3)
```

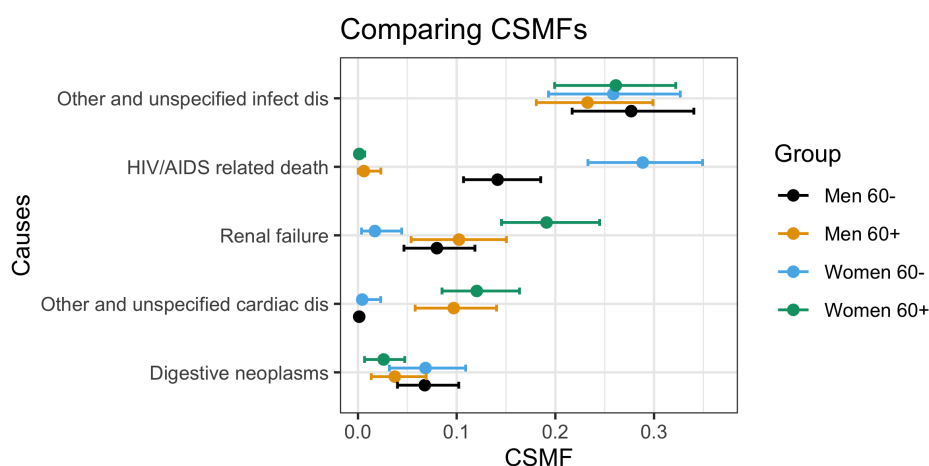


Figure 4: Estimated CSMFs for different sub-populations. The points indicate posterior means of the CSMF and the error bars indicate 95% credible intervals of the CSMF.

By default, the comparison plots will select all the CODs that are included in the top causes (specified by the `top` argument) for each of the sub-populations. We can also plot only subsets of them by specifying the causes of interest, as shown in Figure 5.

```
plotVA(fit_sub, type = "compare", title = "Comparing CSMFs",
  causelist = c("HIV/AIDS related death",
    "Pulmonary tuberculosis",
    "Other and unspecified infect dis",
    "Other and unspecified NCD"))
```

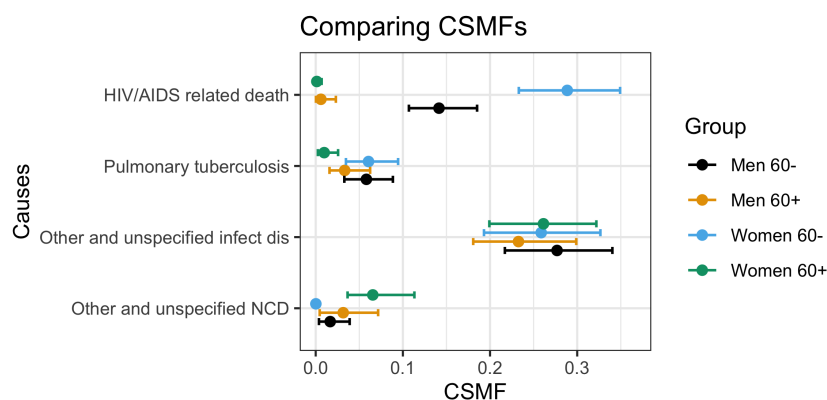


Figure 5: Estimated fraction of deaths due to selected CODs for different sub-populations. The points indicate posterior means of the CSMF and the error bars indicate 95% credible intervals of the CSMF.

Figure 6 shows the visualization of the top CSMFs for a chosen sub-population using the `which.sub` argument.

```
plotVA(fit_sub, which.sub = "Women 60-", title = "Women 60-")
```

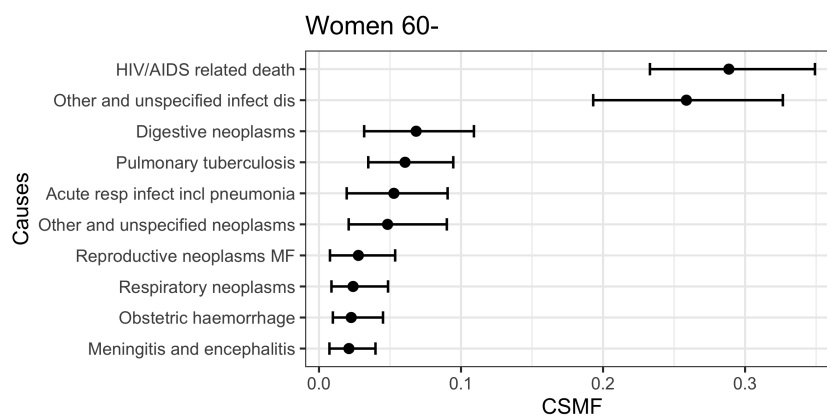


Figure 6: Top 10 CSMFs for a specified sub-population (women under 60 years old).

Similar to before, the `stackplotVA()` function can also be used to compare different sub-populations in aggregated cause groups, as shown in Figure 7.

