

# ‘eHDPrep’: an ‘R’ package for Electronic Health Data Quality Control and Semantic Enrichment

Tom Toner, Ian Overton

## Contents

<b>Quick Start</b>	<b>2</b>
<b>Introduction</b>	<b>2</b>
<b>Data</b>	<b>2</b>
<b>Quality control</b>	<b>3</b>
High level functions . . . . .	4
Data Import . . . . .	4
Assess input data quality . . . . .	4
Apply quality control . . . . .	7
Review of all quality control . . . . .	11
Data export . . . . .	13
Low level functions . . . . .	14
Measure completeness . . . . .	14
Internal consistency . . . . .	18
Merge variables . . . . .	19
Encoding missing values . . . . .	21
Encoding categorical data . . . . .	22
Encoding ordinal data . . . . .	22
Encoding genotype (SNP) data . . . . .	23
Extract information from free text variables . . . . .	24
Review quality control . . . . .	27
Encoding data as numeric matrix . . . . .	30
<b>Semantic enrichment</b>	<b>31</b>
Required inputs . . . . .	31
Example data . . . . .	32
High level functionality . . . . .	34
Low level functionality . . . . .	36
Convert edge table to ontology . . . . .	37
Join ontology and data variable names . . . . .	38
Compute meta-variable information . . . . .	39
Review meta-variables’ source variables . . . . .	41
Generate semantic aggregations . . . . .	42
<b>References</b>	<b>43</b>

## Quick Start

For quality control of health datasets, there are several high-level functions in ‘eHDPrep’:

1. `import_dataset()` - import the dataset in .csv, .tsv, or .xlsx format.
2. `assess_quality()` - assess data quality including diagnostics.
3. `apply_quality_ctrl()` - apply quality control measures to the dataset.
4. `review_quality_ctrl()` - review changes made during quality control.
5. `export_dataset()` - export dataset to .csv or .tsv format.

A synthetic example dataset, `example_data`, is used in this vignette and examples to demonstrate functionality.

‘eHDPrep’ also provides functionality for semantic enrichment with `semantic_enrichment()` where meta-variables are discovered from the semantic relationships between input variables as recorded in user-provided ontologies. A small ontology, `example_ontology`, is included with the package.

## Introduction

Data preparation is a key foundation for reliable analysis of health data, ‘eHDPrep’ has been developed for this purpose. The functionality is broadly divided between two themes:

- **Quality Control (QC)**
- **Semantic Enrichment (SE)**

Additionally, two “levels” of functions are provided:

- “High-level” functions wrap several “low-level” functions, allowing the user to perform fast, general quality control and SE. This is appropriate for inexperienced R users or those who require rapid data preparation.
- “Low-level” functions require more user interaction, but can be parameterised more extensively to accommodate specific aspects of a dataset. Some of the “low-level” functions are not provided in the “high-level” functions because they require additional user guidance; for example the merging function: `merge_cols()` (see **Merge variables**).

Finally, this package is built using several packages from the ‘tidyverse’ and follows its structures and grammars (Wickham et al. 2019). Therefore, the `data` object can typically be piped through the functions of ‘eHDPrep’ which will be modified as described in the function’s documentation and returned. We recommend that users have experience with the pipe operator and core ‘tidyverse’ packages before using ‘eHDPrep’.

## Data

We have created a small synthetic health dataset (a `tibble` named `example_data`) to demonstrate the functionality of this package. It contains 10 variables and 1000 observations and is documented in `?example_data`.

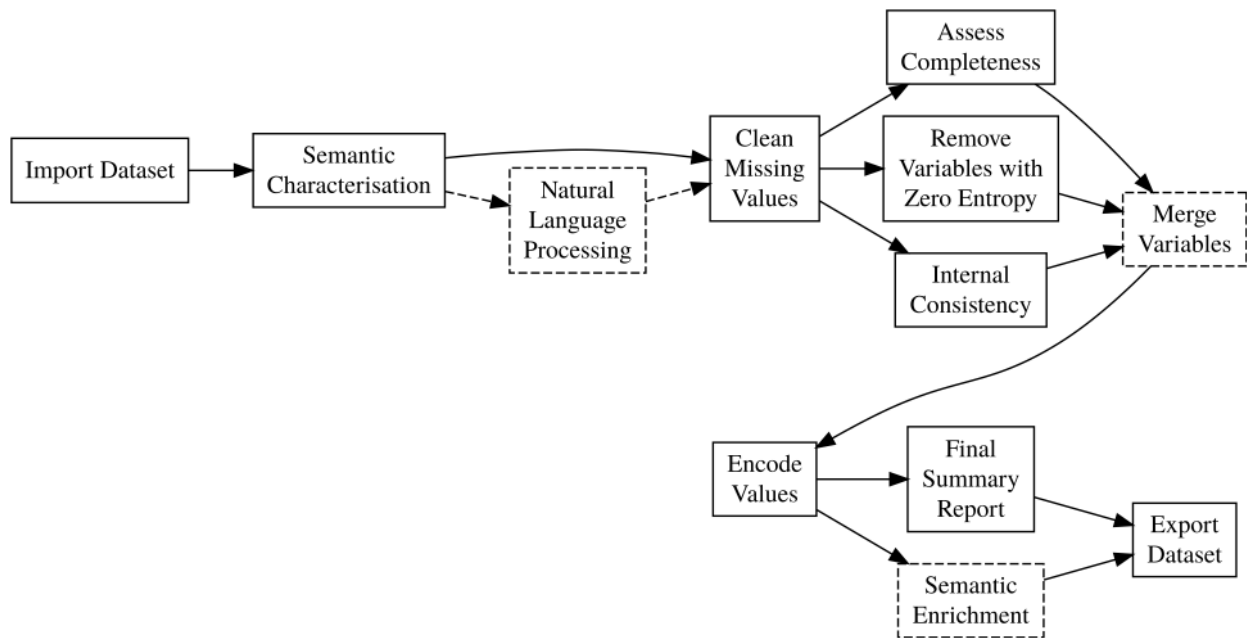
```

data(example_data)
tibble::glimpse(example_data)
#> Rows: 1,000
#> Columns: 12
#> $ patient_id      <int> 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 1~
#> $ tumoursize      <dbl> 61.71058, 64.18932, 47.81393, 40.93006, 62.11775, 13.64088, ~
#> $ t_stage         <chr> "T3a", "T3b", "T1", "T3a", "T4", "T1", "T1", "T3b", "T2", "T~
#> $ n_stage         <chr> "N2", "N1", "N2", "N0", "N1", "N2", "N2", "N1", "N1", "N0", ~
#> $ diabetes        <chr> "Yes", "Yes", "No", "No", "Yes", "No", "No", "No", "No", "No~
#> $ diabetes_type  <chr> "Type I", "Type II", "Type I", NA, "Type I", NA, NA, NA, NA, ~
#> $ hypertension   <chr> "Yes", "Yes", "Yes", "Yes", "No", "Yes", "No", "No", "Yes", ~
#> $ rural_urban     <chr> "rural", "urban", "rural", "rural", "urban", "urban", "urban~
#> $ marital_status <chr> "married", "divorced", "divorced", "single", "single", "sing~
#> $ SNP_a           <chr> "cc", "cc", "cc", "c", "gg", "g", "c", "gg", "g", "g", "gg", ~
#> $ SNP_b           <chr> "tt", "ta", "t", "tt", "t", "t", "t", "tt", "t", "a", "a", ~
#> $ free_text       <chr> "We need grain to keep our mules healthy.", "The gold ring f~

```

## Quality control

The quality control functions aim to assess, improve, and compare the quality of a dataset along multiple quality dimensions: completeness, validity, accuracy, consistency, and uniqueness (Roebuck 2011). A suggested workflow for quality control is shown below. The order of these steps is defined by dependency, where later steps benefit from earlier steps.



**Figure 1:** Suggested workflow of low-level quality control functions in eHDPRep. Dashed lines and boxes represent optional steps.

## High level functions

Quality control can be performed with little code using the high-level functions. It is suggested that the functions are applied in the order that they appear in this section.

### Data Import

'eHDPrep' provides methods to import a dataset into 'R' from several file types where functionality from `readxl` and `readr` is wrapped into the function `import_dataset()`:

```
# Not run, just examples:
#excel
data <- import_dataset(file = "./dataset.xlsx", format = "excel")
#csv
data <- import_dataset(file = "./dataset.csv", format = "csv")
#tsv
data <- import_dataset(file = "./dataset.tsv", format = "tsv")
```

### Assess input data quality

An initial assessment of a dataset's quality provides a good basis for its semantic characterisation in understanding variables which require particular attention during quality control. `assess_quality()` will return a list with three top-level elements.

1. A list of completeness measures:
  - i. A tibble describing row completeness
  - ii. A tibble describing variable (column) completeness
  - iii. A bar plot showing row and variable completeness
  - iv. A heatmap of completeness, clustered on both axes
  - v. A function to ensure completeness heatmap is plotted on a blank canvas
2. A report of internal inconsistencies (requires `consis_tbl` to be provided; see [Internal Consistency](#) for more information).
3. A character vector of variables with no entropy (contains only one unique value; see Shannon (1948)).

```
data(example_data)

# create a consistency table containing consistency rules
# below states: if a patient has a type of diabetes, they should have diabetes
ct <- tibble::tribble(~varA, ~varB, ~lgl_test, ~varA_boundaries, ~varB_boundaries,
  "diabetes_type", "diabetes", NA, "Type I", "Yes",
  "diabetes_type", "diabetes", NA, "Type II", "Yes")

res <- assess_quality(data = example_data, id_var = patient_id, consis_tbl = ct)
```

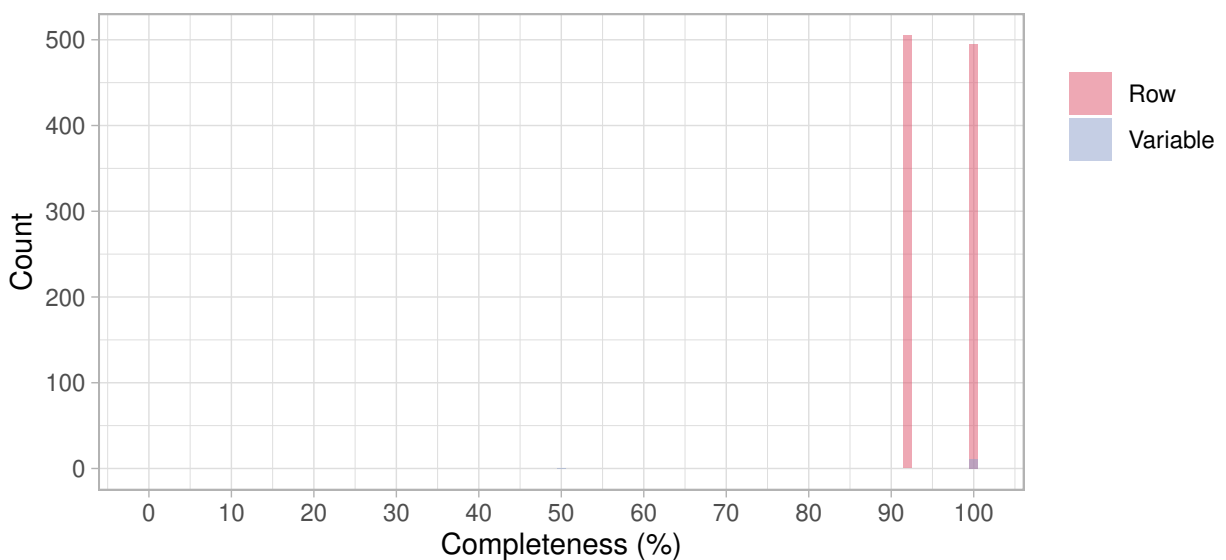
```
res$completeness$row_completeness
#> # A tibble: 1,000 x 4
#>   patient_id  NAs NAs_percent Completeness
#>   <chr>      <int>      <dbl>      <dbl>
```

```

#> 1 4          1      8.3      92.
#> 2 6          1      8.3      92.
#> 3 7          1      8.3      92.
#> 4 8          1      8.3      92.
#> 5 9          1      8.3      92.
#> 6 10         1      8.3      92.
#> 7 12         1      8.3      92.
#> 8 15         1      8.3      92.
#> 9 17         1      8.3      92.
#> 10 18        1      8.3      92.
#> # ... with 990 more rows
res$completeness$variable_completeness
#> # A tibble: 12 x 4
#>   Variable      NAs NAs_percent Completeness
#>   <chr>         <int>    <dbl>         <dbl>
#> 1 diabetes_type  505      50.          5.0e1
#> 2 patient_id     0         0             1 e2
#> 3 tumoursize     0         0             1 e2
#> 4 t_stage        0         0             1 e2
#> 5 n_stage        0         0             1 e2
#> 6 diabetes       0         0             1 e2
#> 7 hypertension   0         0             1 e2
#> 8 rural_urban    0         0             1 e2
#> 9 marital_status 0         0             1 e2
#> 10 SNP_a         0         0             1 e2
#> 11 SNP_b         0         0             1 e2
#> 12 free_text     0         0             1 e2

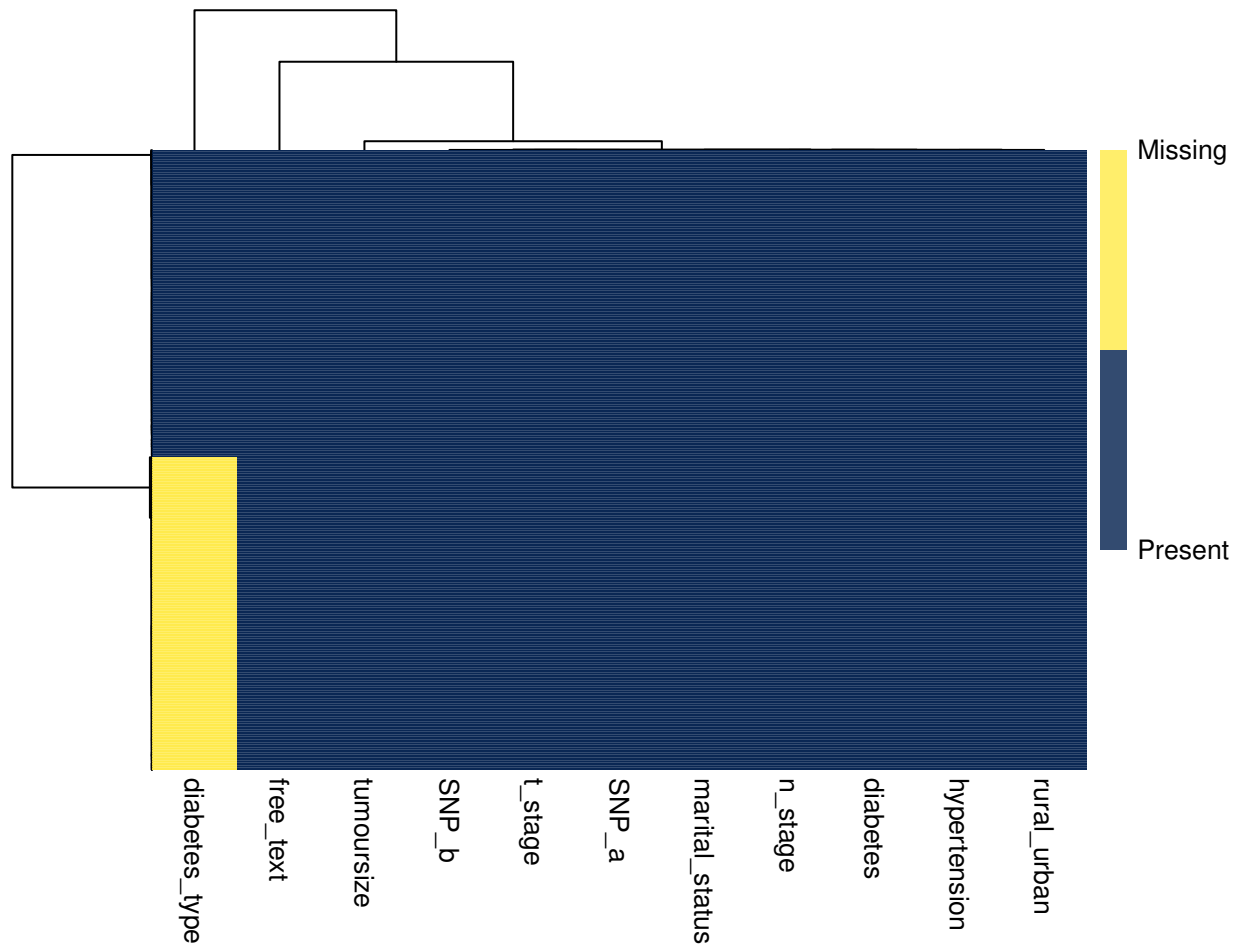
```

```
res$completeness$completeness_plot
```



**Figure 2:** Percentage completeness (x-axis) by count (y-axis) for both rows (red) and variables (purple) of 'example\_data'.

```
plot.new()
res$completeness$completeness_heatmap
```



**Figure 3:** Completeness heatmap for ‘example\_data’. Yellow cells represent missing values and blue cells represent non-missing values.

```
res$internal_inconsistency
#> # A tibble: 4 x 8
#>   var_a      var_b    lgl_test var_a_range var_b_range  row values_a
#>   <chr>      <chr>    <lgl>    <chr>      <chr>      <int> <chr>
#> 1 diabetes_type diabetes NA      Type I     Yes         3 Type I
#> 2 diabetes_type diabetes NA      Type I     Yes        190 Type I
#> 3 diabetes_type diabetes NA      Type I     Yes        873 Type I
#> 4 diabetes_type diabetes NA      Type II    Yes        715 Type II
#>   values_b
#>   <chr>
#> 1 No
#> 2 missing
#> 3 missing
#> 4 missing
```

```
res$vars_with_zero_entropy
#> character(0)
```

## Apply quality control

To apply quality control to a dataset in one function, as `apply_quality_ctrl()` does, it is important to ensure variables are processed appropriately according to their data type. 'R' and 'eHDPRep' suggest data types with `assume_var_classes()` which writes the results to a .csv file. The user can amend this externally and import back into 'R' with `import_var_classes()`.

```
tmp = tempfile(fileext = ".csv")
assume_var_classes(data = example_data, out_file = tmp)

# (user makes manual edits externally)

import_var_classes(file = tmp)
#> Rows: 12 Columns: 2
#> -- Column specification -----
#> Delimiter: ","
#> chr (2): var, datatype
#>
#> i Use `spec()` to retrieve the full column specification for this data.
#> i Specify the column types or set `show_col_types = FALSE` to quiet this message.
#> # A tibble: 12 x 2
#>   var          datatype
#>   <chr>         <chr>
#> 1 patient_id   integer
#> 2 tumoursize   numeric
#> 3 t_stage      character
#> 4 n_stage      character
#> 5 diabetes     character
#> 6 diabetes_type character
#> 7 hypertension character
#> 8 rural_urban  character
#> 9 marital_status character
#> 10 SNP_a       character
#> 11 SNP_b       character
#> 12 free_text   character
```

The permitted datatypes are: "id", "numeric", "double", "integer", "character", "factor", "ordinal", "ordinal\_tstage", "ordinal\_nstage", "genotype", "freetext", "logical". Note that ordinal variables are not modified by `apply_quality_ctrl()` as the ordinal classes would need to be specified for each variable. 'eHDPRep' provides two special ordinal data types "ordinal\_tstage" and "ordinal\_nstage" for two common cancer staging measures where the orders are precoded.

