



ricu: R's Interface to Intensive Care Data

Nicolas Bennett*
ETH Zürich

Drago Plečko*
ETH Zürich

Ida-Fong Ukor
Monash Health

Nicolai Meinshausen
ETH Zürich

Peter Bühlmann
ETH Zürich

Abstract

Providing computational infrastructure for handling diverse intensive care unit (ICU) datasets, the R package **ricu** enables writing dataset-agnostic analysis code, thereby facilitating multi-center training and validation of machine learning models. The package is designed with an emphasis on extensibility both to new datasets as well as clinical data concepts, and currently supports the loading of around 100 patient variables corresponding to a total of 319,402 ICU admissions from 4 data sources collected in Europe and the United States. By allowing for the addition of user-specified medical concepts and data sources the aim of **ricu** is to foster robust, data-based intensive care research, allowing the user to externally validate their method or conclusion with relative ease, and in turn facilitating reproducible and therefore transparent work in this field.

Keywords: electronic health records, computational physiology, critical care medicine.

1. Introduction

Collection of electronic health records has seen a significant rise in recent years (Evans 2016), opening up opportunities and providing the grounds for a large body of data-driven research oriented towards helping clinicians in decision-making and therefore improving patient care and health outcomes (Jiang, Jiang, Zhi, Dong, Li, Ma, Wang, Dong, Shen, and Wang 2017). One example of a problem that has received much attention from the machine learning community is early prediction of sepsis in ICU (Desautels, Calvert, Hoffman, Jay, Kerem, Shieh, Shimabukuro, Chettipally, Feldman, Barton *et al.* 2016; Nemati, Holder, Razmi, Stanley, Clifford, and Buchman 2018; Futoma, Hariharan, Sendak, Brajer, Clement, Bedoya, O'Brien,

*These authors contributed equally.

and Heller 2017; Kam and Kim 2017). Interestingly, there is evidence that a large proportion of the publications are based on the same dataset (Fleuren, Klausch, Zwager, Schoonmade, Guo, Roggeveen, Swart, Girbes, Thorat, Ercole, Hoogendoorn, and Elbers 2020), the Medical Information Mart for Intensive Care III (MIMIC-III; Johnson, Pollard, Shen, Li-wei, Feng, Ghassemi, Moody, Szolovits, Celi, and Mark 2016), which shows a systematic lack of external validation. Part of this problem might well be the need for computational infrastructure handling multiple datasets. The MIMIC-III dataset consists of 26 different tables containing about 20GB of data. While much work and care has gone into data preprocessing in order to provide a self-contained ready -to-use data resource with MIMIC-III, seemingly simple tasks such as computing a sepsis-related organ failure assessment (SOFA) score (Vincent, Moreno, Takala, Willatts, De Mendonça, Bruining, Reinhart, Suter, and Thijs 1996) remains a non-trivial effort¹. This is only exacerbated when aiming to co-integrate multiple different datasets of this form, spanning hospitals and even countries, in order to capture effects of differing practice and demographics.

The aim of the **ricu** package is to provide computational infrastructure allowing users to investigate complex research questions in the context of critical care medicine as easily as possible by providing a unified interface to a heterogeneous set of data sources. The package enables users to write dataset-agnostic code which can simplify implementation and shorten the time necessary for prototyping code querying different datasets. In its current form, the package handles four large-scale, publicly available intensive care databases out of the box: MIMIC-III from the Beth Israel Deaconess Medical Center in Boston, Massachusetts (Johnson *et al.* 2016), the eICU Collaborative Research Database (Pollard, Johnson, Raffa, Celi, Mark, and Badawi 2018), containing data collected from 208 hospitals across the United States, the High Time Resolution ICU Dataset (HiRID) from the Department of Intensive Care Medicine of the Bern University Hospital, Switzerland (Faltys, Zimmermann, Lyu, Hüser, Hyland, Rättsch, and Merz 2021) and AmsterdamUMCdb from the Amsterdam University Medical Center (Thorat, Peppink, Driessen, Sijbrands, Kompanje, Kaplan, Bailey, Kesecioglu, Cecconi, Churpek, Clermont, van der Schaar, Ercole, Girbes, Elbers, Force, and the SCCM/ESICM Joint Data Science Task 2021). Furthermore, **ricu** was designed with extensibility in mind such that adding further public and/or private user-provided datasets is possible. Being implemented in R, a programming language popular among statisticians and data analysts, it is our hope to contribute to accessible and reproducible research by using a familiar environment and requiring only few system dependencies, thereby simplifying setup considerably.

To our knowledge, infrastructure that provides a common interface to multiple such datasets is a novel contribution. While there have been efforts (Adibuzzaman, Musselman, Johnson, Brown, Pitluk, and Grama 2016; Wang, McDermott, Chauhan, Ghassemi, Hughes, and Naumann 2020) attempting to abstract away some specifics of a dataset, these have so far exclusively focused on MIMIC-III, the most popular of public ICU datasets and have not been

¹There is considerable heterogeneity in number of patients satisfying the Sepsis-3 criterion (of which SOFA provides a major component; Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, Coopersmith, Hotchkiss, Levy, Marshall, Martin, Opal, Rubenfeld, van der Poll, Vincent, and Angus 2016) among studies investigating MIMIC-III. Reported Sepsis-3 prevalence ranges from 11.3% (Desautels *et al.* 2016), over 23.9% (Nemati *et al.* 2018) and 25.4% (Wang, Sun, Schroeder, Ameko, Moore, and Barnes 2018), up to 49.1% (Johnson, Aboab, Raffa, Pollard, Deliberato, Celi, and Stone 2018). While some of this variation may be explained by differing patient inclusion criteria, diversity in label implementation must also contribute significantly.

designed with dataset interoperability in mind.

Given the somewhat narrow focus of the targeted datasets, combined with the fact that in some cases data is even extracted from identical patient care management systems, it may come as a surprise as to how heterogeneous the resulting datasets are. In MIMIC-III and HiRID, for example, time-stamps are reported as absolute times (albeit randomly shifted due to data privacy concerns), whereas eICU and AUMC use relative times (with origins being admission times). Another example, involves different types of patient identifiers and their use among datasets. Common to all is the notion of an ICU admission ID, but apart from that, the amount of available information varies: While ICU (and hospital) readmissions for a given patient can be identified in some, this is not possible in other datasets. Furthermore, use of identifier systems might not be consistent over tables. In MIMIC-III, for example, some tables refer to ICU stay IDs while others use hospital stay IDs, which slightly complicates data retrieval for a given ID system. Additionally, table layouts vary (*long* versus *wide* data arrangement) and data organization in general is far from consistent over datasets.

2. Quick start guide

The following list gives a quick outline of the steps required for setting up and starting to use **ricu**, alongside some section references on where to find further details. A more comprehensive version of this overview is available as a [separate vignette](#).