```
stackplotVA(fit_sub)
stackplotVA(fit_sub, type = "dodge")
```

Physician coding

When physician-coded causes of death are available for all or a subset of the deaths, we can incorporate such information in the InSilicoVA model. The physician-coded causes can be either the same as the CODs used for the final algorithm, or consist of causes at a higher level of aggregation. When there is more than one physician code for each death and the physician identity is known, we can first de-bias the multiple codes provided from different physicians using the process described in [McCormick et al. \(2016\)](#). For the purpose of implementation, we only need to specify which columns are physician IDs, and which are their coded causes, respectively.

```
data(SampleCategory)
data(RandomPhysician)
head(RandomPhysician[, 245:250])
```

```
#> smobph scosts      code1 rev1      code2 rev2
#> 1      .      .      NCD doc9      NCD doc6
```

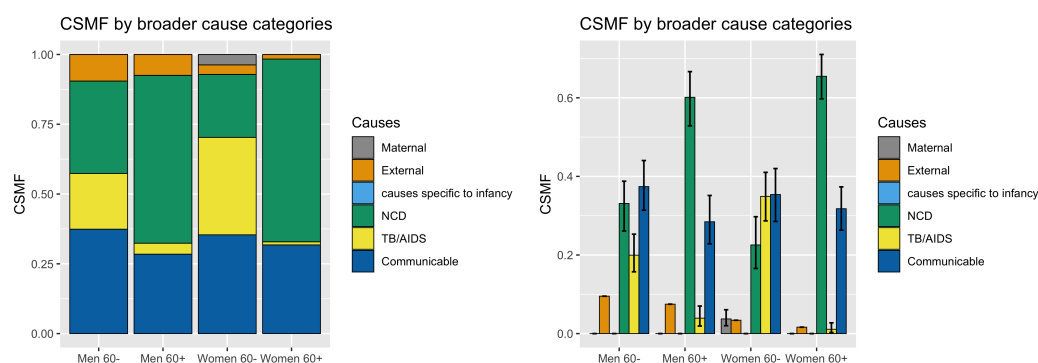



Figure 7: Aggregated CSMFs for four different sub-populations. Left: comparison using the stacked bar chart. Right: comparison using the bar chart arranged side to side. The height of the bars indicate posterior means of the CSMF and the error bars indicate 95% credible intervals of the CSMF.

```
#> 2      .      .      NCD doc4      NCD doc3
#> 3      .      .      NCD doc1      NCD doc5
#> 4      .      .      TB/AIDS doc4      TB/AIDS doc7
#> 5      .      .      TB/AIDS doc5      TB/AIDS doc9
#> 6      .      .      Communicable doc9      Communicable <NA>
```

```
doctors <- paste0("doc", c(1:15))
causelist <- c("Communicable", "TB/AIDS", "Maternal",
               "NCD", "External", "Unknown")
phydebias <- physician_debias(RandomPhysician,
                              phy.id = c("rev1", "rev2"), phy.code = c("code1", "code2"),
                              phylist = doctors, causelist = causelist, tol = 0.0001, max.itr = 100)
```

The de-biased step essentially creates a prior probability distribution for each death over the broader categories of causes. Then to run InSilicoVA with the de-biased physician coding, we can simply pass the fitted object from the previous step to the model. Additional arguments are needed to specify both the external cause category, since external causes are handled by separate heuristics, and the unknown category, which is equivalent to a uniform probability distribution over all other categories, i.e., the same as the case where no physician coding exists.