The data types for `example_data` are shown below:

```
data_types
#> # A tibble: 12 x 2
#>   var          datatype
#>   <chr>         <chr>
#> 1 patient_id   id
#> 2 tumoursize   numeric
```

```

#> 3 t_stage      ordinal_tstage
#> 4 n_stage      ordinal_nstage
#> 5 diabetes     factor
#> 6 diabetes_type factor
#> 7 hypertension factor
#> 8 rural_urban  factor
#> 9 marital_status factor
#> 10 SNP_a       genotype
#> 11 SNP_b       genotype
#> 12 free_text   freetext

```

Data types are modified as follows:

Data type	Modification Summary
id	Ignored
numeric	Ignored
double	Ignored
integer	Ignored
ordinal	Ignored
logical	Ignored
ordinal_tstage	Converted to ordered factor with predetermined levels
ordinal_nstage	Converted to ordered factor with predetermined levels
factor; character	<i>If &gt;2 categories:</i> converted to multiple variables using one-hot encoding (see <a href="#">Encoding categorical data</a> ). <i>If 2 categories, specified in <code>bin_cats</code> parameter:</i> converted to ordered factor with two levels (see <code>?encode_binary_cats</code> )
genotype	Converted to ordered factors using SNP allele frequency in the variable (see <a href="#">Encoding genotype (SNP) data</a> )
freetext	Groups of words which appear within two words each other in the variable with a minimum frequency of occurrence set by <code>min_freq</code> are converted to logical variables describing each group (see <a href="#">Extract information from free text variables</a> )

Quality Control with the function `apply_quality_control()` is performed upon the `example_data` with the following parameters (please see below):

- **data:** The dataset to be quality controlled.
- **id\_var:** The variable which identifies each row. Note it is not surrounded by quotes.
- **class\_tbl:** The object shown above describing variables' data types.
- **bin\_cats:** A character vector showing how variables with two options should be encoded with the syntax `negative_finding = positive_finding`. If positivity/negativity is not associated with the binary categories of a variable (e.g. `rural_urban` in `example_data`) then the ordering can be arbitrarily decided.
- **min\_freq:** The minimum frequency of occurrence for groups of proximal words in free-text variables. Those which meet this threshold are added as logical variables (see `?extract_freetext` and `?skipgram_append`). This is ignored if there are no free-text variables specified in `class_tbl`.



```

apply_quality_ctrl(data = example_data,
                  id_var = patient_id,
                  class_tbl = data_types,
                  bin_cats =c("No" = "Yes", "rural" = "urban"),
                  min_freq = 0.6)
#> # A tibble: 1,000 x 18
#>   patient_id tumoursize t_stage n_stage diabetes diabetes_type hypert~1 rural~2
#>   <dbl>      <dbl> <ord> <ord> <fct>      <chr>      <fct>      <fct>
#> 1         1         62. T3a   N2     Yes       Type I     Yes       rural
#> 2         2         64. T3b   N1     Yes       Type II    Yes       urban
#> 3         3         48. T1    N2     No        Type I     Yes       rural
#> 4         4         41. T3a   N0     No        <NA>      Yes       rural
#> 5         5         62. T4    N1     Yes       Type I     No        urban
#> 6         6         14. T1    N2     No        <NA>      Yes       urban
#> 7         7         63. T1    N2     No        <NA>      No        urban
#> 8         8         44. T3b   N1     No        <NA>      No        rural
#> 9         9         44. T2    N1     No        <NA>      Yes       rural
#> 10        10         32. T1    N0     No        <NA>      No        rural
#>   SNP_a SNP_b board_w~3 leas_~4 sixte~5 white~6 marit~7 marit~8 marit~9 marit~*
#>   <ord> <ord>      <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl>
#> 1 C/C   T/T         0     0     0     0     0     1     0     0
#> 2 C/C   A/T         0     0     0     0     1     0     0     0
#> 3 C/C   T/T         0     0     0     0     1     0     0     0
#> 4 C/C   T/T         0     0     0     0     0     0     1     0
#> 5 G/G   T/T         0     0     0     0     0     0     1     0
#> 6 G/G   T/T         0     0     0     0     0     0     1     0
#> 7 C/C   T/T         0     0     0     0     0     1     0     0
#> 8 G/G   T/T         0     0     0     0     0     0     1     0
#> 9 G/G   T/T         0     0     0     0     0     0     1     0
#> 10 G/G  A/A         0     0     0     0     0     1     0     0
#> # ... with 990 more rows, and abbreviated variable names 1: hypertension,
#> # 2: rural_urban, 3: board_will, 4: leas_ran, 5: sixteen_week, 6: white_back,
#> # 7: marital_status_divorced, 8: marital_status_married, 9: marital_status_single,
#> # *: marital_status_NA

```

The variables `diabetes` and `diabetes_type` demonstrate some of the limitations of using the high-level functions which do not support variable merging due to required additional user configuration. For this dataset, we can first merge the two diabetes variables using a low-level function (see `merge_cols()` in [Merge Variables](#)) before `apply_quality_ctrl()` to produce a dataset with higher uniqueness. Note the data types need to be updated to include the new merged variable:

Updated `class_tbl`:

```

data_types_diabetes_m
#> # A tibble: 11 x 2
#>   var          datatype
#>   <chr>        <chr>
#> 1 patient_id   id
#> 2 tumoursize   numeric
#> 3 t_stage      ordinal_tstage
#> 4 n_stage      ordinal_nstage
#> 5 diabetes_merged factor
#> 6 hypertension factor
#> 7 rural_urban  factor

```

```

#> 8 marital_status factor
#> 9 SNP_a genotype
#> 10 SNP_b genotype
#> 11 free_text freetext

```

Quality control using low-level function, `merge_cols()`, to merge variables (see [Merge Variables](#)):

```

require(magrittr) # for pipe: %>%
#> Loading required package: magrittr
example_data %>%
  # first merge diabetes variables
  merge_cols(primary_var = diabetes_type,
             secondary_var = diabetes,
             merge_var_name = "diabetes_merged",
             rm_in_vars = TRUE) %>%
  # pass data with diabetes_merged to high-level QC function
  apply_quality_ctrl(id_var = patient_id, class_tbl = data_types_diabetes_m,
                    bin_cats = c("No" = "Yes", "rural" = "urban")) ->
  post_QC_example_data
#> New names:
#> * `diabetes_merged_Type I` -> `diabetes_merged_Type.I`
#> * `diabetes_merged_Type II` -> `diabetes_merged_Type.II`

post_QC_example_data
#> # A tibble: 1,000 x 16
#>   patient_id tumoursize t_stage n_stage hypertension rural_urban SNP_a SNP_b
#>   <dbl>      <dbl> <ord> <ord> <fct>      <fct>      <ord> <ord>
#> 1         1         62. T3a  N2    Yes        rural      C/C    T/T
#> 2         2         64. T3b  N1    Yes        urban      C/C    A/T
#> 3         3         48. T1   N2    Yes        rural      C/C    T/T
#> 4         4         41. T3a  N0    Yes        rural      C/C    T/T
#> 5         5         62. T4   N1    No         urban      G/G    T/T
#> 6         6         14. T1   N2    Yes        urban      G/G    T/T
#> 7         7         63. T1   N2    No         urban      C/C    T/T
#> 8         8         44. T3b  N1    No         rural      G/G    T/T
#> 9         9         44. T2   N1    Yes        rural      G/G    T/T
#> 10        10         32. T1   N0    No         rural      G/G    A/A
#>   diabetes_merged_No diabetes~1 diabe~2 diabe~3 marit~4 marit~5 marit~6 marit~7
#>   <dbl>      <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl>
#> 1         0         1         0         0         0         1         0         0
#> 2         0         0         1         0         1         0         0         0
#> 3         0         1         0         0         1         0         0         0
#> 4         1         0         0         0         0         0         1         0
#> 5         0         1         0         0         0         0         1         0
#> 6         1         0         0         0         0         0         1         0
#> 7         1         0         0         0         0         1         0         0
#> 8         1         0         0         0         0         0         1         0
#> 9         1         0         0         0         0         0         1         0
#> 10        1         0         0         0         0         1         0         0
#> # ... with 990 more rows, and abbreviated variable names 1: diabetes_merged_Type.I,
#> # 2: diabetes_merged_Type.II, 3: diabetes_merged_NA, 4: marital_status_divorced,
#> # 5: marital_status_married, 6: marital_status_single, 7: marital_status_NA

```

The function `merge_cols()` may be run with the parameter `to_numeric_matrix = TRUE`, which automat-

ically converts the dataset to numeric values, facilitated by prior encoding of any **category**, **ordinal**, or **genotype** data:

```
example_data %>%
  # first merge diabetes variables
  merge_cols(primary_var = diabetes_type,
             secondary_var = diabetes,
             merge_var_name = "diabetes_merged",
             rm_in_vars = TRUE) %>%
  # pass data with diabetes_merged to high-level QC function
  apply_quality_ctrl(id_var = patient_id, class_tbl = data_types_diabetes_m,
                    bin_cats = c("No" = "Yes", "rural" = "urban"),
                    # Relevant line:
                    to_numeric_matrix = TRUE) ->
  post_QC_example_data_m
#> New names:
#> * `diabetes_merged_Type I` -> `diabetes_merged_Type.I`
#> * `diabetes_merged_Type II` -> `diabetes_merged_Type.II`

# concise summary of output:
tibble::glimpse(post_QC_example_data_m)
#> Rows: 1,000
#> Columns: 15
#> $ tumoursize      <dbl> 61.71058, 64.18932, 47.81393, 40.93006, 62.11775, 1~
#> $ t_stage         <dbl> 3, 4, 1, 3, 5, 1, 1, 4, 2, 1, 5, 4, 3, 2, 5, 3, 3, ~
#> $ n_stage         <dbl> 3, 2, 3, 1, 2, 3, 3, 2, 2, 1, 3, 1, 3, 1, 2, 2, 1, ~
#> $ hypertension   <dbl> 2, 2, 2, 2, 1, 2, 1, 1, 2, 1, 2, 1, 1, 1, 1, 2, 1, ~
#> $ rural_urban     <dbl> 1, 2, 1, 1, 2, 2, 2, 1, 1, 1, 2, 2, 2, 2, 2, 1, 1, ~
#> $ SNP_a           <dbl> 1, 1, 1, 1, 2, 2, 1, 2, 2, 2, 2, 1, 2, 1, 2, 2, 2, ~
#> $ SNP_b           <dbl> 2, 3, 2, 2, 2, 2, 2, 2, 2, 1, 1, 3, 1, 3, 2, 1, 2, ~
#> $ diabetes_merged_No <dbl> 0, 0, 0, 1, 0, 1, 1, 1, 1, 1, 0, 1, 0, 0, 1, 0, 1, ~
#> $ diabetes_merged_Type.I <dbl> 1, 0, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 1, 0, 0, 1, 0, ~
#> $ diabetes_merged_Type.II <dbl> 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, ~
#> $ diabetes_merged_NA <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, ~
#> $ marital_status_divorced <dbl> 0, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, ~
#> $ marital_status_married <dbl> 1, 0, 0, 0, 0, 0, 1, 0, 0, 1, 1, 1, 1, 0, 1, 0, 1, ~
#> $ marital_status_single <dbl> 0, 0, 0, 1, 1, 1, 0, 1, 1, 0, 0, 0, 0, 1, 0, 0, 0, ~
#> $ marital_status_NA <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, ~
```

This is useful for preparation for later analysis, including machine learning applications, or for further preparation with **Semantic Enrichment**.

## Review of all quality control

‘eHDPRep’ provides functionality for users to review the results of quality control operations that have been applied to the input data. `review_quality_ctrl()` provides information of quality control modifications at multiple levels of detail.

```
qc_review <- review_quality_ctrl(before_tbl = example_data,
                                after_tbl = post_QC_example_data,
                                id_var = patient_id)
```

The `variable_level_changes` list element is a tibble with variable names in the first column. The second column can contain up to three unique values describing the presence of the variable in the post-quality control dataset (Added, Removed, Preserved):

```
qc_review$variable_level_changes
#> # A tibble: 20 x 2
#>   variable           presence
#>   <chr>              <chr>
#> 1 patient_id        Preserved
#> 2 tumoursize        Preserved
#> 3 t_stage           Preserved
#> 4 n_stage           Preserved
#> 5 diabetes          Removed
#> 6 diabetes_type     Removed
#> 7 hypertension     Preserved
#> 8 rural_urban       Preserved
#> 9 marital_status    Removed
#> 10 SNP_a            Preserved
#> 11 SNP_b            Preserved
#> 12 free_text        Removed
#> 13 diabetes_merged_No Added
#> 14 diabetes_merged_Type.I Added
#> 15 diabetes_merged_Type.II Added
#> 16 diabetes_merged_NA Added
#> 17 marital_status_divorced Added
#> 18 marital_status_married Added
#> 19 marital_status_single Added
#> 20 marital_status_NA Added
```