1. Package installation:

- the latest release of **ricu** can be installed from CRAN as `install.packages("ricu")`
- alternatively, the latest development version is available from [Github](#) by running `remotes::install_github("eth-mds/ricu")`

2. Requesting access to datasets and data source setup:

- demo datasets can be set up by installing the data packages `mimic.demo` and/or `eicu.demo`, passing `"https://eth-mds.github.io/physionet-demo"` as `repos` argument to `install.packages()` (see code snippet in [Section 3](#))
- the complete MIMIC-III, eICU and HiRID datasets can be accessed by setting up an account at [PhysioNet](#)
- access to AUMCdb is available via the [Amsterdam Medical Data Science Website](#)
- the obtained credentials can be configured for PhysioNet datasets by setting environment variables `RICU_PHYSIONET_USER` and `RICU_PHYSIONET_PASS`, while the download token for AUMCdb can be set as `RICU_AUMC_TOKEN`
- datasets are downloaded and set up either automatically upon the first access attempt or manually by running `setup_data_src()`; the environment variable `RICU_DATA_PATH` can be set to control data location
- dataset availability can be queried by calling `src_data_avail()`

A more detailed description of the supported datasets is given in [Section 3](#), summarized in [Table 1](#), while [Section 5](#) provides implementation details, elaborating on how datasets are represented in code.

3. Loading of data corresponding to clinical concepts using `load_concepts()`:

- currently, over 100 data concepts are available for the 4 supported datasets (see `concept_availability()/explain_dictionary()` for names, availability etc.)
- both concepts and data sources can be specified as strings; for example, glucose and age data can be loaded from MIMIC-III as `load_concepts(c("age", "glu"), "mimic")`

Section 4 goes into more detail on how data concepts are represented within **ricu** and an overview of the pre-configured concepts is available from Section 4.2.

4. Extending the concept dictionary:

- data concepts can be specified in code using the constructors `concept()/item()` or `new_concept()/new_item()`
- for session persistence, data concepts can also be specified as JSON formatted objects
- JSON-based concept dictionaries can either extend or replace others and they can be pointed to by setting the environment variable `RICU_CONFIG_PATH`

The JSON format used to encode data concepts is discussed in more detail in Section 4.3.

5. Adding new datasets:

- a JSON-based dataset configuration file is required, from which the configuration objects described in Section 5.3 are created
- in order for concepts to be available from the new dataset, the dictionary requires extension by adding new data items

Further information about adding a custom dataset is available from Section 5.4. Some code used when AUMCdb was not yet fully integrated with **ricu** is available from [Github](#) and is used for demonstration purposes for setting up AUMCdb as external dataset `aumc_ext`.

The final section (6) shows briefly how **ricu** could be used in practice to address clinical questions by presenting two small examples.

3. Ready to use datasets

Several large-scale ICU datasets collected from multiple hospitals in the US and Europe can be set up for access using **ricu** with minimal user effort. Provisions in terms of required configuration information alongside functions for download and setup are part of **ricu**, opening up easy access to these datasets. Data itself, however, is not part of **ricu** and while the supported datasets are publicly available, access has to be granted by the dataset creators individually. Three datasets, MIMIC-III, eICU and HiRID are hosted on PhysioNet ([Goldberger, Amaral,](#)

Glass, Hausdorff, Ivanov, Mark, Mietus, Moody, Peng, and Stanley 2000), access to which requires an [account](#), while the fourth, AmsterdamUMCdb is currently distributed via a separate platform, requiring a [download link](#).

For both MIMIC-III and eICU, small subsets of data are available as demo datasets that do not require credentialed access to PhysioNet. As the terms for distribution of these demo datasets are less restrictive, they can be made available as data packages **mimic.demo** and **eicu.demo**. Due to size constraints, however they are not available via CRAN, but can be installed from Github as

```
R> install.packages(
+   c("mimic.demo", "eicu.demo"),
+   repos = "https://eth-mds.github.io/physionet-demo"
+ )
```

Provisions for datasets configured to be attached during package loading are made irrespective of whether data is actually available. Upon access of an incomplete dataset, the user is asked for permission to download in interactive sessions and an error is thrown otherwise. Credentials can either be provided as environment variables (RICU_PHYSIONET_USER and RICU_PHYSIONET_PASS for access to PhysioNet data, as well as RICU_AUMC_TOKEN for AmsterdamUMCdb) and if the corresponding variables are unset, user input is again required in interactive sessions. For non-interactive sessions, functionality is exported such that data can be downloaded and set up ahead of first access (see `?setup_src_data`).

Contingent on being granted access by the data owners, Download requires a stable Internet connection, as well as 50 to 100 GB of temporary disk storage for unpacking and preparing the data for efficient access. In terms of permanent storage, 5 to 10 GB per dataset are required, while memory requirements are kept reasonably low by iterating over row-chunks for set-up operations. Laptop class hardware (8-16 GB of memory) should suffice for setup and many analysis tasks which focus only on subsets of rows (and columns). Initial data source set up (depending on available download speeds and CPU/disk type) may take upwards of an hour per dataset.

The following paragraphs serve to give quick introductions to the included datasets to offer some guidance, outlining some strengths and weaknesses of each of the datasets. Especially the PhysioNet datasets **MIMIC-III** and **eICU** offer good documentation on the respective websites. This section is concluded with a table summarizing similarities and differences among the datasets, outlined in the following paragraphs (see Table 1).

3.1. MIMIC-III

The **Medical Information Mart for Intensive Care III (MIMIC-III)** represents the third iteration of the arguably most influential initiative for collecting and providing to the public large-scale ICU data². The dataset comprises de-identified health related data of roughly 46,000 patients admitted to critical care units of BIDMC during the years 2001-2012. Amounting to

²The initial MIMIC (at the time short for Multi-parameter Intelligent Monitoring for Intensive Care) data release dates back 20 years and contained data on roughly 100 patients recorded from patient monitors in the medical, surgical, and cardiac intensive care units of Boston's Beth Israel Hospital during the years 1992-1999 (Moody and Mark 1996). Significantly broadened in scope, MIMIC-II was released 10 years after, now including data on almost 27,000 adult hospital admissions collected from ICUs of Beth Israel Deaconess Medical Center

just over 61,000 individual ICU admission, data is available on demographics, routine vital sign measurements (at approximately 1 hour resolution), laboratory tests, medication, as well as critical care procedures, organized as a 26-table relational structure.

```
R> mimic
```

```
<mimic_env[26]>
      admissions      callout      caregivers      chartevents
[58,976 x 19] [34,499 x 24] [7,567 x 4] [330,712,483 x 15]
      cptevents      d_cpt      d_icd_diagnoses      d_icd_procedures
[573,146 x 12] [134 x 9] [14,567 x 4] [3,882 x 4]
      d_items      d_labitems      datatimeevents      diagnoses_icd
[12,487 x 10] [753 x 6] [4,485,937 x 14] [651,047 x 5]
      drgcodes      icustays      inpatientevents_cv      inpatientevents_mv
[125,557 x 8] [61,532 x 12] [17,527,935 x 22] [3,618,991 x 31]
      labevents microbiologyevents      noteevents      outputevents
[27,854,055 x 9] [631,726 x 16] [2,083,180 x 11] [4,349,218 x 13]
      patients      prescriptions      procedureevents_mv      procedures_icd
[46,520 x 8] [4,156,450 x 19] [258,066 x 25] [240,095 x 5]
      services      transfers
[73,343 x 6] [261,897 x 13]
```