```
fit_ins_phy <- codeVA(RandomVA1, model = "InSilicoVA",
                     phy.debias = phydebias, phy.cat = SampleCategory,
                     phy.external = "External", phy.unknown = "Unknown",
                     Nsim = 10000, auto.length = FALSE)
```

Figure 8 compares the previous results without including physicians codes.

```
plotVA(fit_ins_who, title = "Without physician coding")
plotVA(fit_ins_phy, title = "With physician coding")
```

Removal of physically impossible causes

The originally proposed InSilicoVA assumes all causes of death are possible for each observation. The impact from such an assumption is mild when data are abundant, but could be problematic when either the sample size is small or the proportion of missing data is high. In both cases, physically impossible causes might get assigned with non-ignorable posterior mass. Since version 1.1.5 of **InSilicoVA**, when the input is in the WHO format, the algorithm automatically checks and removes impossible causes before fitting the model. The k -th cause is defined as physically impossible for the i -th death if $P(s_{ij} = 1 | y_i = k) = 0$ where s_{ij} is an indicator that the decedent belongs to a particular sex or age group. We then consider a cause to be physically impossible for the underlying population if it is impossible for all the observations in the input data. For example, with the new implementation, CSMF for pregnancy-related causes will not be estimated if the input data consist of only male deaths.

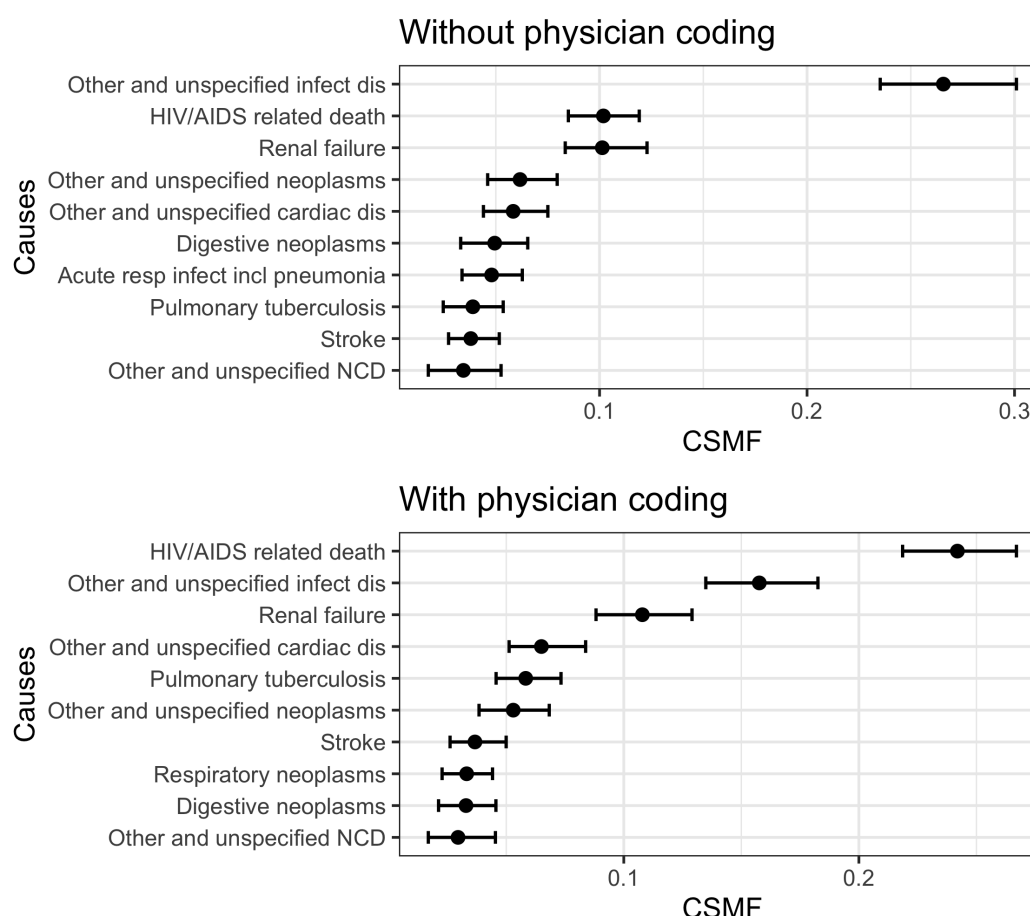


Figure 8: Comparing fitted CSMF with and without physicians

Other related software packages

Since the release of the [openVA](#) package on CRAN, there have been several new developments in both methodology and software that build on the [openVA](#) suite of packages and further extend its functionalities. Here we briefly survey some of the related methods, software packages, and ongoing work in the VA community that are related to [openVA](#).

First, the ability to easily fit and compare existing methods using the [openVA](#) package facilitated the development of several new VA methods in the last several years. Most of the development focuses on building statistical models to relax the conditional independence assumption of symptoms given a cause of death (e.g., [Li et al., 2020](#); [Kuniyama et al., 2020](#); [Moran et al., 2021](#); [Li et al., 2021](#); [Wu et al., 2021](#)). These methods tend to be computationally more demanding compared to the algorithms currently included in the [openVA](#) package, but usually provide improved inference. It is future work to include some of these latest developments in the [openVA](#) package for routine use. Most of these methods have publicly available implementations, such as the [farva](#) package ([Moran, 2020](#)) on GitHub. In another direction of research, a class of transfer learning methods focuses on building models to correct for bias in existing methods when predicting out of domain. These methods take the predicted cause of death assignments and distributions obtained with the [openVA](#) package and learn an ensemble of the predictions calibrated to the target population ([Datta et al., 2020](#); [Fiksel et al., 2021](#)). The [calibratedVA](#) package ([Fiksel and Datta, 2018](#)) is available to implement these models.