The `value_level_changes` element is a tibble which shows changes made during quality control where each row records a value modification:

```
qc_review$value_level_changes
#> # A tibble: 2,019 x 6
#>   patient_id new_var old_var old_value new_value mod_type
#>   <chr>      <chr> <chr> <chr>    <chr>    <chr>
#> 1 31         t_stage t_stage equivocal <NA>      Removal
#> 2 34         t_stage t_stage equivocal <NA>      Removal
#> 3 44         t_stage t_stage equivocal <NA>      Removal
#> 4 48         t_stage t_stage equivocal <NA>      Removal
#> 5 261        t_stage t_stage equivocal <NA>      Removal
#> 6 263        t_stage t_stage equivocal <NA>      Removal
#> 7 348        t_stage t_stage equivocal <NA>      Removal
#> 8 454        t_stage t_stage equivocal <NA>      Removal
#> 9 468        t_stage t_stage equivocal <NA>      Removal
#> 10 569        t_stage t_stage equivocal <NA>      Removal
#> # ... with 2,009 more rows

# summary of above
qc_review$value_level_changes %>%
  dplyr::distinct(across(!patient_id))
#> # A tibble: 13 x 5
#>   new_var old_var old_value new_value mod_type
#>   <chr>   <chr>   <chr>    <chr>    <chr>
```

```

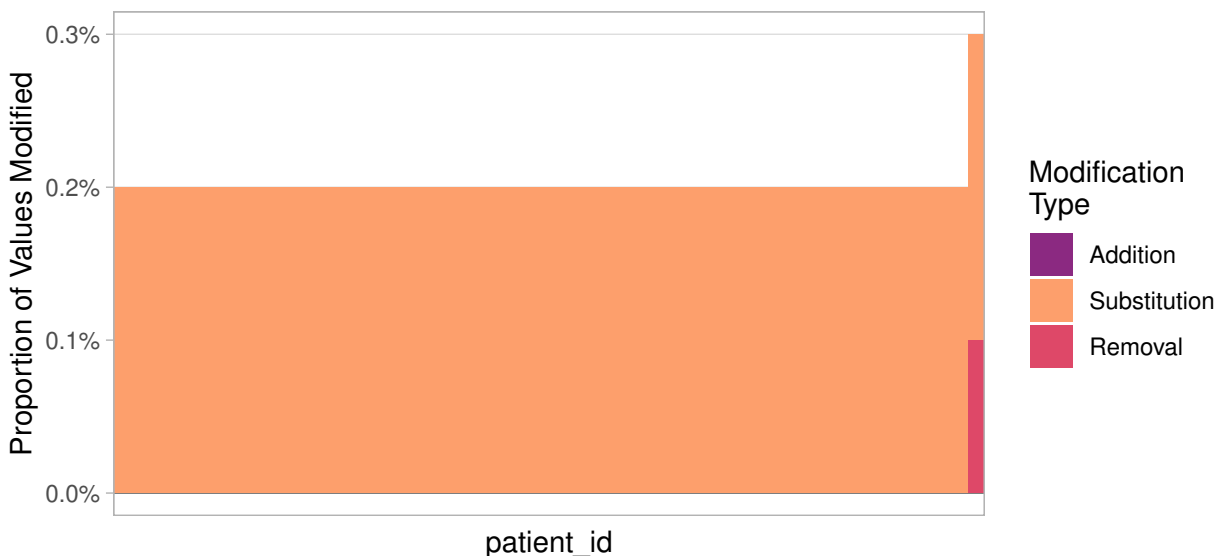
#> 1 t_stage t_stage equivocal <NA> Removal
#> 2 SNP_a SNP_a cc C/C Substitution
#> 3 SNP_a SNP_a c C/C Substitution
#> 4 SNP_a SNP_a gg G/G Substitution
#> 5 SNP_a SNP_a g G/G Substitution
#> 6 SNP_a SNP_a gc C/G Substitution
#> 7 SNP_a SNP_a cg C/G Substitution
#> 8 SNP_b SNP_b tt T/T Substitution
#> 9 SNP_b SNP_b ta A/T Substitution
#> 10 SNP_b SNP_b t T/T Substitution
#> 11 SNP_b SNP_b a A/A Substitution
#> 12 SNP_b SNP_b at A/T Substitution
#> 13 SNP_b SNP_b aa A/A Substitution

```

Note in the above that “gc” has been encoded, via `encode_genotypes()`, as “C/G” to create a standard representation of this SNP allele. Positional information for SNP allele should be recorded elsewhere, if required.

The `value_level_changes_plt` element visualises the content of the `value_level_changes` element. It is a bar plot with rows on the x-axis and the proportion of each row’s values which were modified (removed, substituted, or added) on the y-axis. This can be useful when many changes have occurred and the source table contains a large amount of data.

```
qc_review$value_level_changes_plt
```



**Figure 4:** Proportion of values modified per patient in ‘example\_data’ following quality control. This plot summarises the modifications made to the data during quality control.

## Data export

Modified data can be exported with `export_dataset()` as either `.csv` or `.tsv`:

```

#csv
export_dataset(x = post_QC_example_data,
              file = "./post_QC_example_data.csv",
              format = "csv")

#tsv
export_dataset(x = post_QC_example_data,
              file = "./post_QC_example_data.csv",
              format = "tsv")

```

## Low level functions

This section describes functions that can provide more granular access to the ‘eHDPrep’ quality control operations. While the functionality is largely available within ‘high-level’ functions, directly calling low-level functions provides greater scope to adjust individual parameter values and allows for finer-grained assessment of each step in the quality control process. Operations that may only be performed using low-level functions are: `merge_cols()`, `compare_info_content()`, `compare_info_content_plt()` (see [Merge variables](#)).

## Measure completeness

Completeness in variables and rows can be calculated in tibbles and visualised in a bar plot as shown below:

```

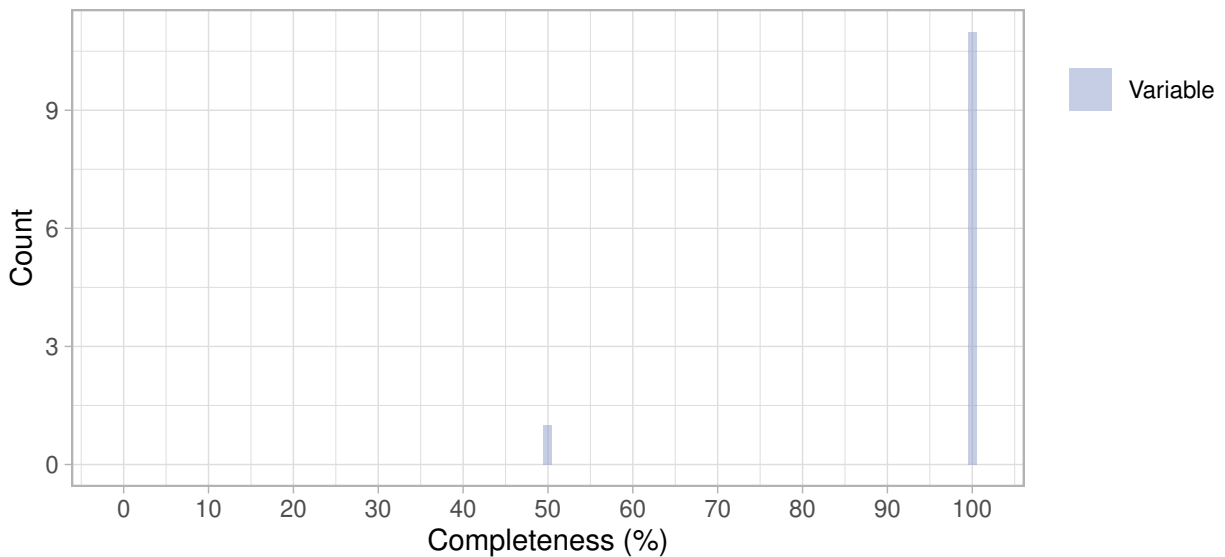
variable_completeness(example_data)
#> # A tibble: 12 x 4
#>   Variable      NAs NAs_percent Completeness
#>   <chr>         <int>      <dbl>         <dbl>
#> 1 diabetes_type    505         50.         5.0e1
#> 2 patient_id        0            0            1 e2
#> 3 tumoursize        0            0            1 e2
#> 4 t_stage           0            0            1 e2
#> 5 n_stage           0            0            1 e2
#> 6 diabetes          0            0            1 e2
#> 7 hypertension     0            0            1 e2
#> 8 rural_urban       0            0            1 e2
#> 9 marital_status   0            0            1 e2
#> 10 SNP_a            0            0            1 e2
#> 11 SNP_b            0            0            1 e2
#> 12 free_text        0            0            1 e2

row_completeness(data = example_data, id_var = patient_id)
#> # A tibble: 1,000 x 4
#>   patient_id  NAs NAs_percent Completeness
#>   <chr>       <int>      <dbl>         <dbl>
#> 1 4            1         8.3           92.
#> 2 6            1         8.3           92.
#> 3 7            1         8.3           92.
#> 4 8            1         8.3           92.
#> 5 9            1         8.3           92.
#> 6 10           1         8.3           92.
#> 7 12           1         8.3           92.
#> 8 15           1         8.3           92.
#> 9 17           1         8.3           92.
#> 10 18          1         8.3           92.

```

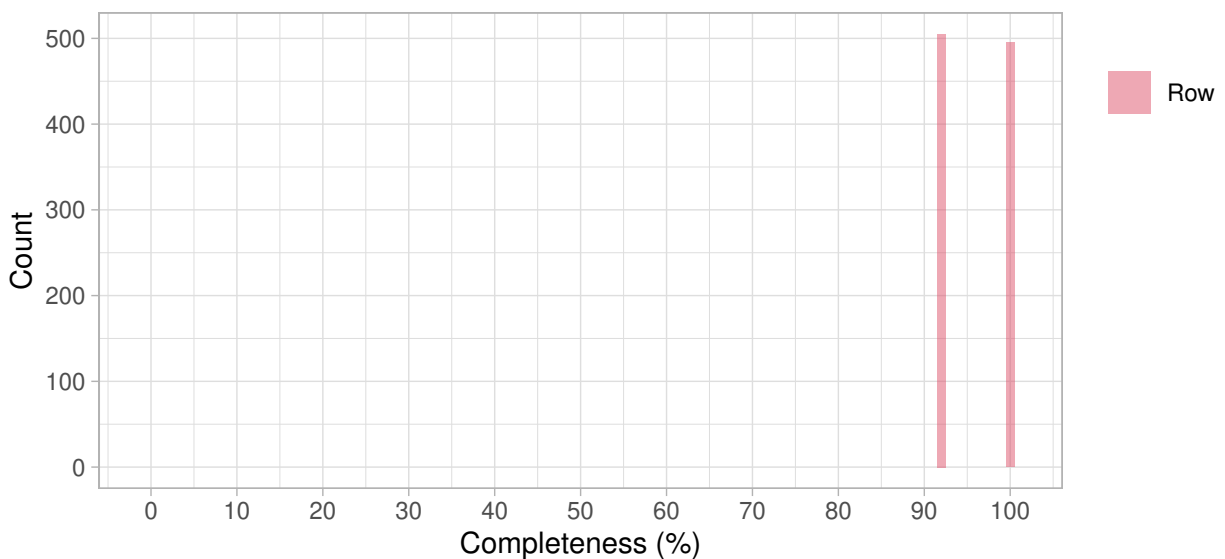
```
#> # ... with 990 more rows
```

```
plot_completeness(data = example_data, id_var = patient_id, plot = "variables")
```



**Figure 5:** Percentage completeness (x-axis) by count (y-axis) for variables of ‘example\_data.’

```
plot_completeness(data = example_data, id_var = patient_id, plot = "rows")
```



**Figure 6:** Percentage completeness (x-axis) by count (y-axis) for rows of ‘example\_data.’

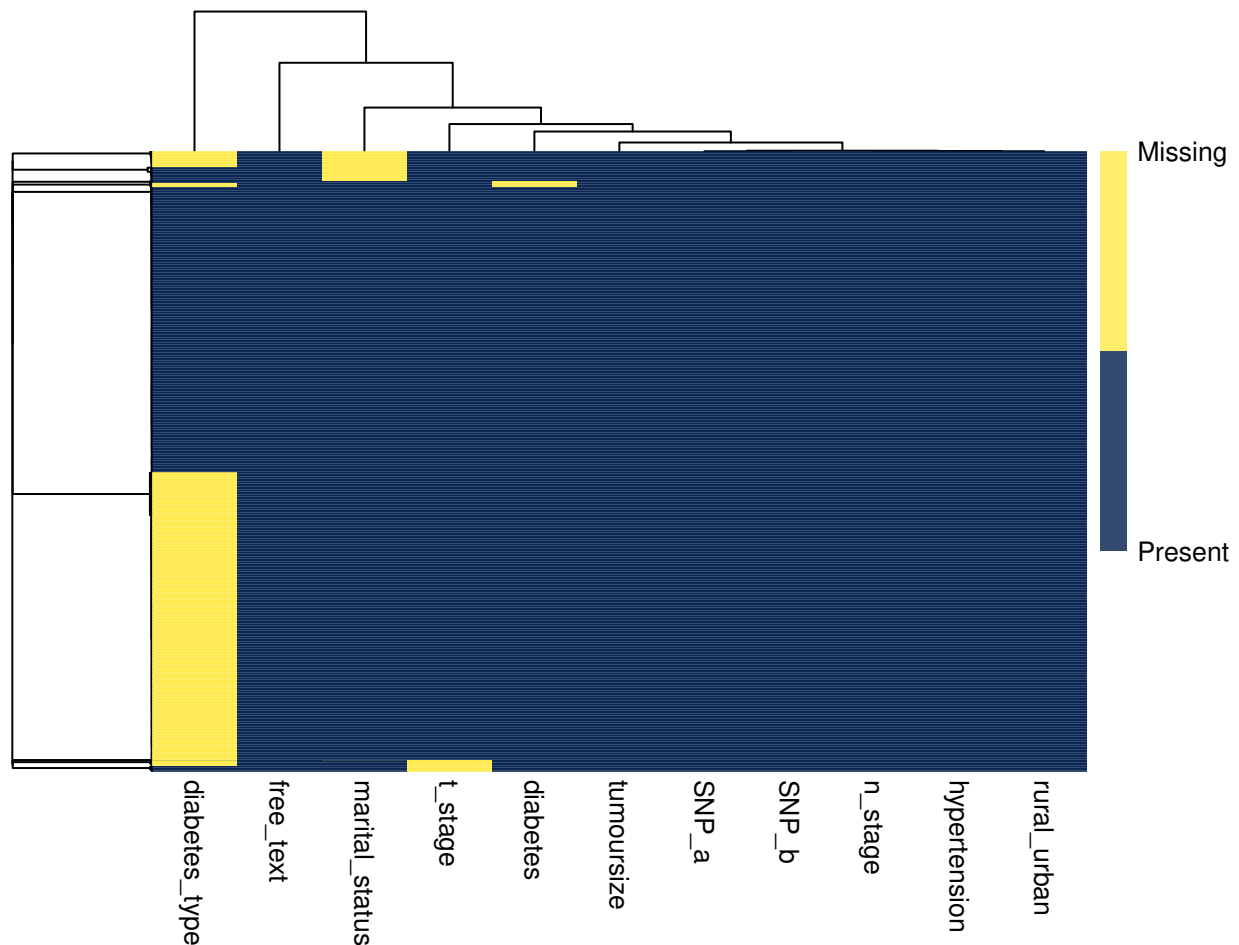
An overview of the dataset completeness is generated by `completeness_heatmap()` which utilises ‘pheatmap’ (Kolde 2019). Additional parameters are passed to `pheatmap()` through `...` (see `?pheatmap` for all options). Additional parameters are supplied in creating the heatmap below where the row names are hidden because they clutter the plot. The completeness heatmap may be useful for identifying structural patterns in the missingness, for example

indicative of non-random missingness. There are three underlying methods which are used to encode the data so that non-numeric data can be visualised:

1. (Default). Missing values are numerically encoded with a highly negative number, numerically distant from all values in data. Non-missing values in categorical variables are replaced with the number of unique values in the variable. Clustering uses these values. Cells are coloured by presence (yellow = missing; blue = present).
2. Same as 1 but cells are coloured by the values input to the clustering algorithm (instead of missing or present).
3. Boolean values are used for clustering (present values = 1; missing values = 0). Cells are coloured by presence (yellow = missing; blue = present).

```
# show_rownames is passed to pheatmap() through the `...` parameter
hm <- completeness_heatmap(data = strings_to_NA(example_data),
                           id_var = patient_id,
                           show_rownames = F)

plot.new()
hm
```



**Figure 7:** Completeness heatmap of ‘example\_data’ after pre-defined strings have been converted to ‘NA’. Yellow cells represent missing values and blue cells represent non-missing values.