One thing of note from a data-organizational perspective is that a change in electronic health care systems occurred in 2008. Owing to this, roughly 48,000 ICU admissions spanning the years 2001 through 2008 are documented using the CareVue system, while for 2008 and onwards, data was extracted from the MetaVision system. Item identifiers differ between the two systems, requiring queries to consider both ID mappings (heart rate for example being available both as `itemid` number 211 for CareVue and 220045 for MetaVision) as does documentation of infusions and other procedures that are considered as input events (c.f. `inpatientevents_cv` and `inpatientevents_mv` tables). Especially with respect to such input event data, MetaVision data generally is of superior quality.

In terms of patient identifiers, MIMIC-III allows for identifying both individual patients (`subject_id`) across hospital admissions (`hadm_id`) and for connecting ICU (re-)admissions (`icustay_id`) to hospital admissions. Using the respective one-to-many relationships, **ricu** can retrieve patient data using any of the above IDs, irrespective of how the raw data is organized.

3.2. eICU

Unlike the single-center focus of other datasets, the **eICU Collaborative Research Database** constitutes an amalgamation of data from critical care units of over 200 hospitals throughout the continental United States. Large-scale data collected via the Philips eICU program which provides telehealth infrastructure for intensive care units, is available from the Philips eICU Research Institute (eRI), albeit neither publicly nor freely. Only data corresponding

(BIDMC) from 2001 to 2008 (Lee, Scott, Villarroel, Clifford, Saeed, and Mark 2011). The next iteration, MIMIC-IV has recently been released as first stable version (Johnson, Bulgarelli, Pollard, Horng, Celi, and Mark 2021) and experimental support in **ricu** is available as dataset `miiv`.

to roughly 200,000 ICU admissions, sampled from a larger population of over 3 million ICU admissions and stratified by hospital, is being made available via PhysioNet. Patients with discharge dates in 2014 or 2015 were considered, with stays in low acuity units being removed.

```
R> eicu
```

```
<eicu_env[31]>
```

admissiondrug	admissiondx	allergy
[874,920 x 14]	[626,858 x 6]	[251,949 x 13]
apacheapsvar	apachepatientresult	apachepredvar
[171,177 x 26]	[297,064 x 23]	[171,177 x 51]
careplancareprovider	careplaneol	careplangeneral
[502,765 x 8]	[1,433 x 5]	[3,115,018 x 6]
careplangoal	careplaninfectiousdisease	customlab
[504,139 x 7]	[8,056 x 8]	[1,082 x 7]
diagnosis	hospital	infusiondrug
[2,710,672 x 7]	[208 x 4]	[4,803,719 x 9]
intakeoutput	lab	medication
[12,030,289 x 12]	[39,132,531 x 10]	[7,301,853 x 15]
microlab	note	nurseassessment
[16,996 x 7]	[2,254,179 x 8]	[15,602,498 x 8]
nursecare	nursecharting	pasthistory
[8,311,132 x 8]	[151,604,232 x 8]	[1,149,180 x 8]
patient	physicalexam	respiratorycare
[200,859 x 29]	[9,212,316 x 6]	[865,381 x 34]
respiratorycharting	treatment	vitalaperiodic
[20,168,176 x 7]	[3,688,745 x 5]	[25,075,074 x 13]
vitalperiodic		
[146,671,642 x 19]		

The data is organized into 31 tables and includes patient demographics, routine vital signs, laboratory measurements, medication administrations, admission diagnoses, as well as treatment information. Owing to the wide range of hospitals participating in this data collection initiative, spanning small, rural, non-teaching health centers with fewer than 100 beds to large teaching hospitals with an excess of 500 beds, data availability varies. Even if data was being recorded at the bedside it might end up missing from the eICU dataset due to technical limitations of the collection process. As for patient identifiers, while it is possible to link ICU admissions corresponding to the same hospital stay, it is not possible to identify patients across hospital stays.

Data resolution again varies considerably over included variables. The `vitalperiodic` table stands out as one of the few examples of a *wide* table organization (laying out variables as columns), as opposed to the *long* presentation (following an entity–attribute–value) of most other tables containing patient measurement data. The average time step in `vitalperiodic` is around 5 minutes, but data missingness ranges from around 1% for heart rate and pulse oximetry to around 80-90% for blood pressure measurements, therefore giving approximately hourly resolution for such variables.

3.3. HiRID

Developed for early prediction of circulatory failure (Hyland, Faltys, Hüser, Lyu, Gumbusch, Esteban, Bock, Horn, Moor, Rieck, Zimmermann, Bodenham, Borgwardt, Rätsch, and Merz 2020), the **High Time Resolution ICU Dataset (HiRID)** contains data on almost 34,000 admissions to the Department of Intensive Care Medicine of the Bern University Hospital, Switzerland, an interdisciplinary 60-bed unit. Given the clear focus on a concrete application during data collection, this dataset is the most limited in terms of breadth of available information, which is also reflected in a comparatively simple data layout comprising only 5 tables³.

```
R> hirid
```

```
<hirid_env[5]>
      general      observations      ordinal      pharma
[33,905 x 5] [776,921,131 x 8] [72 x 3] [16,270,399 x 14]
variables
[712 x 5]
```

Collected during the period of January 2008 through June 2016, roughly 700 distinct variables covering routine vital signs, diagnostic test results and treatment parameters are available with variables monitored at the bedside being recorded with two minute time resolution. In terms of demographic information and patient identifier systems however, the data is limited. It is not possible to identify ICU admissions corresponding to individual patients and apart from patient age, sex, weight and height, very little information is available to characterize patients. There is no medical history, no admission diagnoses, only in-ICU mortality information, no unstructured patient data and no information on patient discharge. Furthermore, data on body fluid sampling has been omitted, complicating for example the construction of a Sepsis-3 label (Singer *et al.* 2016).

3.4. AmsterdamUMCdb

As a second European dataset, also focusing on increased time-resolution over the US datasets, **AmsterdamUMCdb** has been made available in late 2019, containing data on over 23,000 intensive care unit and high dependency unit admissions of adult patients during the years 2003 through 2016. The department of Intensive Care at Amsterdam University Medical Center is a mixed medical-surgical ICU with up to 32 bed ICU and 12 bed high dependency units with an average of 1000-2000 yearly admissions. Covering middle ground between the US datasets and HiRID in terms of breadth of included data, while providing a maximal time-resolution of 1 minute, AmsterdamUMCdb constitutes a well organized high quality ICU data resource organized succinctly as a 7-table relational structure.