Outside of research community that develops new VA algorithms, [openVA](#) has also been used extensively by governments and health care organizations, particularly in locations that lack a strong vital registration system and use VA data to identify the leading causes of death. To facilitate the work of these users, [openVA](#) has been wrapped into a web application, the openVA App ([Thomas, 2021](#)), using the [shiny](#) package ([Chang et al., 2021](#)). The open source openVA App is available on GitHub and provides an intuitive interface to [openVA](#) that does not require one to learn R, but provides visual and tabular output produced by the different VA algorithms. It also runs the official Tariff algorithm by calling the Python source code of SmartVA-Analyze ([Institute for Health Metrics and Evaluation, 2021a](#)) and processing the output to be consistent with the other algorithms. The [openVA](#) R package

has also been a key component in a larger data analysis pipeline that pulls VA data from an Open Data Kit (ODK) Collect server and deposits the assigned causes of death to another server running the District Health Information Software 2 (DHIS2), which is a common information management system used in low and middle-income countries. This open-source software is implemented as a Python package, *openva-pipeline*, and is available on GitHub and the Python Package Index (Thomas et al., 2021a). Finally, the R package *CrossVA* (Thomas et al., 2020) and the Python package *pyCrossVA* (Choi et al., 2021) provide additional toolkits to convert raw VA data from its original format from the ODK server to the standardized formats discussed before. Both packages are open source and available on GitHub. The *pyCrossVA* package is also available on the Python Package Index.

Conclusion

In this paper, we introduce the *openVA* package. This is the first open-source software that implements and compares the major VA methods. The *openVA* package allows researchers to easily access the most recent tools that were previously difficult to work with or unavailable. It also enables the compatibility of multiple data input formats and significantly reduces the tedious work to pre-process different data formats specific to each algorithm. The software framework of the *openVA* package allows for the integration of new methods developed in the future. The *openVA* package makes all the steps involved in analyzing VA data – i.e., data processing, model tuning and fitting, summarizing results, and evaluation metrics – transparent and reproducible. This contributes significantly to the public health community using VA.

Finally, we make note of several features that will be helpful for future development. First, many users of the *openVA* package may not be familiar with the command line tools or do not have access to R on their local machines. A well designed graphical user interface can be very useful in such settings. The work on the shiny web application, *openVA app*, is a first step towards making the package more accessible. The authors intend to extend it to a better front end hosted on secure centralized servers. Second, although we aim to provide users with all the available methods for assigning causes of death, there is a lack of tools for comparing the accuracy and robustness between algorithms. Thus, much future work is needed to systematically assess, compare, and combine these methods in a better analytic framework. Finally, the development of VA algorithms is still an active area of research and it would be possible to extend the *openVA* suite to incorporate better VA algorithms and new types of data such as free-text narratives.

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