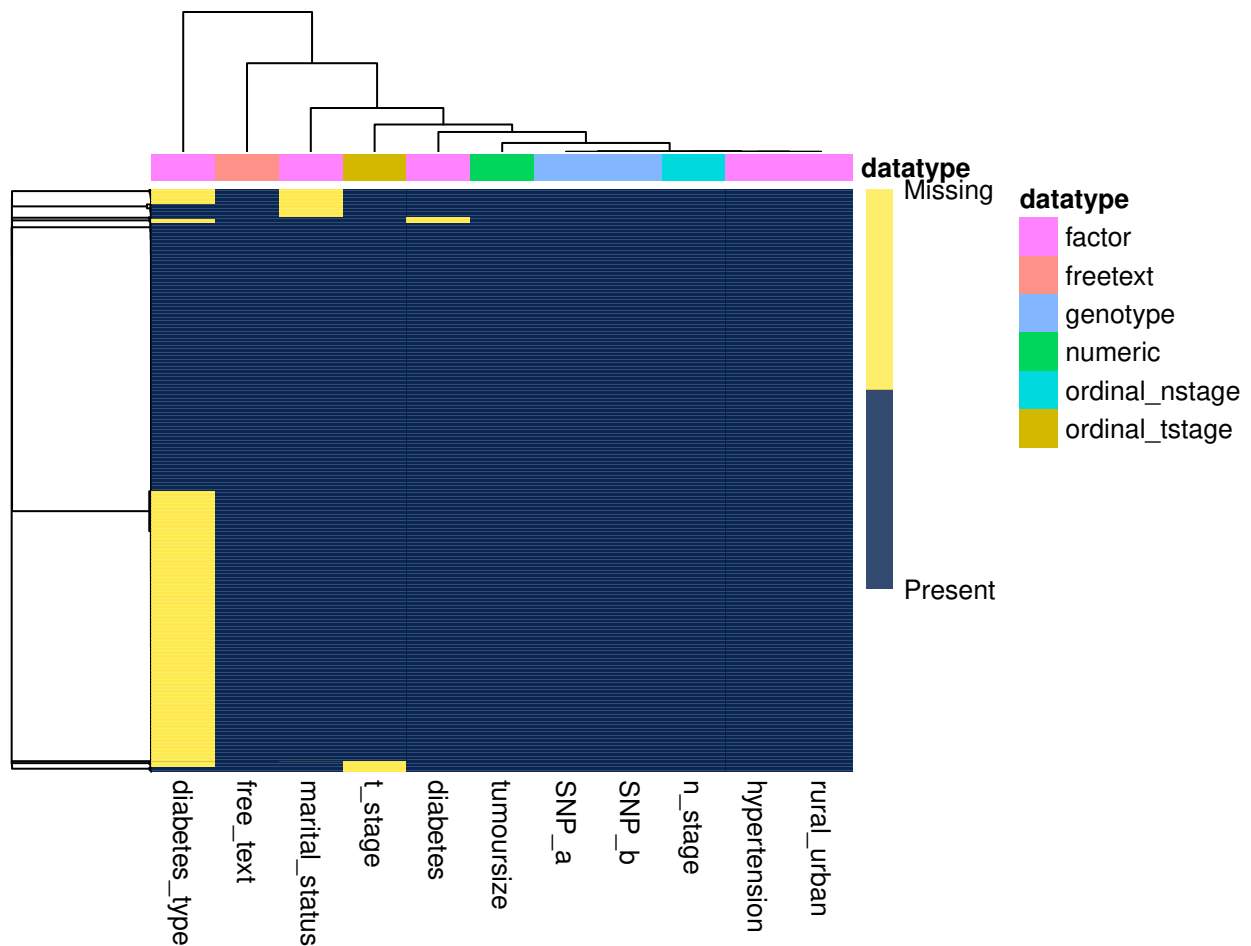
Variable-level annotations can be provided with the `annotation_tbl` parameter to further characterise



completeness patterns. Below, the `data_types` tibble is used:

```
hm <- completeness_heatmap(data = strings_to_NA(example_data),
  id_var = patient_id,
  show_rownames = FALSE,
  annotation_tbl = data_types)

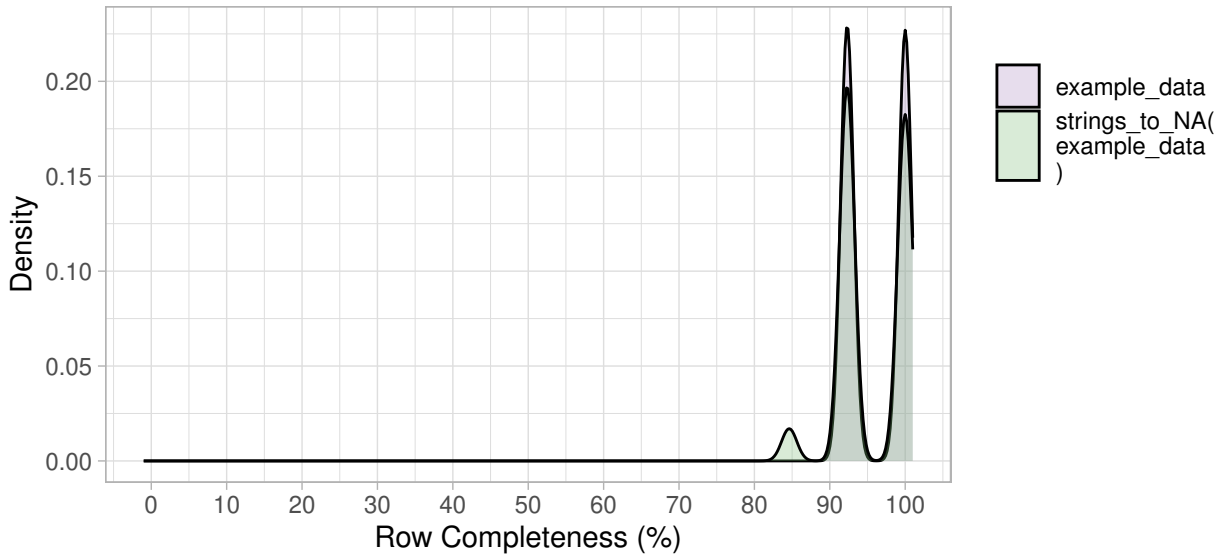
plot.new()
hm
```



**Figure 8:** Completeness heatmap of ‘example\_data’ after pre-defined strings have been converted to ‘NA’. Yellow cells represent missing values and blue cells represent non-missing values. Variables are annotated by their data type.

Comparison of dataset completeness before and after quality control is available using the `compare_completeness()` function. The plot below reveals a decrease in reported completeness following quality control because the input `example_data` encoded missingness as strings (for example ‘not recorded’) which were converted to NA values during quality control.

```
compare_completeness(tbl_a = example_data, tbl_b = strings_to_NA(example_data),
  dim = 1, tbl_a_lab = "example_data",
  tbl_b_lab = "strings_to_NA(\nexample_data\n)")
```



**Figure 9:** Density plot comparing percentage row completeness of ‘example\_data‘ before specified strings have been converted to ‘NA‘ (purple) and after (green).

### Internal consistency

Relationships between the values of different, but related, variables for a given patient may be used to define rules that identify internal inconsistencies. For example the `number_of_lymph_nodes` examined should be greater than or equal to the `number_of_positive_lymph_nodes`. `identify_inconsistency()` can test pairs of variables in multiple ways:

1. Logical operators (<, <=, ==, !=, >=, >)
2. Comparing permitted categories (e.g. cat1 in varA only if cat2 in varB)
3. Comparing permitted numeric ranges (e.g. 20-25 in varC only if 10-20 in varD)
4. Mixtures of 2 and 3 (e.g. cat1 in varA only if 20-25 in varC)

The internal consistency tests rely on such rules being specified in a separate data frame (argument: `consis_tbl`). An example of this type of table is shown below. Column headers are not important but column order is important. See `?validate_consistency_tbl` for all requirements.

```
example_incon_rules <- tibble::tribble(~varA, ~varB, ~lgl_test, ~varA_boundaries, ~varB_boundaries,
                                     "diabetes_type", "diabetes", NA, "Type I", "Yes",
                                     "diabetes_type", "diabetes", NA, "Type II", "Yes"
                                     )

example_incon_rules
#> # A tibble: 2 x 5
#>   varA      varB    lgl_test varA_boundaries varB_boundaries
#>   <chr>    <chr>    <lgl>    <chr>          <chr>
#> 1 diabetes_type diabetes NA          Type I         Yes
#> 2 diabetes_type diabetes NA          Type II        Yes
```

These rules are interpreted as:

- in rows where `diabetes_type` equals `Type I`, `diabetes` should equal `Yes`.
- in rows where `diabetes_type` equals `Type II`, `diabetes` should equal `Yes`.

Note: The order of variables in each row is important here, switching `diabetes` and `diabetes_type` in the first row of `example_incon_rules` would be interpreted as where `diabetes` equals `Yes`, `diabetes_type` should always equal `Type I`.

This format of a user-defined consistency table should be validated as shown below:

```
# validate the consistency rule table
validate_consistency_tbl(data = example_data, consis_tbl = example_incon_rules)
#> Consistency table is valid.
```

The tests are run against the data and all instances (rows). When no inconsistencies are found, a confirmatory message is returned along with the data (invisibly). However, when inconsistencies are found, a warning is thrown and a table detailing the inconsistencies is returned:

```
identify_inconsistency(data = example_data, consis_tbl = example_incon_rules)
#> Warning: One or more inconsistencies were identified. They are shown in the
#> returned tibble.
#> # A tibble: 4 x 8
#>   var_a      var_b    lgl_test var_a_range var_b_range  row values_a
#>   <chr>      <chr>    <lgl>    <chr>      <chr>      <int> <chr>
#> 1 diabetes_type diabetes NA      Type I      Yes          3 Type I
#> 2 diabetes_type diabetes NA      Type I      Yes         190 Type I
#> 3 diabetes_type diabetes NA      Type I      Yes         873 Type I
#> 4 diabetes_type diabetes NA      Type II     Yes         715 Type II
#>   values_b
#>   <chr>
#> 1 No
#> 2 missing
#> 3 missing
#> 4 missing
```

The first five columns represent the rules set in `consis_tbl`. The additional columns describe:

6. The inconsistent row(s)
7. The value in the variable reported in column 1
8. The value in the variable reported in column 2 (inconsistent with the corresponding value in the variable in column 1, given the rules in `consis_tbl`).

## Merge variables

Merging variables can improve the uniqueness and completeness of the dataset, also reducing its dimensionality. In `example_data`, `diabetes` and `diabetes_type` record observations of the same disease at different levels and are merged below:

```
merge <- merge_cols(data = example_data,
                    primary_var = diabetes_type,
                    secondary_var = diabetes,
                    merge_var_name = "diabetes_merged")
```

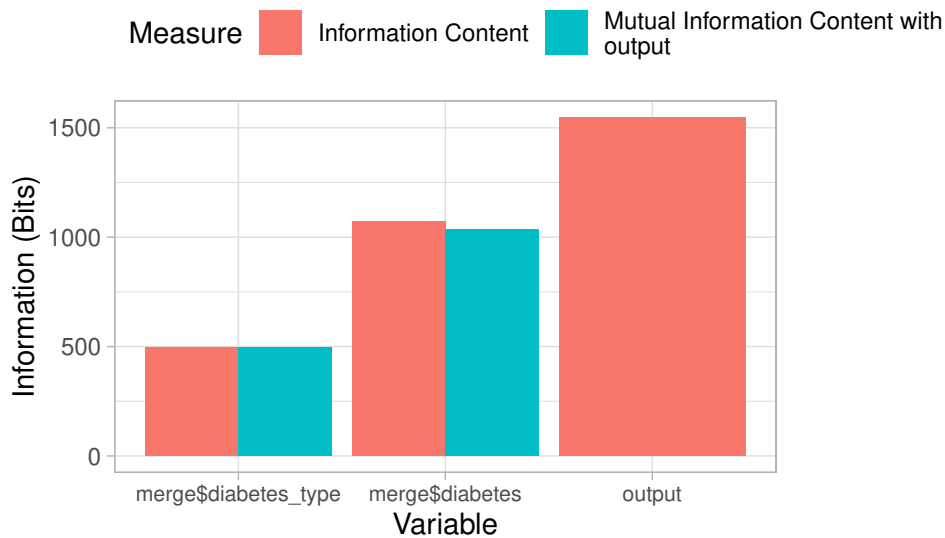
By default, the input variables (e.g. `diabetes` and `diabetes_type`) are preserved. They can be removed with the parameter `rm_in_vars = TRUE`.

`compare_info_content` and `compare_info_content_plt` can support merging strategies by identifying when a pairwise merge operation results in loss of information:

```
merge_IC <- compare_info_content(input1 = merge$diabetes,
                               input2 = merge$diabetes_type,
                               composite = merge$diabetes_merged)

merge_IC
#> # A tibble: 5 x 3
#>   Information Variable Measure
#>   <chr>      <chr>      <chr>
#> 1 1070.74650282141 merge$diabetes "Information Content"
#> 2 494.9635676875 merge$diabetes_type "Information Content"
#> 3 1548.12947181663 output "Information Content"
#> 4 1035.17075316701 merge$diabetes "Mutual Information Content with\noutput"
#> 5 494.9635676875 merge$diabetes_type "Mutual Information Content with\noutput"

compare_info_content_plt(compare_info_content_res = merge_IC)
```



**Figure 10:** Comparison of information content between two input variables and each input variable’s mutual information with the merged variable (output). This plot can inform variable merging strategies. Mutual information of ‘mergediabetes’with‘output’islowerthaninformationcontentof‘mergediabetes’ which informs the user that some information loss has occurred in this merging strategy.

In the above bar chart, the variable `diabetes` has higher information content than its mutual information with the output variable; shown in the bars for `merge$diabetes`. Therefore information loss has occurred in the merge operation, due to two features of the input variables (`diabetes_type` and `diabetes`). Firstly missing values in `diabetes` are represented as “missing”. Secondly there is an internal inconsistency where `diabetes` is recorded as “No” but `diabetes_type` is recorded as “Type 1”. This example reveals that additional preprocessing is required before the variable merge can be successfully achieved.

## Encoding missing values

Missing values can be recorded in several ways (e.g. “unknown”, “missing”). ‘R’ uses NA as a standard representation of missing values which allows for the user and packages to process them appropriately (e.g. `mean(x, na.rm = T)`).

‘eHDPrep’ can convert values representing missingness to NA with two functions:

- `strings_to_NA()` will encode a series of predefined strings which represent missingness or specific strings specified in the argument `strings_to_replace` as NA.
  - predefined strings: “Undetermined”, “unknown”, “missing”, “fail”, “fail / unknown”, “equivocal”, “equivocal / unknown”, “\*”
- `nums_to_NA()` will replace (only) numbers specified in `nums_to_replace` with NA in numeric variables.

```
# default values
example_data_NAs1 <- strings_to_NA(data = example_data)

# predefined value "equivocal" is removed
unique(example_data_NAs1$t_stage)
#> [1] "T3a" "T3b" "T1" "T4" "T2" NA

# custom values (T1 does not represent missingness, just used as an example)
example_data_NAs2 <- strings_to_NA(data = example_data,
                                   strings_to_replace = "T1")

# custom value "T1" is removed
unique(example_data_NAs2$t_stage)
#> [1] "T3a"      "T3b"      NA          "T4"      "T2"      "equivocal"

# numeric value is removed in patient_id
nums_to_NA(data = example_data, patient_id, nums_to_replace = c(1,3))
#> # A tibble: 1,000 x 12
#>   patient_id tumoursize t_stage n_stage diabetes diabetes_type hypertension
#>   <int>      <dbl> <chr> <chr> <chr> <chr> <chr>
#> 1         NA        62. T3a  N2    Yes   Type I   Yes
#> 2          2        64. T3b  N1    Yes   Type II  Yes
#> 3         NA        48. T1   N2    No    Type I   Yes
#> 4          4        41. T3a  N0    No    <NA>    Yes
#> 5          5        62. T4   N1    Yes   Type I   No
#> 6          6        14. T1   N2    No    <NA>    Yes
#> 7          7        63. T1   N2    No    <NA>    No
#> 8          8        44. T3b  N1    No    <NA>    No
#> 9          9        44. T2   N1    No    <NA>    Yes
#> 10         10        32. T1   N0    No    <NA>    No
#>   rural_urban marital_status SNP_a SNP_b free_text
#>   <chr>      <chr>      <chr> <chr> <chr>
#> 1 rural      married    cc    tt    We need grain to keep our mules healt-
#> 2 urban      divorced   cc    ta    The gold ring fits only a pierced ear.
#> 3 rural      divorced   cc    t    The vamp of the shoe had a gold buckl-
#> 4 rural      single     c     tt   Wipe the grease off his dirty face.
#> 5 urban      single     gg    t    Look in the corner to find the tan sh-
#> 6 urban      single     g     t    Float the soap on top of the bath wat-
```

```

#> 7 urban      married      c      t      Feel the heat of the weak dying flame.
#> 8 rural      single       gg     tt     A stuffed chair slipped from the movi~
#> 9 rural      single       g      t      The beam dropped down on the workmen'~
#> 10 rural     married      g      a      Screen the porch with woven straw mat~
#> # ... with 990 more rows

```

## Encoding categorical data

Categorical (nominal) data can present problems when analysed; either resulting in an error or improper analysis; for example, treating the relationships between categories as if they were ordinal. To combat this, `encode_cats()` utilises one hot encoding and creates a new variable for each unique value in the input categorical variable. The values in each new variable describe the presence of the unique value where 1 means present and 0 means not present. This is demonstrated below with `marital_status`.

```

encode_cats(data = example_data, marital_status) %>%
  dplyr::select(dplyr::starts_with("marital_status"))
#> # A tibble: 1,000 x 4
#>   marital_status_divorced marital_status_married marital_status_single
#>   <dbl>                 <dbl>                 <dbl>
#> 1             0             1             0
#> 2             1             0             0
#> 3             1             0             0
#> 4             0             0             1
#> 5             0             0             1
#> 6             0             0             1
#> 7             0             1             0
#> 8             0             0             1
#> 9             0             0             1
#> 10            0             1             0
#>   marital_status_unknown
#>   <dbl>
#> 1             0
#> 2             0
#> 3             0
#> 4             0
#> 5             0
#> 6             0
#> 7             0
#> 8             0
#> 9             0
#> 10            0
#> # ... with 990 more rows

```

## Encoding ordinal data

The relationships in ordinal variables can be encoded numerically while preserving the labels in 'R' with 'ordered factors' using `encode_ordinals()`. The numeric relations can later be extracted if fully numeric variables are required. The `ord_levels` parameter should describe the order of categories in ascending order:

```

example_data %>%
  encode_ordinals(ord_levels = c("N0", "N1", "N2"), n_stage) %>%
  dplyr::select(n_stage)

```

```

#> # A tibble: 1,000 x 1
#>   n_stage
#>   <ord>
#> 1 N2
#> 2 N1
#> 3 N2
#> 4 N0
#> 5 N1
#> 6 N2
#> 7 N2
#> 8 N1
#> 9 N1
#> 10 N0
#> # ... with 990 more rows

# demonstrating how ordered factors can be converted to numeric vectors
example_data %>%
  encode_ordinals(ord_levels = c("N0", "N1", "N2"), n_stage) %>%
  dplyr::select(n_stage) %>%
  dplyr::mutate(dplyr::across(n_stage, as.numeric))
#> # A tibble: 1,000 x 1
#>   n_stage
#>   <dbl>
#> 1     3
#> 2     2
#> 3     3
#> 4     1
#> 5     2
#> 6     3
#> 7     3
#> 8     2
#> 9     2
#> 10    1
#> # ... with 990 more rows

```

## Encoding genotype (SNP) data

In `encode_genotypes()`, variables which record single nucleotide polymorphism (SNP) information are standardised to a “A/B” syntax. Homozygous SNPs (e.g. recorded as “A”) are encoded in two character form (e.g. “A/A”) while heterozygous SNPs are ordered alphabetically (e.g. “GA” becomes “A/G”). Alleles are encoded as ordinal factors, ordered by observed allele frequency (in the supplied cohort). The most frequent allele is assigned level 1, the second most frequent value is assigned level 2, and the least frequent values is assigned level 3). This method embeds the numeric relationship between the allele frequencies while preserving value labels.

```

encode_genotypes(data = example_data, SNP_a, SNP_b) %>%
  dplyr::select(dplyr::starts_with("SNP"))
#> # A tibble: 1,000 x 2
#>   SNP_a SNP_b
#>   <ord> <ord>
#> 1 C/C   T/T
#> 2 C/C   A/T
#> 3 C/C   T/T

```

```

#> 4 C/C T/T
#> 5 G/G T/T
#> 6 G/G T/T
#> 7 C/C T/T
#> 8 G/G T/T
#> 9 G/G T/T
#> 10 G/G A/A
#> # ... with 990 more rows

```

## Extract information from free text variables

Medical notes and other free text variables can contain additional information but require Natural Language Processing (NLP). Information on the presence of words, phrases, or groups of proximal words can be extracted with the functionality below; utilising the ‘quanteda’ package (Benoit et al. 2018). A knowledge of NLP terminology can be beneficial however the crucial term for this functionality is ‘skipgram’ which, in this context, is a series of words in a string which can have interrupting words (‘skips’) between them (see examples in `?quanteda::tokens_skipgrams`). The high-level function `extract_freetext()` can be applied to extract skipgrams in free text variables by their frequency.