³The data is available in three states: as raw data and in preprocessed form, with preprocessed data being represented by two intermediary pipeline stages from (Hyland *et al.* 2020). While **ricu** focuses exclusively on raw data, the *merged* stage represents a selection of variables that were deemed most predictive for determining circulatory failure, which are then merged into 18 meta-variables, representing different clinical concepts. Time stamps in *merged* data are left unchanged, yielding irregular time series, whereas for the *imputed* stage, data is down-sampled to a 5 minute grid and missing values are imputed using a scheme discussed in (Hyland *et al.* 2020).


```
R> aumc
```

```
<aumc_env[7]>
```

admissions	drugitems	freetextitems
[23,106 x 17]	[4,907,269 x 31]	[651,248 x 11]
listitems	numericitems	procedureorderitems
[30,744,065 x 11]	[977,625,612 x 15]	[2,188,626 x 8]
processitems		
[256,715 x 6]		

A slightly different approach to data anonymization was chosen for this dataset, yielding demographic information such as patient weight, height and age only available as binned variables instead of raw numeric values. Apart from this, there is information on patient origin, mortality, admission diagnoses, as well as numerical measurements including vital parameters, lab results, outputs from drains and catheters, information on administered medication, and other medical procedures. In terms of patient identifiers, it is possible to link ICU admissions corresponding to the same individual, but it is not possible to identify separate hospital admissions.

Note: The following code blocks are run using demo (`mimic_demo` and `eicu_demo`) instead of full (`mimic`, `eicu`, `aumc` and `hirid`) datasets and therefore might be less useful. For data set up, please consult the manual at `?attach_src`. The full version of this vignette is available from [CRAN](#).

4. Data concepts

One of the key components of **ricu** is a scheme for specifying how to retrieve data corresponding to pre-defined clinical concepts from a given data source. This abstraction provides a mechanism for hiding away the data source specific implementation of a concept, in turn enabling dataset agnostic code for analysis. Heart rate, for example can be loaded from datasets `mimic_demo` and `eicu_demo` using the `hr` concept as

```
R> src <- "mimic_demo"
R> demo <- c(src, "eicu_demo")
R>
R> load_concepts("hr", demo, verbose = FALSE)
```

```
# A 'ts_tbl': 152,197 x 4
# Id vars:      'source', 'icustay_id'
# Units:       'hr' [bpm]
# Index var:   'charttime' (1 hours)
```

	source	icustay_id	charttime	hr
	<chr>	<int>	<drtn>	<dbl>
1	eicu_demo	141764	0 hours	119
2	eicu_demo	141764	1 hours	105

Table 1: Comparison of datasets supported by **ricu**, highlighting some of the major similarities and distinguishing features among the four data sources described in the preceding paragraphs. Values followed by parenthesized ranges represent medians and are accompanied by quartiles.

	MIMIC (demo)	eICU (demo)
Number of tables	25	31
Disk storage [GB]	0.01	0.06
Available concepts *	89	86
Admission counts		
ICU	136	2,520
Hospital	129	2,174
Unique patients	100	-
Stay lengths [day]		
ICU stays	2.11 (1.23 - 4.33)	1.47 (0.79 - 2.78)
Hospital stays	6.63 (3.31 - 10.65)	4.14 (2.12 - 7.90)
Frequency [1/day]		
Vital signs	1.00	12.00
(heart rate)	(1.00 - 1.00)	(12.00 - 12.00)
Lab tests	0.04	0.04
(bilirubin)	(0.04 - 0.08)	(0.04 - 0.05)

* These values represent the number of atomic concepts per data source. Additionally, 29 recursive concepts are available, which build on source-specific atomic concepts in a source-agnostic manner (see Section 4.3 for details).

```

      3 eicu_demo      141764    2 hours    95
      4 eicu_demo      141764    3 hours   106
      5 eicu_demo      141764    4 hours   102
      ...
152,193 mimic_demo    298685  314 hours    60
152,194 mimic_demo    298685  315 hours    56
152,195 mimic_demo    298685  316 hours    50
152,196 mimic_demo    298685  317 hours    48
152,197 mimic_demo    298685  318 hours     0
# ... with 152,187 more rows

```

This requires some form of infrastructure for specifying how to retrieve data subsets (Section 4.3), which is both extensible (to new concepts and new datasets) and flexible enough to handle concept-specific pre-processing, while providing abstractions that allow for code re-use for common data transformation tasks. Building on this, **ricu** has included a dictionary with over 100 concepts implemented for all four supported datasets (where possible; see also Section 4.2).

4.1. Data classes

In order to represent tabular ICU data, **ricu** provides several classes, all inheriting from `data.table`. The most basic of which, `id_tbl`, marks one (or several) columns as `id_vars` which serve to define a grouping (i.e. identify patients or unit stays). Inheriting from `id_tbl`, `ts_tbl` is capable of representing grouped time series data. In addition to `id_var` column(s), a single column is marked as `index_var` and is required to hold a base R `difftime` vector. Furthermore, `ts_tbl` contains a scalar-valued `difftime` object as `interval` attribute, specifying the time series step size. More recently, a further class `win_tbl`, inheriting from `ts_tbl` has been added. Objects of this class can be used for time-stamped measurements associated with a validity period. A set of drug infusions, consisting of both rates and intervals can as such be conveniently represented by a `win_tbl` object.

Meta data is transiently added to `data.table` objects by classes inheriting from `id_tbl` and for S3 generic functions which allow for object modifications, down-casting is implicit:

```

R> (dat <- ts_tbl(a = 1:5, b = hours(1:5), c = rnorm(5)))

# A 'ts_tbl': 5 x 3
# Id var:      'a'
# Index var:   'b' (1 hours)
      a b          c
<int> <drtn> <dbl>
1     1 1 hours 2.06
2     2 2 hours 0.718
3     3 3 hours 1.87
4     4 4 hours 1.41
5     5 5 hours 1.19

R> dat[["b"]] <- dat[["b"]] + mins(30)
R> dat

```

```
# An 'id_tbl': 5 x 3
# Id var:      'a'
      a b      c
<int> <drtn> <dbl>
1      1 5400 secs 2.06
2      2 9000 secs 0.718
3      3 12600 secs 1.87
4      4 16200 secs 1.41
5      5 19800 secs 1.19
```

Due to time series step size of `dat` being specified as 1 hour, an internal inconsistency is encountered when shifting time stamps by 30 minutes, as time steps are no longer multiples of the time series interval, in turn causing down-casting to `id_tbl`. If column `a` were to be removed, direct down-casting to `data.table` would be required in order to resolve inconsistencies⁴.

Coercion to base classes `data.frame` and `data.table` is easily possible using `as.data.frame()` and `as.data.table()`, which simply strips away the extra attributes. Coercion is also available as `data.table`-style by-reference operation (albeit user caution is advised as this does break with base R by-value or copy-on-modify semantics and may lead to unexpected behavior) by passing `by_ref = TRUE` to any of the above coercion functions.

In its current form, `win_tbl` objects can both be used to represent for example drug rates or drug amounts administered over a specified time-period. When calling the utility function `expand()` however, which creates a `ts_tbl` from a `win_tbl` by assigning values to the corresponding time steps, values are assumed to be *valid* for the given interval.

```
R> (dat <- win_tbl(a = 1:5, b = hours(1:5), c = mins(rep(90, 5)),
+               d = runif(5)))
```

```
# A 'win_tbl': 5 x 4
# Id var:      'a'
# Index var:    'b' (1 hours)
# Duration var: 'c'
      a b      c      d
<int> <drtn> <drtn> <dbl>
1      1 1 hours 90 mins 0.0355
2      2 2 hours 90 mins 0.128
3      3 3 hours 90 mins 0.331
4      4 4 hours 90 mins 0.352
5      5 5 hours 90 mins 0.467
```

```
R> expand(dat)
```

```
# A 'ts_tbl': 10 x 3
# Id var:      'a'
```

⁴Updating an object inheriting from `id_tbl` using `data.table::set()` bypasses consistency checks as this is not an S3 generic function and therefore its behavior cannot be tailored to requirements of `id_tbl` objects. It therefore is up to the user to avoid creating invalid `id_tbl` objects in such a way.

```
# Index var: 'b' (1 hours)
      a b          d
<int> <drtn> <dbl>
1      1 1 hours 0.0355
2      1 2 hours 0.0355
3      2 2 hours 0.128
4      2 3 hours 0.128
5      3 3 hours 0.331
6      3 4 hours 0.331
7      4 4 hours 0.352
8      4 5 hours 0.352
9      5 5 hours 0.467
10     5 6 hours 0.467
```

In a case where `d` represented drug amounts instead of drug rates, the current implementation of `expand()` would produce incorrect results. One would expect the overall amount in such a scenario to be evenly divided by – and the resulting fractions assigned to – the corresponding time steps. Allowing for this distinction is being considered but as of yet has not been implemented.

Utilizing the attached meta-data of objects inheriting from `id_tbl`, several utility functions can be called with concise semantics (as seen in the above example, where `expand()` is able to determine the required column names from the `win_tbl` object by default). Utilities include functions for sorting, checking for duplicates, aggregating data per combination of `id_vars` (and time step/time duration), checking time series data for gaps, verifying whether the time series is regular and converting between irregular and regular time series, as well as functions for several types of moving window operations. Adding to those class-specific implementations, `id_tbl` objects inherit from `data.table` (and therefore from `data.frame`), ensuring compatibility with a wide range of functionality targeted at these base-classes.

4.2. Ready to use concepts

The current selection of clinical concepts that is included with **ricu** covers many physiological variables that are available throughout the included datasets. Treatment-related information on the other hand, being more heterogeneous in nature and therefore harder to harmonize across datasets, has been added on an as-needed basis and therefore is more limited in breadth. A quick note on loading from multiple sources simultaneously: In the introductory example, heart rate was loaded from multiple data sources, resulting in a column `source` being added. This allows for identifying patient IDs corresponding to the respective data sources and the extra column is added to the set of `id_vars`. In the following calls to `load_concepts()`, only data from a single source is requested and therefore no corresponding column is added.

Available concepts can be enumerated using `load_dictionary()` and the utility function `explain_dictionary()` can be used to display some concept meta-data.

```
R> dict <- load_dictionary(demo)
R> head(dict)
```

```
<concept[6]>
```

```

                                abx                                adh_rate
antibiotics <lgl_cncpt[4]>      vasopressin rate <num_cncpt[3]>
                                adm                                age
patient admission type <fct_cncpt[2]>      patient age <num_cncpt[2]>
                                alb                                alp
                                albumin <num_cncpt[2]>      alkaline phosphatase <num_cncpt[2]>

```

```
R> explain_dictionary(head(dict))
```

	name	category	description
1	abx	medications	antibiotics
2	adh_rate	medications	vasopressin rate
3	adm	demographics	patient admission type
4	age	demographics	patient age
5	alb	chemistry	albumin
6	alp	chemistry	alkaline phosphatase

The following sub-sections serve to introduce some of the included concepts as well as highlight limitations that come with current implementations. Grouping the available concepts by category yields the following counts

```
R> table(vapply(dict, '[', character(1L), "category"))
```

blood gas	chemistry	demographics	hematology	medications	microbiology
10	21	6	20	17	1
neurological	outcome	output	respiratory	vitals	
8	19	2	10	6	

Physiological data

The largest and most well established group of concepts (covering more than half of all currently included concepts) includes physiological patient measurements such as routine vital signs, respiratory variables, fluid discharge amounts, as well as many kinds of laboratory tests including blood gas measurements, chemical analysis of body fluids and hematology assays.

```
R> load_concepts(c("alb", "glu"), src, interval = mins(15L),
+               verbose = FALSE)
```

```

# A 'ts_tbl': 1,965 x 4
# Id var:      'icustay_id'
# Units:      'alb' [g/dL], 'glu' [mg/dL]
# Index var:  'charttime' (15 mins)
      icustay_id charttime    alb    glu
      <int> <drtn>      <dbl> <dbl>

```

```

1      201006 -3495 mins  NA      116
2      201006 -2745 mins  NA       83
3      201006 -1275 mins  NA       91
4      201006   15 mins   2.4     175
5      201006   675 mins  NA      129
...
1,961   298685 15600 mins  NA      159
1,962   298685 16365 mins   2.2    153
1,963   298685 17400 mins  NA      182
1,964   298685 17595 mins  NA      122
1,965   298685 17955 mins   2.5    121
# ... with 1,955 more rows

```

Most concepts of this kind are represented by `num_cncpt` objects with an associated unit of measurement and a range of permissible values. Data is mainly returned as `ts_tbl` objects, representing time-dependent observations. Apart from conversion to a common unit (possibly using the `convert_unit()` callback function), little has to be done in terms of pre-processing: values are simply reported at time-points rounded to the requested interval.

Patient demographics

Moving on from dynamic, time-varying patient data, this group of concepts focuses on static patient information. While the assumption of remaining constant throughout a stay is likely to hold for variables such as patient sex or height this is only approximately true for others including age or weight. Nevertheless such effects are ignored and concepts of this group will be mainly returned as `id_tbl` objects with no corresponding time-stamps included.