There are three underlying stages of extracting skipgrams:

1. Identify skipgrams in a character variable (`skipgram_identify()`). The variable is also preprocessed here where:
  - Punctuation, numbers, symbols, stop-words (see `?tm::stopwords`) are removed.
  - Text is standardised to lower case
  - Words are stemmed (see `?quanteda::tokens_wordstem`).
2. Measure skipgram frequency across the variable (`skipgram_freq()`)
3. Append specified skipgrams to dataset as logical variables (`skipgram_append()`)

In medical notes, a clear signal may appear where certain skipgrams provide information suitable for analysis. The variable `free_text` in `example_data` comprises sample sentences from `stringr::sentences`. While these are not medical notes they are established examples of short pieces of text. As `free_text` does not contain true signals, we set generous parameters below: The number of interrupting words is set to five in the example below (`max_interrupt_words = 5`) however values of one or two are more likely to be useful in real-world applications. Additionally, the minimum frequency of skipgrams across the cohort to consider (`min_freq = 0.5`) is used below although 5 or 10 may be more suitable with real data. Ultimately, user evaluation and tuning is required.

```

# Identify skipgrams in example_data$free_text
skipgrams <- skipgram_identify(x = example_data$free_text,
                              ids = example_data$patient_id,
                              num_of_words = 2,
                              max_interrupt_words = 5)

skipgrams
#> # A tibble: 1,000 x 1,335
#>   doc_id need_grain mule_heal~1 gold_~2 gold_~3 ring_~4 pierc~5 gold_~6 dirti~7
#>   <chr>      <dbl>      <dbl>  <dbl>  <dbl>  <dbl>  <dbl>  <dbl>  <dbl>
#> 1 1          1          1      0      0      0      0      0      0
#> 2 2          0          0      1      1      1      1      0      0
#> 3 3          0          0      0      0      0      0      1      0

```



```

#> 4 4          0          0          0          0          0          0          0          1
#> 5 5          0          0          0          0          0          0          0          0
#> 6 6          0          0          0          0          0          0          0          0
#> 7 7          0          0          0          0          0          0          0          0
#> 8 8          0          0          0          0          0          0          0          0
#> 9 9          0          0          0          0          0          0          0          0
#> 10 10        0          0          0          0          0          0          0          0
#>   tan_shirt bath_water weak_die weak_~8 die_f~9 stuf_~* stuf_~* chair~* move_~*
#>   <dbl>      <dbl>      <dbl>      <dbl>      <dbl>      <dbl>      <dbl>      <dbl>      <dbl>
#> 1         0          0          0          0          0          0          0          0
#> 2         0          0          0          0          0          0          0          0
#> 3         0          0          0          0          0          0          0          0
#> 4         0          0          0          0          0          0          0          0
#> 5         1          0          0          0          0          0          0          0
#> 6         0          1          0          0          0          0          0          0
#> 7         0          0          1          1          1          0          0          0
#> 8         0          0          0          0          0          1          1          1
#> 9         0          0          0          0          0          0          0          0
#> 10        0          0          0          0          0          0          0          0
#> # ... with 990 more rows, 1,317 more variables: beam_drop <dbl>, workmen_head <dbl>,
#> #   woven_straw <dbl>, woven_mat <dbl>, straw_mat <dbl>, worn_floor <dbl>,
#> #   fish_twist <dbl>, bent_hook <dbl>, quick_snip <dbl>, abrupt_start <dbl>,
#> #   clan_gather <dbl>, dull_night <dbl>, trust_fund <dbl>, bank_earli <dbl>,
#> #   dens_crowd <dbl>, two_distinct <dbl>, two_way <dbl>, distinct_way <dbl>,
#> #   empti_flask <dbl>, empti_stood <dbl>, flask_stood <dbl>, tin_tray <dbl>,
#> #   fig_tree <dbl>, cool_green <dbl>, cool_grass <dbl>, green_grass <dbl>, ...

# Summarise frequency of skipgrams to consider which should be added to the
# data.
skipgram_freq(skipgram_tokens = skipgrams, min_freq = 0.5)
#> # A tibble: 41 x 3
#>   skipgram      count percentage
#>   <chr>         <dbl>      <dbl>
#> 1 board_will         6         0.6
#> 2 leas_ran           6         0.6
#> 3 sixteen_week       6         0.6
#> 4 white_back         6         0.6
#> 5 alway_show         5         0.5
#> 6 bad_strain         5         0.5
#> 7 catch_pink         5         0.5
#> 8 catch_salmon       5         0.5
#> 9 cone_cent          5         0.5
#> 10 cone_cost         5         0.5
#> # ... with 31 more rows

# Append chosen skipgrams to example_data
## a) by minimum frequency
skipgram_append(skipgram_tokens = skipgrams,
                id_var = patient_id,
                min_freq = 0.6,
                data = example_data)
#> `skipgrams2append` not provided. Searching for skipgrams with a `min_freq` of 0.6%
#> 4 skipgrams have been appended the data.

```

```

#> # A tibble: 1,000 x 16
#>   patient_id tumoursize t_stage n_stage diabetes diabetes_type hypertension
#>   <dbl>      <dbl> <chr>  <chr>  <chr>      <chr>      <chr>
#> 1         1         62. T3a    N2      Yes      Type I      Yes
#> 2         2         64. T3b    N1      Yes      Type II     Yes
#> 3         3         48. T1     N2      No       Type I      Yes
#> 4         4         41. T3a    N0      No       <NA>       Yes
#> 5         5         62. T4     N1      Yes      Type I      No
#> 6         6         14. T1     N2      No       <NA>       Yes
#> 7         7         63. T1     N2      No       <NA>       No
#> 8         8         44. T3b    N1      No       <NA>       No
#> 9         9         44. T2     N1      No       <NA>       Yes
#> 10        10         32. T1     N0      No       <NA>       No
#>   rural_urban marital_sta~1 SNP_a SNP_b free_~2 board~3 leas_~4 sixte~5 white~6
#>   <chr>      <chr>      <chr> <chr> <chr>      <dbl> <dbl> <dbl> <dbl>
#> 1 rural      married    cc    tt    We nee~    0     0     0     0
#> 2 urban      divorced  cc    ta    The go~    0     0     0     0
#> 3 rural      divorced  cc    t    The va~    0     0     0     0
#> 4 rural      single    c     tt    Wipe t~    0     0     0     0
#> 5 urban      single    gg    t    Look i~    0     0     0     0
#> 6 urban      single    g     t    Float ~    0     0     0     0
#> 7 urban      married  c     t    Feel t~    0     0     0     0
#> 8 rural      single    gg    tt    A stuf~    0     0     0     0
#> 9 rural      single    g     t    The be~    0     0     0     0
#> 10 rural     married  g     a    Screen~    0     0     0     0
#> # ... with 990 more rows, and abbreviated variable names 1: marital_status,
#> # 2: free_text, 3: board_will, 4: leas_ran, 5: sixteen_week, 6: white_back

```

## b) by specific skipgram(s)

```

skipgram_append(skipgram_tokens = skipgrams,
                id_var = patient_id,
                skipgrams2append = c("sixteen_week", "bad_strain"),
                data = example_data)

```

#> 2 skipgrams have been appended the data.

```

#> # A tibble: 1,000 x 14
#>   patient_id tumoursize t_stage n_stage diabetes diabetes_type hypertension
#>   <dbl>      <dbl> <chr>  <chr>  <chr>      <chr>      <chr>
#> 1         1         62. T3a    N2      Yes      Type I      Yes
#> 2         2         64. T3b    N1      Yes      Type II     Yes
#> 3         3         48. T1     N2      No       Type I      Yes
#> 4         4         41. T3a    N0      No       <NA>       Yes
#> 5         5         62. T4     N1      Yes      Type I      No
#> 6         6         14. T1     N2      No       <NA>       Yes
#> 7         7         63. T1     N2      No       <NA>       No
#> 8         8         44. T3b    N1      No       <NA>       No
#> 9         9         44. T2     N1      No       <NA>       Yes
#> 10        10         32. T1     N0      No       <NA>       No
#>   rural_urban marital_status SNP_a SNP_b free_text                sixte~1 bad_s~2
#>   <chr>      <chr>      <chr> <chr> <chr>      <dbl> <dbl>
#> 1 rural      married    cc    tt    We need grain to keep~    0     0
#> 2 urban      divorced  cc    ta    The gold ring fits on~    0     0
#> 3 rural      divorced  cc    t    The vamp of the shoe ~    0     0
#> 4 rural      single    c     tt    Wipe the grease off h~    0     0

```

```

#> 5 urban      single      gg      t      Look in the corner to~      0      0
#> 6 urban      single      g       t      Float the soap on top~      0      0
#> 7 urban      married     c       t      Feel the heat of the ~      0      0
#> 8 rural      single      gg      tt     A stuffed chair slipp~      0      0
#> 9 rural      single      g       t      The beam dropped down~      0      0
#> 10 rural     married     g       a      Screen the porch with~      0      0
#> # ... with 990 more rows, and abbreviated variable names 1: sixteen_week,
#> # 2: bad_strain

```

The high-level function `extract_freetext()` is a wrapper for the low-level functions in the above example. However use of `extract_freetext()` is limited to appending skipgrams by minimum frequency and selection of skipgrams by name to append is not possible because they are not defined at the point the `extract_freetext()` function is called.:

```

extract_freetext(data = example_data,
                 id_var = patient_id,
                 min_freq = 0.6, free_text)
#> `skipgrams2append` not provided. Searching for skipgrams with a `min_freq` of 0.6%
#> 4 skipgrams have been appended the data.
#> # A tibble: 1,000 x 15
#>   patient_id tumoursize t_stage n_stage diabetes diabetes_type hypertension
#>   <dbl>      <dbl> <chr> <chr> <chr> <chr> <chr>
#> 1         1         62. T3a  N2    Yes   Type I   Yes
#> 2         2         64. T3b  N1    Yes   Type II  Yes
#> 3         3         48. T1   N2    No    Type I   Yes
#> 4         4         41. T3a  N0    No    <NA>     Yes
#> 5         5         62. T4   N1    Yes   Type I   No
#> 6         6         14. T1   N2    No    <NA>     Yes
#> 7         7         63. T1   N2    No    <NA>     No
#> 8         8         44. T3b  N1    No    <NA>     No
#> 9         9         44. T2   N1    No    <NA>     Yes
#> 10        10         32. T1   N0    No    <NA>     No
#>   rural_urban marital_status SNP_a SNP_b board_will leas_ran sixteen_~1 white~2
#>   <chr> <chr> <chr> <chr> <dbl> <dbl> <dbl> <dbl>
#> 1 rural      married     cc  tt      0      0      0      0
#> 2 urban      divorced    cc  ta      0      0      0      0
#> 3 rural      divorced    cc  t       0      0      0      0
#> 4 rural      single      c   tt      0      0      0      0
#> 5 urban      single      gg  t       0      0      0      0
#> 6 urban      single      g   t       0      0      0      0
#> 7 urban      married     c   t       0      0      0      0
#> 8 rural      single      gg  tt      0      0      0      0
#> 9 rural      single      g   t       0      0      0      0
#> 10 rural     married     g   a       0      0      0      0
#> # ... with 990 more rows, and abbreviated variable names 1: sixteen_week,
#> # 2: white_back

```

## Review quality control

Quality control modifications may have unintended effects on the data which could remain undetected until later stages of analysis. `count_compare()` can avoid this situation by reporting changes at each step and reporting a tally of values in relevant variables. The code below uses the earlier variable merging operation ([Merge Variables](#)) as an example:

```

# merge data
example_data_merged <- merge_cols(data = example_data,
                                primary_var = diabetes_type,
                                secondary_var = diabetes,
                                merge_var_name = "diabetes_merged",
                                rm_in_vars = T)

# review this step's effects on the involved variables:
count_compare(before_tbl = example_data,
              after_tbl = example_data_merged,
              cols2compare = c("diabetes", "diabetes_type", "diabetes_merged"),
              kableout = F)

#> $before_tbl
#> # A tibble: 7 x 3
#>   diabetes diabetes_type     n
#>   <chr>      <chr>      <int>
#> 1 No        <NA>          498
#> 2 Yes      Type I         247
#> 3 Yes      Type II        244
#> 4 missing <NA>           7
#> 5 missing Type I           2
#> 6 No      Type I           1
#> 7 missing Type II          1
#>
#> $after_tbl
#> # A tibble: 4 x 2
#>   diabetes_merged     n
#>   <chr>              <int>
#> 1 No                498
#> 2 Type I            250
#> 3 Type II           245
#> 4 missing           7

```

Documentation of quality control modifications is important for writing methodology and summarising changes. The remaining quality control review functions are intended for review once all quality control has been implemented, as in [Review quality control](#), but can be used at any point; as below with `report_var_mods()` and `mod_plot()` comparing the merging operation example and a `strings_to_NA()` example with the original data:

```

#variable level modifications
report_var_mods(before_tbl = example_data,
               after_tbl = example_data_merged)

#> # A tibble: 13 x 2
#>   variable      presence
#>   <chr>         <chr>
#> 1 patient_id   Preserved
#> 2 tumoursize   Preserved
#> 3 t_stage      Preserved
#> 4 n_stage      Preserved
#> 5 diabetes     Removed
#> 6 diabetes_type Removed
#> 7 hypertension Preserved
#> 8 rural_urban  Preserved

```

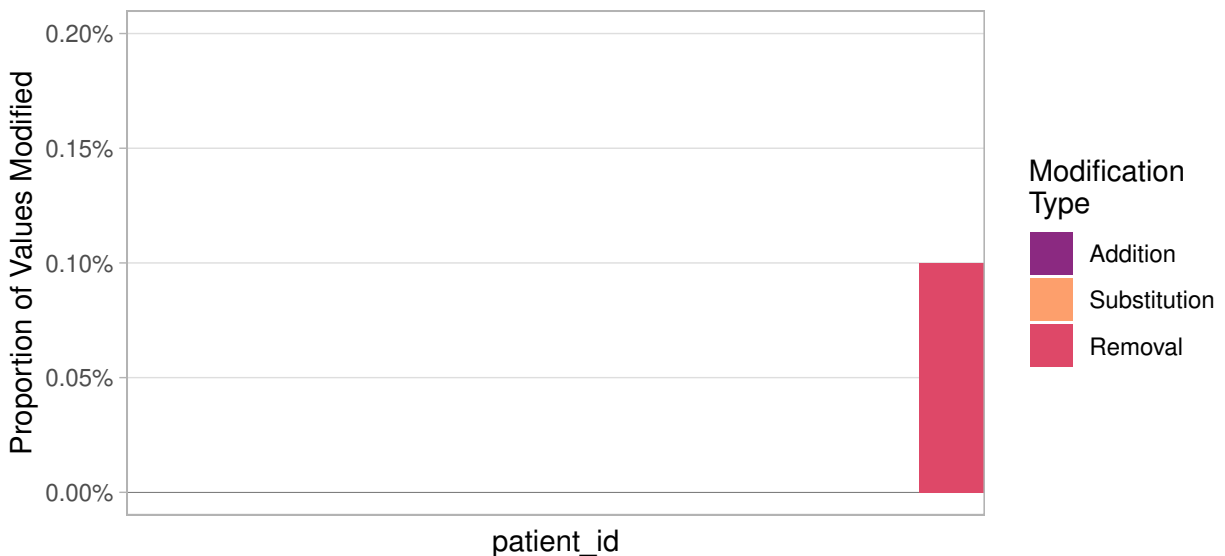
```

#> 9 marital_status Preserved
#> 10 SNP_a Preserved
#> 11 SNP_b Preserved
#> 12 free_text Preserved
#> 13 diabetes_merged Added

# value level modifications showing which exact missingness values
# were removed
mod_track(before_tbl = example_data,
          after_tbl = strings_to_NA(example_data),
          id_var = patient_id)
#> `vars2compare` not supplied. Attempting to compare all variables...
#> # A tibble: 78 x 6
#>   patient_id new_var old_var old_value new_value mod_type
#>   <chr>      <chr> <chr> <chr> <chr> <chr>
#> 1 31        t_stage t_stage equivocal <NA> Removal
#> 2 34        t_stage t_stage equivocal <NA> Removal
#> 3 44        t_stage t_stage equivocal <NA> Removal
#> 4 48        t_stage t_stage equivocal <NA> Removal
#> 5 261       t_stage t_stage equivocal <NA> Removal
#> 6 263       t_stage t_stage equivocal <NA> Removal
#> 7 348       t_stage t_stage equivocal <NA> Removal
#> 8 454       t_stage t_stage equivocal <NA> Removal
#> 9 468       t_stage t_stage equivocal <NA> Removal
#> 10 569      t_stage t_stage equivocal <NA> Removal
#> # ... with 68 more rows

# plot value level modifications
mod_track(before_tbl = example_data,
          after_tbl = strings_to_NA(example_data),
          id_var = patient_id, plot = T)
#> `vars2compare` not supplied. Attempting to compare all variables...