Whenever requesting concepts which are returned with associated time-stamps (e.g. glucose) alongside time-constant data (e.g. age), merging will duplicate static data over all time-points.

```
R> load_concepts(c("age", "glu"), src, verbose = FALSE)
```

```

# A 'ts_tbl': 1,914 x 4
# Id var:      'icustay_id'
# Units:       'age' [years], 'glu' [mg/dL]
# Index var:   'charttime' (1 hours)
      icustay_id charttime   age   glu
      <int> <drtn>    <dbl> <dbl>
1      201006 -58 hours  68.9   116
2      201006 -45 hours  68.9    83
3      201006 -21 hours  68.9    91
4      201006  0 hours  68.9   175
5      201006 11 hours  68.9   129
...
1,910   298685 260 hours  80.1   159
1,911   298685 272 hours  80.1   153
1,912   298685 290 hours  80.1   182
1,913   298685 293 hours  80.1   122

```



```
1,914      298685 299 hours  80.1   121
# ... with 1,904 more rows
```

Despite a best-effort approach, data availability can be a limiting factor. While for physiological variables, there is good agreement even across continents, data-privacy considerations, as well as lack of a common standard for data encoding, may cause issues that are hard to resolve. In some cases, this can be somewhat mitigated while in others, this is a limitation to be kept in mind. In AmsterdamUMCdb, for example, patient age, height and weight are not available as continuous variables, but as factor with patients binned into groups. Such variables are then approximated by returning the respective mid-points of groups for `aumc` data⁵. Other concepts, such as `adm` (categorizing admission types) or a prospective `icd` concept (diagnoses as ICD-9 codes) can only return data if available from the data source in question. Unfortunately, neither `aumc` nor `hirid` contain ICD-9 encoded diagnoses, and in the case of `hirid`, no diagnosis information is available at all.

Treatment-related information

The largest group of concepts dealing with treatment-related information is described by the `medications` category. In addition to drug administrations, only basic ventilation information is currently provided as ready to use concept. Just like availability of common ICU procedures, patient medication is also underdeveloped, covering mainly vasopressor administrations, as well as corticosteroids, antibiotics and dextrose infusions. The current concepts retrieving treatment-related information are mostly focused on providing data required for constructing clinical scores described in Section 4.2.4. While this group of concepts lends itself to use of `win_tbl` objects, bear in mind that when requesting multiple concepts which do not all return data as `win_tbls`, all `win_tbl` objects are converted to `ts_tbl` in order to be merged with the non-`win_tbl` objects.

Ventilation is represented by several concepts: a ventilation indicator variable (`vent_ind`), as well as ventilation durations (`vent_dur`) are constructed from start and events (`vent_start` and `vent_end`). This includes any kind of mechanical ventilation (invasive via an endotracheal or tracheostomy tube), as well as non-invasive ventilation via face or nasal masks. In line with other concepts belonging to this group, the current state is far from being comprehensive and expansion to further ventilation parameters is desirable.

The singular concept addressing antibiotics (`abx`) returns an indicator signaling whenever an antibiotic was administered. This includes any route of administration (intravenous, oral, topical, etc.) and does neither report dosage, nor active ingredient. Finally, vasopressor administration is reported by several concepts representing different vasoactive drugs (including dopamine, dobutamine, epinephrine, norepinephrine and vasopressin), as well as different administration aspects such as rate, duration (and for use in SOFA scoring, rate administered for at least 60 minutes).

```
R> load_concepts(c("abx", "vent_ind", "norepi_rate", "norepi_dur"), src,
+               verbose = FALSE)
```

⁵Prioritizing consistency over accuracy, one could apply the same binning to datasets which report numeric values, but the concepts included with `ricu` attempt to strike a balance between consistency and amount of applied pre-processing. With the extensible architecture of data concepts, however, such categorical variants of patient demographic concepts could easily be added.

```
# A 'ts_tbl': 12,434 x 6
# Id var:      'icustay_id'
# Units:       'norepi_rate' [mcg/kg/min]
# Index var:   'startdate' (1 hours)
  icustay_id startdate abx   vent_ind norepi_rate norepi_dur
    <int> <drtn>    <lgl> <lgl>      <dbl> <drtn>
1     201006   7 hours TRUE   NA         NA      NA hours
2     201006   8 hours NA     TRUE        NA      60 hours
3     201006   9 hours NA     TRUE      0.0460 NA hours
4     201006  10 hours NA     TRUE      0.0690 NA hours
5     201006  11 hours NA     TRUE      0.0690 NA hours
...
12,430    298685 612 hours NA     TRUE        NA      NA hours
12,431    298685 613 hours NA     TRUE        NA      NA hours
12,432    298685 614 hours NA     TRUE        NA      NA hours
12,433    298685 615 hours NA     TRUE        NA      NA hours
12,434    298685 616 hours NA     TRUE        NA      NA hours
# ... with 12,424 more rows
```

As cautioned in Section 4.2.2, variability in data reporting across datasets can lead to issues: the `prescriptions` table included with MIMIC-III, for example, reports time-stamps as dates only, yielding a discrepancy of up to 24 hours when merged with data where time-accuracy is on the order of minutes. Another problem exists with concepts that attempt to report administration windows, as some datasets do not describe infusions with clear cut start/endpoints but rather report infusion parameters at (somewhat) regular time intervals. This can cause artifacts when the requested time step-size deviates from the data set inherent time grid and introduces uncertainty when attempting to determine start/endpoints for creating a `win_tbl` object.

```
R> load_concepts("dex", "mimic_demo", verbose = FALSE)
```

```
# A 'win_tbl': 10 x 4
# Id var:      'icustay_id'
# Units:       'dex' [ml/hr]
# Index var:   'starttime' (1 hours)
# Duration var: 'dur_var'
  icustay_id starttime dur_var    dex
    <int> <drtn>    <drtn>    <dbl>
1     216185 129 hours   1 mins 15000
2     249805 335 hours 660 mins   9.09
3     253931 159 hours   1 mins  500.
4     277238   2 hours 140 mins  100.
5     277238   3 hours   1 mins 15000
6     277238   5 hours   1 mins 15000
7     285750   4 hours   1 mins 15000
8     286072 101 hours   1 mins  7500
```

```

9      286072 118 hours    1 mins  7500
10     286072 126 hours    1 mins  7500

```

Furthermore for a concept like dextrose administration as implemented in `dex`, where infusions are returned alongside bolus administrations, this can yield large rate values, as the returned unit is ml/hr and in this particular case, values are harmonized such that they correspond to 10% dextrose solutions. A bolus administration of 50 ml D50 will therefore be reported as 15000 ml/hr administered within 1 minute.

Outcomes

A group of more loosely associated concepts can be used to describe patient state. This includes common clinical endpoints, such as death or length of ICU stay, as well as scoring systems such as SOFA, the systemic inflammatory response syndrome (SIRS; [Bone, Sibbald, and Sprung 1992](#)) criterion, the National Early Warning Score (NEWS; [Jones 2012](#)) and the Modified Early Warning Score (MEWS; [Subbe, Kruger, Rutherford, and Gemmel 2001](#)).