```



**Figure 11:** Proportion of values modified per patient in 'example\_data' following conversion of specific values to 'NA'.

`mod_track()` with `plot = TRUE` can visualise the extent and any disparity of value modification within the dataset.

## Encoding data as numeric matrix

As a late or final quality control step, the dataset may be converted to a numeric matrix for future analysis. This will require many of the earlier steps, such as encoding categorical variables (see [Encoding categorical data](#)), to be completed. `encode_as_num_mat()` will convert all columns to numeric and use the row identifier column (`id_var`) as row names:

```
# example of data which has been quality controlled.
example_data %>%
  merge_cols(primary_var = diabetes_type,
             secondary_var = diabetes,
             merge_var_name = "diabetes_merged",
             rm_in_vars = TRUE) %>%
  apply_quality_ctrl(id_var = patient_id,
                    class_tbl = data_types_diabetes_m,
                    bin_cats = c("No" = "Yes", "rural" = "urban"),
                    min_freq = 0.6) ->
  post_qc_data
#> New names:
#> * `diabetes_merged_Type I` -> `diabetes_merged_Type.I`
#> * `diabetes_merged_Type II` -> `diabetes_merged_Type.II`

post_qc_data %>%
  encode_as_num_mat(id_var = patient_id) %>%
  tibble::glimpse()
#> Rows: 1,000
#> Columns: 19
#> $ tumoursize      <dbl> 61.71058, 64.18932, 47.81393, 40.93006, 62.11775, 1~
#> $ t_stage         <dbl> 3, 4, 1, 3, 5, 1, 1, 4, 2, 1, 5, 4, 3, 2, 5, 3, 3, ~
#> $ n_stage         <dbl> 3, 2, 3, 1, 2, 3, 3, 2, 2, 1, 3, 1, 3, 1, 2, 2, 1, ~
#> $ hypertension   <dbl> 2, 2, 2, 2, 1, 2, 1, 1, 2, 1, 2, 1, 1, 1, 1, 2, 1, ~
#> $ rural_urban     <dbl> 1, 2, 1, 1, 2, 2, 2, 1, 1, 1, 2, 2, 2, 2, 2, 1, 1, ~
#> $ SNP_a           <dbl> 1, 1, 1, 1, 2, 2, 1, 2, 2, 2, 2, 1, 2, 1, 2, 2, 2, ~
#> $ SNP_b           <dbl> 2, 3, 2, 2, 2, 2, 2, 2, 2, 1, 1, 3, 1, 3, 2, 1, 2, ~
#> $ board_will      <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, ~
#> $ leas_ran        <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, ~
#> $ sixteen_week    <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, ~
#> $ white_back      <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, ~
#> $ diabetes_merged_No <dbl> 0, 0, 0, 1, 0, 1, 1, 1, 1, 1, 0, 1, 0, 0, 1, 0, 1, ~
#> $ diabetes_merged_Type.I <dbl> 1, 0, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 1, 0, 0, 1, 0, ~
#> $ diabetes_merged_Type.II <dbl> 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, ~
#> $ diabetes_merged_NA <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, ~
#> $ marital_status_divorced <dbl> 0, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, ~
#> $ marital_status_married <dbl> 1, 0, 0, 0, 0, 0, 1, 0, 0, 1, 1, 1, 1, 1, 0, 1, 0, ~
#> $ marital_status_single <dbl> 0, 0, 0, 1, 1, 1, 0, 1, 1, 0, 0, 0, 0, 1, 0, 0, 0, ~
#> $ marital_status_NA <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, ~
```

Note that the text labels in ordinal variables will be removed in the above conversion to a numeric matrix. The mapping between the text labels and the numerical levels can be extracted to another data frame for future reference using `ordinal_label_levels()`, as below:

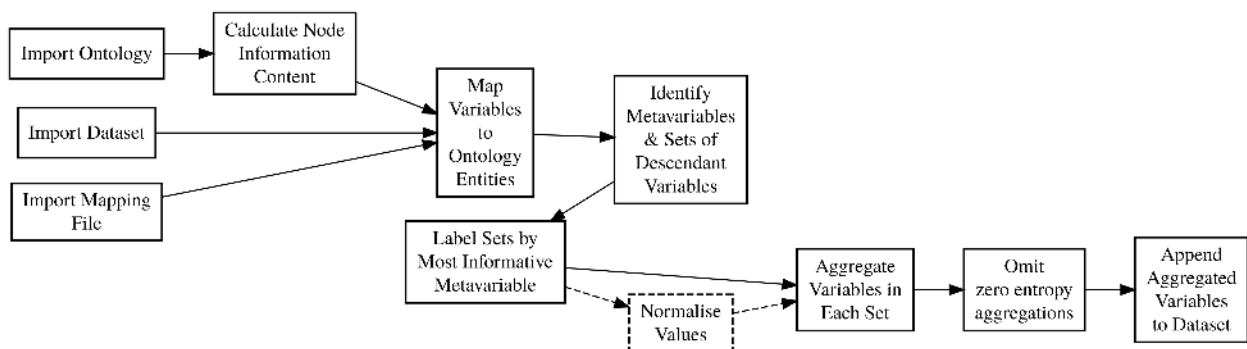
```

post_qc_data %>%
  ordinal_label_levels()
#> # A tibble: 15 x 3
#>   variable label level
#>   <chr>    <chr> <dbl>
#> 1 SNP_a    C/C     1
#> 2 SNP_a    G/G     2
#> 3 SNP_a    C/G     3
#> 4 SNP_b    A/A     1
#> 5 SNP_b    T/T     2
#> 6 SNP_b    A/T     3
#> 7 n_stage NO      1
#> 8 n_stage N1      2
#> 9 n_stage N2      3
#> 10 t_stage T1      1
#> 11 t_stage T2      2
#> 12 t_stage T3a     3
#> 13 t_stage T3b     4
#> 14 t_stage T4      5
#> 15 t_stage <NA>    NA

```

## Semantic enrichment

Data frames are semantically disorganised because no information on the semantic relationships between variables is present. Biomedical ontologies contain extensive semantic information between concepts across medical domains. The semantic commonalities of a dataset’s variables can be incorporated with semantic enrichment (SE). The added information may improve performance of later analysis. An overview of the workflow for SE is shown below where the “Normalise Values” box is dashed as it is an optional step:



**Figure 12:** Workflow of low-level semantic enrichment functions in eHDPprep. The dashed lines and box represent an optional step.

## Required inputs

SE requires three input objects:

1. A numeric dataset (data frame or matrix).
  - All variables must be numeric because SE attempts to aggregate values.

2. An ontology as a graph ('igraph' or 'tidygraph'), a data frame containing an edge table, or a path to an edge table in a csv file.
  - `example_ontology` is a synthetic ontology we have created to demonstrate the semantic commonalities in `example_data`.
  - At present, users must supply an ontology themselves. There are several potential ontologies for health data including SNOMED CT, the Gene Ontology, the Disease Ontology, and the Human Phenotype Ontology (Millar 2016; Gene Ontology Consortium 2019; Schriml et al. 2019; Köhler et al. 2021).
3. A mapping file (csv path or data frame) which links variables in the data with entities in the ontology.
  - `example_mapping_file` is used to demonstrate SE here.
  - The variable name must not be identical to the ontological entity to which it is mapped (e.g. variable `hypertension` cannot be mapped to a ontological entity `hypertension`). This is not typically a problem as most ontologies use a numeric naming system unlikely to be used for variable names.

## Example data

Examples of the three required inputs, described above, are provided with this package.

1. Because SE requires a numeric dataset, quality control is applied to `example_data`:

```
example_data %>%
  # first merge diabetes variables
  merge_cols(primary_var = diabetes_type,
             secondary_var = diabetes,
             merge_var_name = "diabetes_merged",
             rm_in_vars = TRUE) %>%
  # pass data with diabetes_merged to high-level QC function
  apply_quality_ctrl(id_var = patient_id,
                    class_tbl = data_types_diabetes_m,
                    bin_cats = c("No" = "Yes", "rural" = "urban"),
                    to_numeric_matrix = TRUE) ->
  post_qc_data
#> New names:
#> * `diabetes_merged_Type I` -> `diabetes_merged_Type.I`
#> * `diabetes_merged_Type II` -> `diabetes_merged_Type.II`
```

2. The example ontology containing the semantic information of variables in `example_data` is stored in `example_ontology` as a tidygraph `tbl_graph` object:

```
data(example_ontology)
example_ontology
#> # A tbl_graph: 24 nodes and 24 edges
#> #
#> # A directed acyclic simple graph with 1 component
#> #
#> # Node Data: 24 x 1 (active)
#>   name
#>   <chr>
#> 1 Nstage
```



```

#> 2 Tstage
#> 3 Tumoursize
#> 4 property_of_tumour
#> 5 TNM
#> 6 property_of_cancer
#> # ... with 18 more rows
#> #
#> # Edge Data: 24 x 2
#>   from to
#>   <int> <int>
#> 1     1     5
#> 2     2     5
#> 3     3     4
#> # ... with 21 more rows

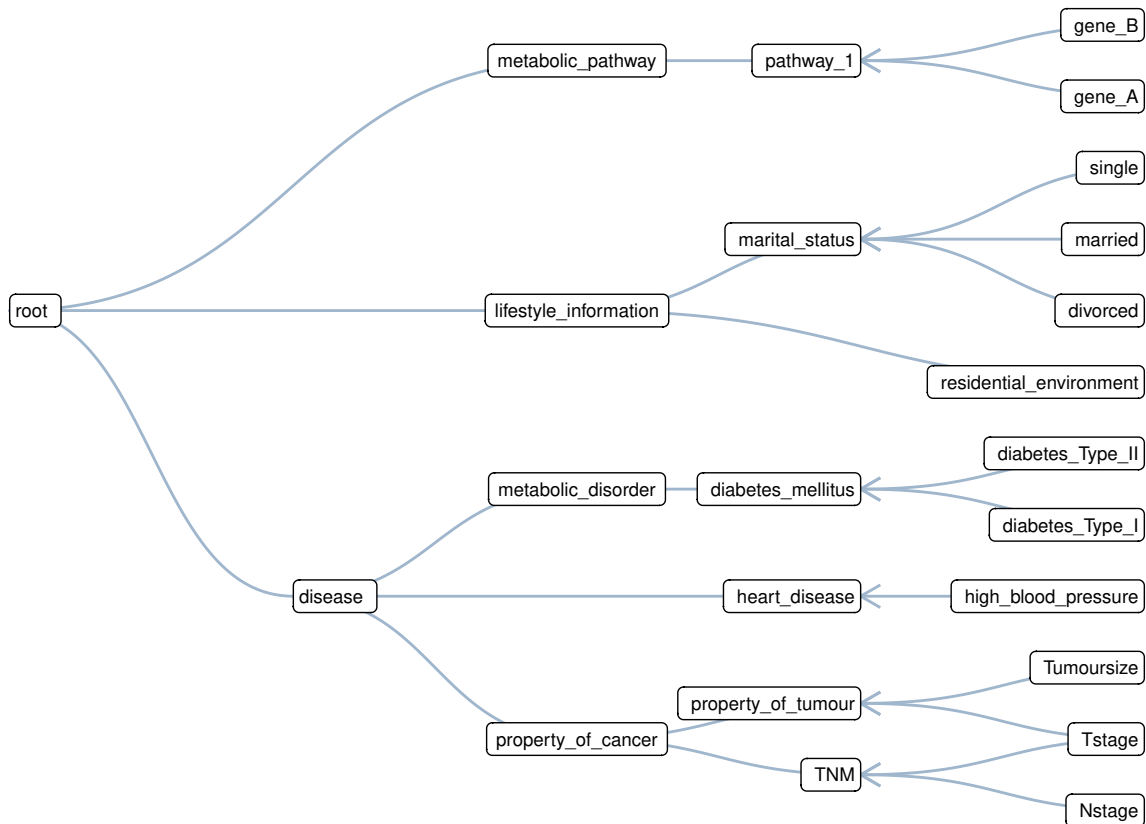
```

example\_ontology is visualised in the network graph below:

```

require(ggplot2)
#> Loading required package: ggplot2
ggraph::ggraph(example_ontology, layout = "sugiyama") +
  ggraph::geom_edge_diagonal(arrow = arrow(length = unit(3, 'mm')),
                             colour = "slategray3") +
  ggraph::geom_node_label(aes(label = name),
                          size = 2.5, repel = FALSE, hjust="inward") +
  theme_void() +
  theme(legend.position = "none") +
  coord_flip()
#> Warning: Using the `size` aesthetic in this geom was deprecated in ggplot2 3.4.0.
#> i Please use `linewidth` in the `default_aes` field and elsewhere instead.

```



**Figure 13:** Visualisation of ‘example\_ontology’ using the ggraph package.

3. The example mapping file, as a data frame, is as follows:

```

data(example_mapping_file)
example_mapping_file
#> # A tibble: 12 x 2
#>   variable      onto_entity
#>   <chr>         <chr>
#> 1 tumoursize   Tumoursize
#> 2 t_stage      Tstage
#> 3 n_stage      Nstage
#> 4 hypertension high_blood_pressure
#> 5 rural_urban  residential_environment
#> 6 SNP_a        gene_A
#> 7 SNP_b        gene_B
#> 8 diabetes_merged_Type.I diabetes_Type_I
#> 9 diabetes_merged_Type.II diabetes_Type_II
#> 10 marital_status_divorced divorced
#> 11 marital_status_married married
#> 12 marital_status_single single
  
```

## High level functionality

With the three inputs (data, ontology, and mapping\_file) supplied, the semantic enrichment of post\_qc\_data can be completed with `semantic_enrichment()`:

```

qc_se_data <- semantic_enrichment(data = post_qc_data,
                                ontology = example_ontology,
                                mapping_file = example_mapping_file,
                                mode = "in",
                                root = "root")

#> Aggregating variables with semantic commonalities to metavariables
#> and appending to `data`...
#> Metavariables will be labelled by the most informative common ancestor.
#> Identifying semantic commonalities...
#> Complete. Duration: 1.2 secs.
#> 9 semantic commonalities found (via common ontological ancestors).
#> Complete. Duration: 40.25 secs.
#> The dataset has been enriched with 35 metavariables
#> (10 metavariables had zero entropy and were therefore not appended).

```

Below is an overview of the enriched dataset with semantic aggregations:

```

tibble::glimpse(qc_se_data)
#> Rows: 1,000
#> Columns: 50
#> $ tumoursize <dbl> 61.71058, 64.18932, 47.81393, 40.93006, 62.117~
#> $ t_stage <dbl> 3, 4, 1, 3, 5, 1, 1, 4, 2, 1, 5, 4, 3, 2, 5, 3~
#> $ n_stage <dbl> 3, 2, 3, 1, 2, 3, 3, 2, 2, 1, 3, 1, 3, 1, 2, 2~
#> $ hypertension <dbl> 2, 2, 2, 2, 1, 2, 1, 1, 2, 1, 2, 1, 1, 1, 1, 2~
#> $ rural_urban <dbl> 1, 2, 1, 1, 2, 2, 2, 1, 1, 1, 2, 2, 2, 2, 2, 1~
#> $ SNP_a <dbl> 1, 1, 1, 1, 2, 2, 1, 2, 2, 2, 2, 1, 2, 1, 2, 2~
#> $ SNP_b <dbl> 2, 3, 2, 2, 2, 2, 2, 2, 2, 1, 1, 3, 1, 3, 2, 1~
#> $ diabetes_merged_No <dbl> 0, 0, 0, 1, 0, 1, 1, 1, 1, 1, 0, 1, 0, 0, 1, 0~
#> $ diabetes_merged_Type.I <dbl> 1, 0, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 1, 0, 0, 1~
#> $ diabetes_merged_Type.II <dbl> 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0~
#> $ diabetes_merged_NA <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0~
#> $ marital_status_divorced <dbl> 0, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1~
#> $ marital_status_married <dbl> 1, 0, 0, 0, 0, 0, 1, 0, 0, 1, 1, 1, 1, 0, 1, 0~
#> $ marital_status_single <dbl> 0, 0, 0, 1, 1, 1, 0, 1, 1, 0, 0, 0, 0, 1, 0, 0~
#> $ marital_status_NA <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0~
#> $ MV_property_of_tumour_SUM <dbl> 1.0506338, 1.3209213, 0.4368958, 0.8805543, 1.~
#> $ MV_property_of_tumour_AVG <dbl> 0.7004225, 0.8806142, 0.2912639, 0.5870362, 1.~
#> $ MV_property_of_tumour_MAX <dbl> 1.0506338, 1.3209213, 0.4368958, 0.8805543, 1.~
#> $ MV_property_of_tumour_MIN <dbl> 0.5000000, 0.5709213, 0.0000000, 0.3805543, 0.~
#> $ MV_property_of_tumour_MUL <dbl> 0.106430411, 0.375623897, 0.000000000, 0.03295~
#> $ MV_TNM_SUM <dbl> 1.50, 1.25, 1.00, 0.50, 1.50, 1.00, 1.00, 1.25~
#> $ MV_TNM_AVG <dbl> 1.0000000, 0.8333333, 0.6666667, 0.3333333, 1.~
#> $ MV_TNM_MAX <dbl> 1.50, 1.25, 1.00, 0.50, 1.50, 1.00, 1.00, 1.25~
#> $ MV_TNM_MIN <dbl> 0.50, 0.50, 0.00, 0.00, 0.50, 0.00, 0.00, 0.50~
#> $ MV_TNM_MUL <dbl> 0.562500000, 0.244140625, 0.000000000, 0.00000~
#> $ MV_property_of_cancer_SUM <dbl> 2.0506338, 1.8209213, 1.4368958, 0.8805543, 2.~
#> $ MV_property_of_cancer_AVG <dbl> 1.0253169, 0.9104606, 0.7184479, 0.4402771, 1.~
#> $ MV_property_of_cancer_MAX <dbl> 2.0506338, 1.8209213, 1.4368958, 0.8805543, 2.~
#> $ MV_property_of_cancer_MIN <dbl> 0.5000000, 0.5000000, 0.0000000, 0.0000000, 0.~
#> $ MV_property_of_cancer_MUL <dbl> 0.593522555, 0.323162519, 0.000000000, 0.00000~
#> $ MV_disease_SUM <dbl> 4.0506338, 3.8209213, 3.4368958, 1.8805543, 3.~
#> $ MV_disease_AVG <dbl> 1.15732395, 1.09169179, 0.98197023, 0.53730122~
#> $ MV_disease_MAX <dbl> 4.0506338, 3.8209213, 3.4368958, 1.8805543, 3.~

```

```

#> $ MV_diabetes_mellitus_SUM <dbl> 1, 1, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 1, 1, 0, 1~
#> $ MV_diabetes_mellitus_AVG <dbl> 0.6666667, 0.6666667, 0.6666667, 0.0000000, 0.~
#> $ MV_diabetes_mellitus_MAX <dbl> 1, 1, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 1, 1, 0, 1~
#> $ MV_marital_status_SUM <dbl> 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1~
#> $ MV_marital_status_AVG <dbl> 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0~
#> $ MV_marital_status_MAX <dbl> 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1~
#> $ MV_lifestyle_information_SUM <dbl> 1, 2, 1, 1, 2, 2, 2, 1, 1, 1, 2, 2, 2, 2, 2, 1~
#> $ MV_lifestyle_information_AVG <dbl> 0.4, 0.8, 0.4, 0.4, 0.8, 0.8, 0.8, 0.4, 0.4, 0~
#> $ MV_lifestyle_information_MAX <dbl> 1, 2, 1, 1, 2, 2, 2, 1, 1, 1, 2, 2, 2, 2, 2, 1~
#> $ MV_pathway_1_SUM <dbl> 0.5, 1.0, 0.5, 0.5, 1.0, 1.0, 0.5, 1.0, 1.0, 0~
#> $ MV_pathway_1_AVG <dbl> 0.3333333, 0.6666667, 0.3333333, 0.3333333, 0.~
#> $ MV_pathway_1_MAX <dbl> 0.5, 1.0, 0.5, 0.5, 1.0, 1.0, 0.5, 1.0, 1.0, 0~
#> $ MV_pathway_1_MIN <dbl> 0.0, 0.0, 0.0, 0.0, 0.5, 0.5, 0.0, 0.5, 0.5, 0~
#> $ MV_pathway_1_MUL <dbl> 0.0000000, 0.0000000, 0.0000000, 0.0000000, 0.0000000~
#> $ MV_root_SUM <dbl> 5.550634, 6.820921, 4.936896, 3.380554, 6.0539~
#> $ MV_root_AVG <dbl> 0.8539437, 1.0493725, 0.7595224, 0.5200853, 0.~
#> $ MV_root_MAX <dbl> 5.550634, 6.820921, 4.936896, 3.380554, 6.0539~

```

Below is an example of how the variables `tumoursize`, `t_stage`, and `n_stage`, which all relate to cancer, have this relationship recognised through their semantic commonality of `property_of_cancer` in `example_ontology`:

```

qc_se_data %>%
  dplyr::select(tumoursize, t_stage, n_stage,
               dplyr::starts_with("MV_property_of_cancer")) %>%
  tibble::glimpse()

#> Rows: 1,000
#> Columns: 8
#> $ tumoursize <dbl> 61.71058, 64.18932, 47.81393, 40.93006, 62.11775,~
#> $ t_stage <dbl> 3, 4, 1, 3, 5, 1, 1, 4, 2, 1, 5, 4, 3, 2, 5, 3, 3~
#> $ n_stage <dbl> 3, 2, 3, 1, 2, 3, 3, 2, 2, 1, 3, 1, 3, 1, 2, 2, 1~
#> $ MV_property_of_cancer_SUM <dbl> 2.0506338, 1.8209213, 1.4368958, 0.8805543, 2.053~
#> $ MV_property_of_cancer_AVG <dbl> 1.0253169, 0.9104606, 0.7184479, 0.4402771, 1.026~
#> $ MV_property_of_cancer_MAX <dbl> 2.0506338, 1.8209213, 1.4368958, 0.8805543, 2.053~
#> $ MV_property_of_cancer_MIN <dbl> 0.5000000, 0.5000000, 0.0000000, 0.0000000, 0.500~
#> $ MV_property_of_cancer_MUL <dbl> 0.593522555, 0.323162519, 0.000000000, 0.00000000~

```

Note:

- The normalisation of values prevents `tumoursize`'s large magnitude (relative to the other variables) having a disproportional effect on the aggregations.
- The prefix “MV\_” stands for “meta-variable”.

In summary, the SE process added 35 aggregation variables to the dataset from 9 meta-variables.

## Low level functionality

There are some exported lower level functions which users may find useful to see the intermediate steps of SE. The should be carried out in the order shown below:

## Convert edge table to ontology

Semantic enrichment in eHDPprep requires an ontology, represented as a `igraph`/`tidygraph` object. As ontologies can also be represented as edge tables, eHDPprep provides a function, `edge_tbl_to_graph`, to convert an edge table to a graph object. Edge tables are typically stored on disk and should first be read into R as a data frame and then supplied to `edge_tbl_to_graph`:

```
example_edge_tbl
#> # A tibble: 25 x 2
#>   from      to
#>   <chr>    <chr>
#> 1 Nstage    TNM
#> 2 Tstage    TNM
#> 3 Tumoursize property_of_tumour
#> 4 Tstage    property_of_tumour
#> 5 property_of_tumour property_of_cancer
#> 6 TNM       property_of_cancer
#> 7 property_of_cancer disease
#> 8 disease   root
#> 9 high_blood_pressure heart_disease
#> 10 heart_disease disease
#> # ... with 15 more rows

example_ontology <- edge_tbl_to_graph(example_edge_tbl)
example_ontology
#> # A tbl_graph: 24 nodes and 24 edges
#> #
#> # A directed acyclic simple graph with 1 component
#> #
#> # Node Data: 24 x 1 (active)
#>   name
#>   <chr>
#> 1 Nstage
#> 2 Tstage
#> 3 Tumoursize
#> 4 property_of_tumour
#> 5 TNM
#> 6 property_of_cancer
#> # ... with 18 more rows
#> #
#> # Edge Data: 24 x 2
#>   from  to
#>   <int> <int>
#> 1     1     5
#> 2     2     5
#> 3     3     4
#> # ... with 21 more rows
```

Node attributes can be included in the edge table (see `?edge_tbl_to_graph`) to be used as labels during meta-variable aggregation (`label_attr` parameter in `metavariable_agg`).

## Join ontology and data variable names

Nodes representing variable names in the dataset can be joined to the ontology to which they have been mapped with `join_vars_to_ontol()`. Prior to joining, this function calculates the information content of each ontological entity using the equation below, developed by Zhou, Wang, and Gu (2008):

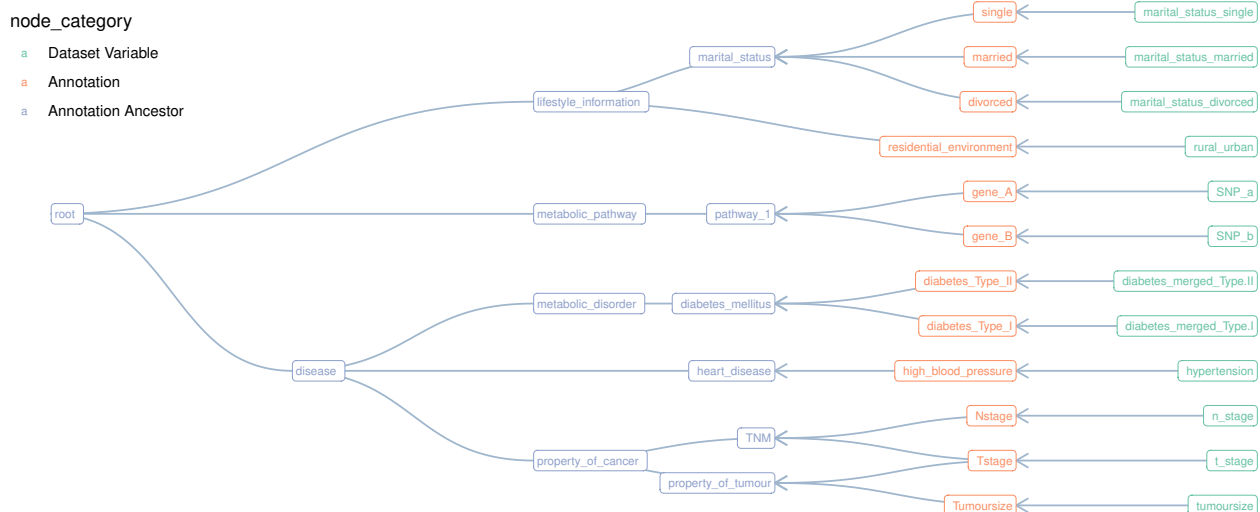
$$IC(c) = k\left(1 - \frac{\log(\text{hypo}(c) + 1)}{\log(\text{node}_{\max})}\right) + (1 - k)\left(\frac{\log(\text{deep}(c))}{\log(\text{deep}_{\max})}\right)$$

Where  $c$  is an ontological entity in `ontol_graph`,  $\text{hypo}(c)$  is the number of hyponyms (descendants) of  $c$ ,  $\text{node}_{\max}$  is the total number of ontological entities in `ontol_graph`,  $\text{deep}(c)$  is the depth of  $c$  (distance from `root`),  $\text{deep}_{\max}$  is the maximum depth in `ontol_graph`, and  $k$  is an adjustable factor to adjust the weight of the two terms (default = 0.5); a higher  $k$  value will reduce the importance/impact of  $c$ 's relative depth in the ontology.

```
joined_nw <- join_vars_to_ontol(ontol_graph = example_ontology,
                              var2entity_tbl = example_mapping_file,
                              root = "root", k = 0.5)
```

This network, with the variable names added as nodes, can be visualised as below. The `node_category` node attribute can be used to colour the nodes:

```
ggraph::ggraph(joined_nw, layout = "sugiyama") +
  ggraph::geom_edge_diagonal(arrow = arrow(length = unit(3, 'mm')),
                             colour = "slategray3") +
  ggraph::geom_node_label(aes(
    label = name, color = node_category), size = 2.5,
    repel = F, hjust="inward") +
  theme_void() +
  scale_color_brewer(palette = "Set2") +
  coord_flip() +
  theme(legend.position = c(0.08, 0.85))
```

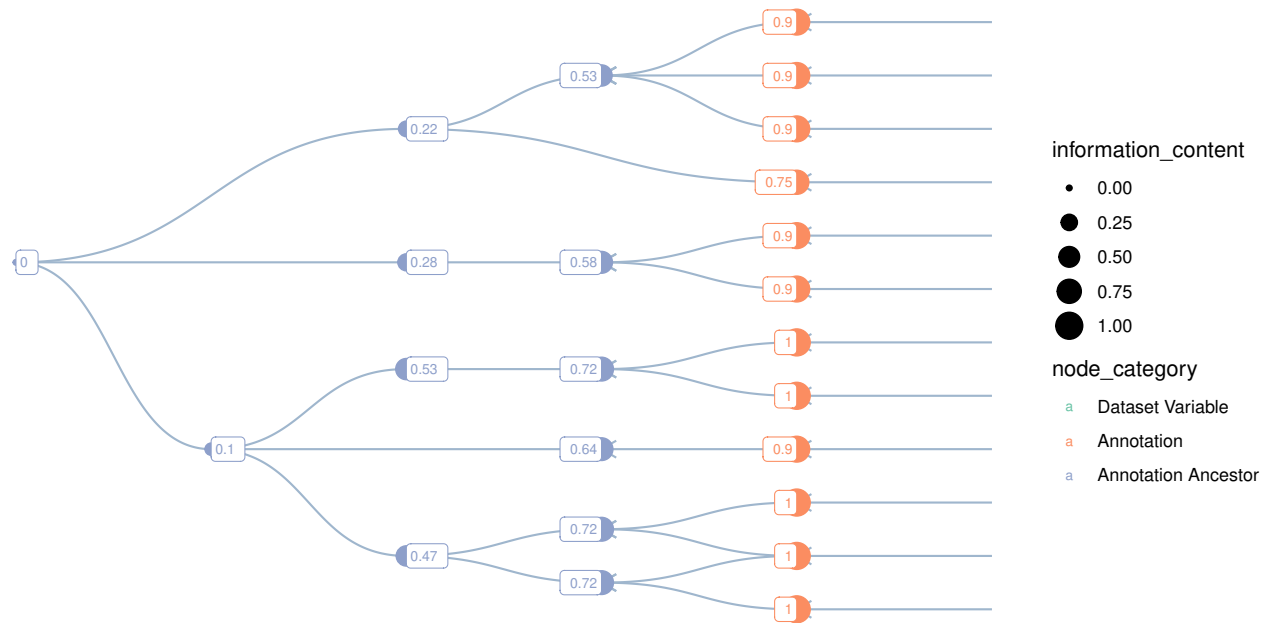


**Figure 14:** Visualisation of ‘example\_ontology’ using the `ggraph` package, coloured by the category of the node.

Node information content can be visualised, as below. Information content is not calculated for dataset variables because they are not part of the original ontology, therefore their node size is 0. This visualisation helps demonstrate how nodes/concepts further down the ontology are more informative than those higher up.