While the more straightforward outcomes can be retrieved directly from data, clinical scores often incorporate multiple variables, based upon which a numeric score is constructed. This can typically be achieved by using concepts of type `rec_cncpt`, specifying the needed components and supplying a callback function that applies rules for score construction.

```

R> load_concepts(c("sirs", "death"), src, verbose = FALSE,
+               keep_components = TRUE)

```

```

# A 'ts_tbl': 14,295 x 8
# Id var:      'icustay_id'
# Index var:   'charttime' (1 hours)
      icustay_id charttime  sirs death temp_comp hr_comp resp_comp wbc_comp
      <int> <drtn>      <dbl> <lgl>      <int>  <int>      <int>  <int>
1      201006 -58 hours    1 NA          NA      NA      NA      1
2      201006 -45 hours    1 NA          NA      NA      NA      1
3      201006 -21 hours    1 NA          NA      NA      NA      1
4      201006 -10 hours    2 NA          NA      NA      1      1
5      201006  0 hours     3 NA           0      1      1      1
...
14,291  298685 314 hours    2 NA           0      0      1      1
14,292  298685 315 hours    2 NA           0      0      1      1
14,293  298685 316 hours    2 NA           0      0      1      1
14,294  298685 317 hours    1 NA           0      0      0      1
14,295  298685 318 hours    1 TRUE          0      0      NA      1
# ... with 14,285 more rows

```

Callback functions can become rather involved (especially for more complex concepts such as SOFA) and may include arbitrary arguments to tune their behavior. As callback functions to `rec_cncpt` objects are typically called internally from `load_concepts()`, arguments not

used by `load_concepts()`, such as `keep_components` in the above example (causing not only the score column, but also individual score components to be retained) are forwarded⁶.

4.3. Concept specification

Similarly to data source configuration (discussed in Section 5.3), concept specification relies on JSON-formatted text files, parsed by `jsonlite` (Ooms 2014). A default dictionary of concepts is included with `ricu` containing a selection of commonly used clinical concepts. Several types of concepts exist within `ricu` and with extensibility in mind, new types can easily be added. A quick remark on terminology before diving into more details on how to specify data concepts: A *concept* corresponds to a clinical variable such as a bilirubin measurement or the ventilation status of a patient, and an *item* encodes how to retrieve data corresponding to a given concept from a data source. A *concept* therefore contains several *items* (zero, one or several are possible per data source).

All concepts consist of minimal meta-data including a name, target class (defaults to `ts_tbl`; see Section 4.1), an aggregation specification⁷ and class information (defaults to `num_concept`), as well as optional `description` and `category` information. Adding to that, depending on concept class, further fields can be added. In the case of the most widespread concept type (`num_cncpt`; used to represent numeric data) this is `unit` which encodes one (or several synonymous) unit(s) of measurement, as well as a minimal and maximal plausible values (specified as `min` and `max`). The concept for heart rate data (`hr`) for example can be specified as

```
{
  "hr": {
    "unit": ["bpm", "/min"],
    "min": 0,
    "max": 300,
    "description": "heart rate",
    "category": "routine vital signs",
    "sources": {
      ...
    }
  }
}
```

Meta-data is used during concept loading for data-preprocessing. For numeric concepts, the

⁶Some care has to be taken as when requesting multiple concepts within the same call to `load_concepts()`, while passing arguments intended for concept-level callback functions, as all involved callback functions will be called with the same forwarded arguments. When for example requesting multiple scores (such as SOFA or SIRS), it is currently not possible to enable `keep_components` for only a subset thereof. Furthermore this set-up requires that all involved callback functions are allowed to be called with the given set of extra arguments.

⁷Every concept needs a default aggregation method which can be used during data loading to return data that is unique per key (either per `id_vars` group or per combination of `id_vars` and `index_var`) otherwise down-stream merging of multiple concepts is ill-defined. The aggregation default can be overridden during loading or as specification of a `rec_cncpt` object. If no aggregation method is explicitly indicated the global default is `first()` for character, `median()` for numeric and `sum()` for logical vectors. For logical data, if a concept of type `lg1_cncpt` is used, the count of `TRUE` values is converted back to logical, thereby providing `any()` type functionality.

specified measurement unit is compared to that of the data (if available), with messages being displayed in case of mismatches, while the range of plausible values is used to filter out measurements that fall outside the specified interval. Other types of concepts include categorical concepts (`fct_cncpt`), concept representing binary data (`lgl_cncpt`), as well as recursive concepts (`rec_cncpt`), which build on other *atomic* concepts⁸.

Specification of how data can be retrieved from a data source is encoded by data *items*. Lists of data items (associated with data source names) are provided as `sources` element (instead of `...` in the above code block). For the demo datasets corresponding eICU and MIMIC-III, heart rate data retrieval is specified as

```
{
  "eicu_demo": [
    {
      "table": "vitalperiodic",
      "val_var": "heartrate",
      "class": "col_itm"
    }
  ],
  "mimic_demo": [
    {
      "ids": [211, 220045],
      "table": "chartevents",
      "sub_var": "itemid"
    }
  ]
}
```

Analogously to how different types of concepts are used to represent different types of data, different types of items handle different types of data loading. The most common scenario is selecting a subset of rows from a table by matching a set of ID values (`sub_itm`). In the above example, heart rate data in MIMIC-III can be located by searching for ID values 211 and 220045 in column `itemid` of table `chartevents` (heart rate data is stored in *long* format). Conversely, heart rate data in eICU is stored in *wide* format, requiring no row-subsetting. Column `heartrate` of table `vitalperiodic` contains all corresponding data and such data situations are handled by the `col_itm` class. Other item classes include `rgx_itm` where a regular expression is used for selecting rows and `fun_itm` where an arbitrary function can be used for data loading. If a data loading scenario is not covered by these classes, adding further `itm` subclasses is encouraged.

In order to extend the current concept library both to new datasets and new concepts, further JSON files can be incorporated by adding their paths to `RICU_CONFIG_PATH`. Concepts with

⁸An example for a recursive concept is the $\text{PaO}_2/\text{FiO}_2$ ratio, used for instance to assess patients with acute respiratory distress syndrome (ARDS) or for sepsis-related organ failure assessment (SOFA) (Villar, Pérez-Méndez, Blanco, Añón, Blanch, Belda, Santos-Bouza, Fernández, Kacmarek, and Spanish Initiative for Epidemiology and Therapies for ARDS (SIESTA) Network 2013; Vincent *et al.* 1996). Given both PaO_2 and FiO_2 as individual concepts, the $\text{PaO}_2/\text{FiO}_2$ ratio is provided by `ricu` as a recursive concept (`pafi`), requesting the two atomic concepts `pao2` and `fio2` and performing some form of imputation for when at a given time step one or both values are missing.

names that already exist are only used for their `sources` entries, such that `hr` for `new_dataset` can be specified as

```
"hr": {
  "sources": {
    "new_dataset": [
      {
        "ids": 6640,
        "table": "numericitems",
        "sub_var": "itemid"
      }
    ]
  }
}
```

whereas concepts with non-existing names are treated as new concepts.