This calculation benefits SE as the common ancestor of a set of variable nodes with the highest information content is chosen to label the group. In the middle branch from the root node, there are two annotation ancestor nodes which are multiple common ancestors of two variables (`SNP_a` and `SNP_b`). The node with the higher information content, `pathway_1`, is chosen to label the semantic commonality between these variables over the less informative node, `metabolic_pathway`.

```
ggraph::ggraph(joined_nw, layout = "sugiyama") +
  ggraph::geom_edge_diagonal(arrow = arrow(length = unit(3, 'mm')),
    colour = "slategray3") +
  ggraph::geom_node_point(aes(
    color = node_category, size = information_content)) +
  ggraph::geom_node_label(aes(
    label = round(information_content, 2),
    color = node_category, size = 2.5, hjust="inward")) +
  scale_color_brewer(palette = "Set2") +
  theme_void() +
  coord_flip()
```



**Figure 15:** Visualisation of ‘example\_ontology’ using the ggraph package, coloured by the category of the node. Node size is proportional to node information content. Node labels denote node information content. Dataset variable nodes (right hand side of figure) are not visible as information content is only applicable to ontological entities.

### Compute meta-variable information

“Meta-variable” is defined here as an ontological entity which is the most informative common ancestor of two or more variables in the joined network. Meta-variables are identified in `metavariable_info()` by first determining the unique sets of variable nodes which are descendants of ontological nodes. The information

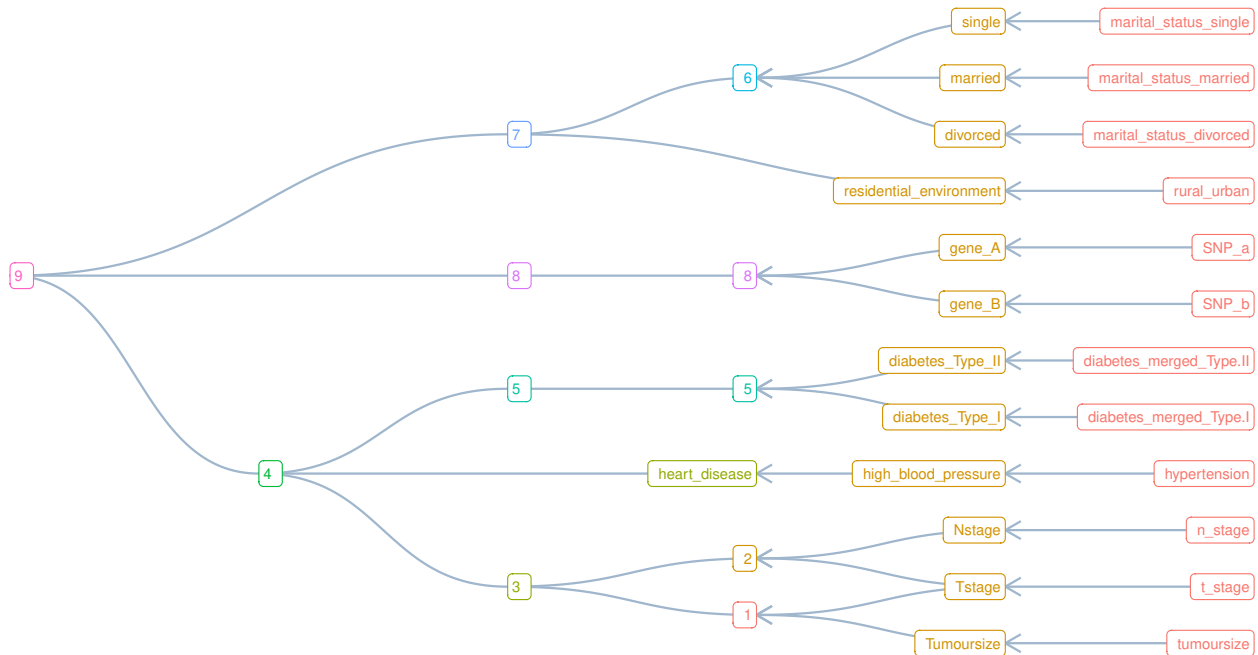
content (IC, calculated above) of nodes which share the same set of variable descendants is compared and the node with the highest IC is used to label the set.

example\_ontology links variable nodes in joined\_nw to identify nine sets, shown in the graph below:

```
example_ontology %>%
  join_vars_to_ontol(var2entity_tbl = example_mapping_file, root = "root") %>%
  metavariable_info() ->
  metavariables_nw
#> Identifying semantic commonalities...
#> Complete. Duration: 1.22 secs.
#> 9 semantic commonalities found (via common ontological ancestors).

metavariables_nw %>%
  # annotations are also considered a set. This isn't helpful for this visualisation
  # Therefore, the sets of non-meta-variables are removed below
  tidygraph::mutate(variable_set = ifelse(!is_metavariable, NA, variable_set)) %>%
  tidygraph::mutate(variable_set = as.factor(variable_set)) %>%
  ggraph::ggraph(layout = "sugiyama") +
  ggraph::geom_edge_diagonal(arrow = arrow(length = unit(3, 'mm')),
    colour = "slategray3") +
  ggraph::geom_node_label(aes(label = ifelse(is_metavariable,
    as.factor(as.numeric(variable_set)),
    name),
    color = ifelse(is_metavariable,
    as.character(as.numeric(variable_set)),
    node_category)),
    repel = F, size = 2.5, hjust="inward") +
  theme_void() +
  theme(legend.position = "none") +
  coord_flip()
```





**Figure 16:** Visualisation of ‘example\_ontology’ using the ggraph package. Ontological entities which link two or more dataset variables as descendants are labelled with numeric identifiers for the set of variables linked. Variable sets 5 and 8 variables are shown to have multiple common ancestors. This demonstrates the need to consider the information content of common ancestors so that the most informative common ancestor is used in the labelling of meta-variables.

Note how variable sets 5 and 8 each have two nodes which share the same set of variables. The information content, calculated during `join_vars_to_ontol()`, of these nodes is compared and the node with the highest information content is used to label the set.

Additionally, a minimum threshold can be applied to the information content to exclude less informative (less specific) meta-variables from subsequent aggregation with the `IC_threshold` parameter).

### Review meta-variables’ source variables

Information describing dataset variables which have been identified as ontological descendants for each meta-variable is contained in the output of `metavariable_info()`. Reviewing this information can be important in understanding how meta-variables were constructed. This is particularly true for meta-variables with a low information content as their label will be less specific to the dataset variables.

`metavariable_variable_descendants()` distils this information from the output of `metavariable_info()` into a table where each row describes one most informative common ancestor (the precursor to meta-variable aggregations), its information content, and one of its descendant/source variables which was used in its creation.

```
metavariable_variable_descendants(metavariablw_nw)
#> # A tibble: 36 x 3
#>   metavariable      information_content descendant_variable
#>   <chr>              <dbl> <chr>
#> 1 property_of_tumour 7.2e-1 t_stage
#> 2 property_of_tumour 7.2e-1 tumoursize
#> 3 TNM                7.2e-1 n_stage
```

```

#> 4 TNM 7.2e-1 t_stage
#> 5 diabetes_mellitus 7.2e-1 diabetes_merged_Type.I
#> 6 diabetes_mellitus 7.2e-1 diabetes_merged_Type.II
#> 7 pathway_1 5.8e-1 SNP_a
#> 8 pathway_1 5.8e-1 SNP_b
#> 9 marital_status 5.3e-1 marital_status_divorced
#> 10 marital_status 5.3e-1 marital_status_married
#> # ... with 26 more rows

```

## Generate semantic aggregations

With the sets of variables identified and the meta-variable used to label each set confirmed, the next step is to perform the aggregations. This functionality requires the previously described low-level SE functions and overlaps with the `semantic_enrichment()` function, but does not carry out some of the checks.

```

example_ontology %>%
  join_vars_to_ontol(var2entity_tbl = example_mapping_file, root = "root") %>%
  metavariable_info() %>%
  metavariable_agg(data = post_qc_data) ->
  qc_se_data
#> Aggregating variables with semantic commonalities to metavariables
#> and appending to `data`...
#> Metavariables will be labelled by the most informative common ancestor.
#> Identifying semantic commonalities...
#> Complete. Duration: 1.22 secs.
#> 9 semantic commonalities found (via common ontological ancestors).
#> Complete. Duration: 39.09 secs.
#> The dataset has been enriched with 35 metavariables
#> (10 metavariables had zero entropy and were therefore not appended).

## summary of output
tibble::glimpse(qc_se_data)
#> Rows: 1,000
#> Columns: 50
#> $ tumoursize <dbl> 61.71058, 64.18932, 47.81393, 40.93006, 62.117~
#> $ t_stage <dbl> 3, 4, 1, 3, 5, 1, 1, 4, 2, 1, 5, 4, 3, 2, 5, 3~
#> $ n_stage <dbl> 3, 2, 3, 1, 2, 3, 3, 2, 2, 1, 3, 1, 3, 1, 2, 2~
#> $ hypertension <dbl> 2, 2, 2, 2, 1, 2, 1, 1, 2, 1, 2, 1, 1, 1, 1, 2~
#> $ rural_urban <dbl> 1, 2, 1, 1, 2, 2, 2, 1, 1, 1, 2, 2, 2, 2, 2, 1~
#> $ SNP_a <dbl> 1, 1, 1, 1, 2, 2, 1, 2, 2, 2, 2, 1, 2, 1, 2, 2~
#> $ SNP_b <dbl> 2, 3, 2, 2, 2, 2, 2, 2, 2, 1, 1, 3, 1, 3, 2, 1~
#> $ diabetes_merged_No <dbl> 0, 0, 0, 1, 0, 1, 1, 1, 1, 1, 0, 1, 0, 0, 1, 0~
#> $ diabetes_merged_Type.I <dbl> 1, 0, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 1, 0, 0, 1~
#> $ diabetes_merged_Type.II <dbl> 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0~
#> $ diabetes_merged_NA <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0~
#> $ marital_status_divorced <dbl> 0, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1~
#> $ marital_status_married <dbl> 1, 0, 0, 0, 0, 0, 1, 0, 0, 1, 1, 1, 1, 0, 1, 0~
#> $ marital_status_single <dbl> 0, 0, 0, 1, 1, 1, 0, 1, 1, 0, 0, 0, 0, 1, 0, 0~
#> $ marital_status_NA <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0~
#> $ MV_property_of_tumour_SUM <dbl> 1.0506338, 1.3209213, 0.4368958, 0.8805543, 1.~
#> $ MV_property_of_tumour_AVG <dbl> 0.7004225, 0.8806142, 0.2912639, 0.5870362, 1.~
#> $ MV_property_of_tumour_MAX <dbl> 1.0506338, 1.3209213, 0.4368958, 0.8805543, 1.~
#> $ MV_property_of_tumour_MIN <dbl> 0.5000000, 0.5709213, 0.0000000, 0.3805543, 0.~

```

```

#> $ MV_property_of_tumour_MUL <dbl> 0.106430411, 0.375623897, 0.000000000, 0.03295~
#> $ MV_TNM_SUM <dbl> 1.50, 1.25, 1.00, 0.50, 1.50, 1.00, 1.00, 1.25~
#> $ MV_TNM_AVG <dbl> 1.0000000, 0.8333333, 0.6666667, 0.3333333, 1.~
#> $ MV_TNM_MAX <dbl> 1.50, 1.25, 1.00, 0.50, 1.50, 1.00, 1.00, 1.25~
#> $ MV_TNM_MIN <dbl> 0.50, 0.50, 0.00, 0.00, 0.50, 0.00, 0.00, 0.50~
#> $ MV_TNM_MUL <dbl> 0.562500000, 0.244140625, 0.000000000, 0.00000~
#> $ MV_property_of_cancer_SUM <dbl> 2.0506338, 1.8209213, 1.4368958, 0.8805543, 2.~
#> $ MV_property_of_cancer_AVG <dbl> 1.0253169, 0.9104606, 0.7184479, 0.4402771, 1.~
#> $ MV_property_of_cancer_MAX <dbl> 2.0506338, 1.8209213, 1.4368958, 0.8805543, 2.~
#> $ MV_property_of_cancer_MIN <dbl> 0.5000000, 0.5000000, 0.0000000, 0.0000000, 0.~
#> $ MV_property_of_cancer_MUL <dbl> 0.593522555, 0.323162519, 0.000000000, 0.00000~
#> $ MV_disease_SUM <dbl> 4.0506338, 3.8209213, 3.4368958, 1.8805543, 3.~
#> $ MV_disease_AVG <dbl> 1.15732395, 1.09169179, 0.98197023, 0.53730122~
#> $ MV_disease_MAX <dbl> 4.0506338, 3.8209213, 3.4368958, 1.8805543, 3.~
#> $ MV_diabetes_mellitus_SUM <dbl> 1, 1, 1, 0, 1, 0, 0, 0, 1, 0, 1, 1, 0, 1~
#> $ MV_diabetes_mellitus_AVG <dbl> 0.6666667, 0.6666667, 0.6666667, 0.0000000, 0.~
#> $ MV_diabetes_mellitus_MAX <dbl> 1, 1, 1, 0, 1, 0, 0, 0, 1, 0, 1, 1, 0, 1~
#> $ MV_marital_status_SUM <dbl> 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1~
#> $ MV_marital_status_AVG <dbl> 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0.5, 0~
#> $ MV_marital_status_MAX <dbl> 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1~
#> $ MV_lifestyle_information_SUM <dbl> 1, 2, 1, 1, 2, 2, 2, 1, 1, 1, 2, 2, 2, 2, 1~
#> $ MV_lifestyle_information_AVG <dbl> 0.4, 0.8, 0.4, 0.4, 0.8, 0.8, 0.8, 0.4, 0.4, 0~
#> $ MV_lifestyle_information_MAX <dbl> 1, 2, 1, 1, 2, 2, 2, 1, 1, 1, 2, 2, 2, 2, 1~
#> $ MV_pathway_1_SUM <dbl> 0.5, 1.0, 0.5, 0.5, 1.0, 1.0, 0.5, 1.0, 1.0, 0~
#> $ MV_pathway_1_AVG <dbl> 0.3333333, 0.6666667, 0.3333333, 0.3333333, 0.~
#> $ MV_pathway_1_MAX <dbl> 0.5, 1.0, 0.5, 0.5, 1.0, 1.0, 0.5, 1.0, 1.0, 0~
#> $ MV_pathway_1_MIN <dbl> 0.0, 0.0, 0.0, 0.0, 0.5, 0.5, 0.0, 0.5, 0.5, 0~
#> $ MV_pathway_1_MUL <dbl> 0.00000000, 0.00000000, 0.00000000, 0.00000000~
#> $ MV_root_SUM <dbl> 5.550634, 6.820921, 4.936896, 3.380554, 6.0539~
#> $ MV_root_AVG <dbl> 0.8539437, 1.0493725, 0.7595224, 0.5200853, 0.~
#> $ MV_root_MAX <dbl> 5.550634, 6.820921, 4.936896, 3.380554, 6.0539~

```

## References

- Benoit, Kenneth, Kohei Watanabe, Haiyan Wang, Paul Nulty, Adam Obeng, Stefan Müller, and Akitaka Matsuo. 2018. “Quanteda: An r Package for the Quantitative Analysis of Textual Data.” *Journal of Open Source Software* 3 (30): 774. <https://doi.org/10.21105/joss.00774>.
- Gene Ontology Consortium, The. 2019. “The Gene Ontology Resource: 20 Years and Still GOing Strong.” *Nucleic Acids Research* 47 (D1): D330–38. <https://doi.org/10.1093/nar/gky1055>.
- Köhler, Sebastian, Michael Gargano, Nicolas Matentzoglou, Leigh C. Carmody, David Lewis-Smith, Nicole A. Vasilevsky, Daniel Danis, et al. 2021. “The Human Phenotype Ontology in 2021.” *Nucleic Acids Research* 49 (D1): D1207–17. <https://doi.org/10.1093/nar/gkaa1043>.
- Kolde, Raivo. 2019. *Pheatmap: Pretty Heatmaps*. <https://CRAN.R-project.org/package=pheatmap>.
- Millar, Jane. 2016. “The Need for a Global Language - SNOMED CT Introduction.” *Studies in Health Technology and Informatics* 225: 683–85.
- Roebuck, Kevin. 2011. *Data Quality: High-Impact Strategies - What You Need to Know: Definitions, Adoptions, Impact, Benefits, Maturity, Vendors*. Lightning Source Incorporated.
- Schriml, Lynn M., Elvira Mitraka, James Munro, Becky Tauber, Mike Schor, Lance Nickle, Victor Felix, et al. 2019. “Human Disease Ontology 2018 update: classification, content and workflow expansion.” *Nucleic Acids Research* 47 (D1): D955–62. <https://doi.org/10.1093/nar/gky1032>.
- Shannon, C. E. 1948. “A Mathematical Theory of Communication.” *The Bell System Technical Journal* 27 (3): 379–423. <https://doi.org/10.1002/j.1538-7305.1948.tb01338.x>.

- Wickham, Hadley, Mara Averick, Jennifer Bryan, Winston Chang, Lucy D'Agostino McGowan, Romain François, Garrett Golemund, et al. 2019. “Welcome to the Tidyverse.” *Journal of Open Source Software* 4 (43): 1686. <https://doi.org/10.21105/joss.01686>.
- Zhou, Zili, Yanna Wang, and Junzhong Gu. 2008. “2008 Second International Conference on Future Generation Communication and Networking Symposia.” In, 3:85–89. <https://doi.org/10.1109/FGCNS.2008.16>.