Central to providing the required flexibility for loading of certain data concepts that require some specific pre-processing are callback functions that can be specified for several *item* types. Functions (with appropriate signatures), designated as `callback` functions, are invoked on individual data items, before concept-related preprocessing is applied. A common scenario for this is unit of measurement conversion: In MIMIC-III data for example, several `itemid` values correspond to temperature measurements, some of which refer to temperatures measured in degrees Celsius whereas others are used for measurements in degrees Fahrenheit. As the information encoding which measurement corresponds to which `itemid` values is no longer available during concept-related preprocessing, this is best resolved at the level of individual data items. Several function factories are available for generating callback functions and `convert_unit()` is intended for covering unit conversions⁹. Data *items* corresponding to the `temp` concept for MIMIC-III are specified as

```
{
  "mimic_demo": [
    {
      "ids": [676, 677, 223762],
      "table": "chartevents",
      "sub_var": "itemid"
    },
    {
      "ids": [678, 679, 223761, 224027],
      "table": "chartevents",
      "sub_var": "itemid",
      "callback": "convert_unit(fahr_to_cels, 'C', 'f')"
    }
  ]
}
```

⁹A more recent addition to `ricu` has been experimental support for automatic unit conversion using the `units` package (Pebesma, Mailund, and Hiebert 2016). In order to leverage these capabilities, a concept can be specified as `unit_cncpt` and values will be converted to the singular unit stated by the concept definition. Source units are taken to be what is returned by the `unit_var` column.

```
]
}
```

indicating that for ID values 676, 677 and 223762 no pre-processing is required and for the remaining ID values the function `fahr_to_cels()` is applied to entries of the `val_var` column where the regular expression "f" is TRUE for the `unit_var` column (the values of which being ultimately replaced with "C").

5. Data sources

Every dataset is represented by an environment with class attributes and associated metadata objects stored as object attributes to that environment. Dataset environments all inherit from `src_env` and from any number of class names constructed from data source name(s) with a suffix `_env` attached. The environment representing MIMIC-III, for example inherits from `src_env` and `mimic_env`, while the corresponding demo dataset inherits from `src_env`, `mimic_env` and `mimic_demo_env`. These sub-classes are later used for tailoring the process of data loading to particularities of individual datasets.

A `src_env` contains an active binding per contained table, which returns a `src_tbl` object representing the requested table. As is the case for `src_env` objects, `src_tbl` objects inherit from additional classes such that certain per-dataset behavior can be customized. The `admissions` table of the MIMIC-III demo dataset for example inherits from `mimic_demo_tbl` and `mimic_tbl` (alongside classes `src_tbl` and `prt`).

```
R> mimic_demo$admissions
```

```
# <mimic_tbl>: [129 x 19]
# ID options:  subject_id (patient) < hadm_id (hadm) < icustay_id (icustay)
# Defaults:   'admission_type' (val)
# Time vars:  'admittime', 'dischtime', 'deathtime', 'edregtime',
#             'edouttime'
      row_id subject_id hadm_id admittime          dischtime
      <int>    <int>    <int> <dtm>          <dtm>
1  12258      10006    142345 2164-10-23 21:09:00 2164-11-01 17:15:00
2  12263      10011    105331 2126-08-14 22:32:00 2126-08-28 18:59:00
3  12265      10013    165520 2125-10-04 23:36:00 2125-10-07 15:13:00
4  12269      10017    199207 2149-05-26 17:19:00 2149-06-03 18:42:00
5  12270      10019    177759 2163-05-14 20:43:00 2163-05-15 12:00:00
...
125 41055      44083    198330 2112-05-28 15:45:00 2112-06-07 16:50:00
126 41070      44154    174245 2178-05-14 20:29:00 2178-05-15 09:45:00
127 41087      44212    163189 2123-11-24 14:14:00 2123-12-30 14:31:00
128 41090      44222    192189 2180-07-19 06:55:00 2180-07-20 13:00:00
129 41092      44228    103379 2170-12-15 03:14:00 2170-12-24 18:00:00
# ... with 119 more rows, and 14 more variables: deathtime <dtm>,
#   admission_type <chr>, admission_location <chr>, discharge_location <chr>,
#   insurance <chr>, language <chr>, religion <chr>, marital_status <chr>,
```



```
# ethnicity <chr>, edregtime <dtm>, edouttime <dtm>, diagnosis <chr>,
# hospital_expire_flag <int>, has_chartevents_data <int>
```

Powered by the **prt** (Bennett 2021) package, `src_tbl` objects represent row-partitioned tabular data stored as multiple binary files created by the **fst** (Klik 2020) package. In addition to standard subsetting, **prt** objects can be subsetted via the base R S3 generic function `subset()` and using non-standard evaluation (NSE):

```
R> subset(mimic_demo$admissions, subject_id > 44000, language:ethnicity)
```

	language	religion	marital_status	ethnicity
1:	ENGL	CATHOLIC	SINGLE	WHITE
2:	ENGL	CATHOLIC	SINGLE	WHITE
3:	ENGL	CATHOLIC	SINGLE	WHITE
4:	ENGL	PROTESTANT QUAKER	MARRIED	WHITE
5:	ENGL	UNOBTAINABLE	SINGLE	BLACK/AFRICAN AMERICAN
6:	ENGL	CATHOLIC	SINGLE	WHITE
7:	ENGL	NOT SPECIFIED	SINGLE	WHITE

This syntax makes it possible to read row-subsets of *long* tables into memory with little memory overhead. While terseness of such an API does introduce potential ambiguity, this is mostly overcome by using the tidy eval framework provided by **rlang** (Henry and Wickham 2020):

```
R> subject_id <- 44000:45000
R> subset(mimic_demo$admissions, .data$subject_id %in% .env$subject_id,
+      subject_id:disctime)
```

	subject_id	hadm_id	admittime	disctime
1:	44083	125157	2112-05-04 08:00:00	2112-05-11 14:15:00
2:	44083	131048	2112-05-22 15:37:00	2112-05-25 13:30:00
3:	44083	198330	2112-05-28 15:45:00	2112-06-07 16:50:00
4:	44154	174245	2178-05-14 20:29:00	2178-05-15 09:45:00
5:	44212	163189	2123-11-24 14:14:00	2123-12-30 14:31:00
6:	44222	192189	2180-07-19 06:55:00	2180-07-20 13:00:00
7:	44228	103379	2170-12-15 03:14:00	2170-12-24 18:00:00

By using **rlang** pronouns (`.data` and `.env`), the distinction can readily be made between a name referring to an object within the context of the data and an object within the context of the calling environment.

5.1. Data source set-up

In order to make a dataset accessible to **ricu**, three steps are necessary, each handled by an exported S3 generic function: `download_src()`, `import_src()` and `attach_src()`. The first two steps, download and import, are one-time procedures, whereas attaching is carried out

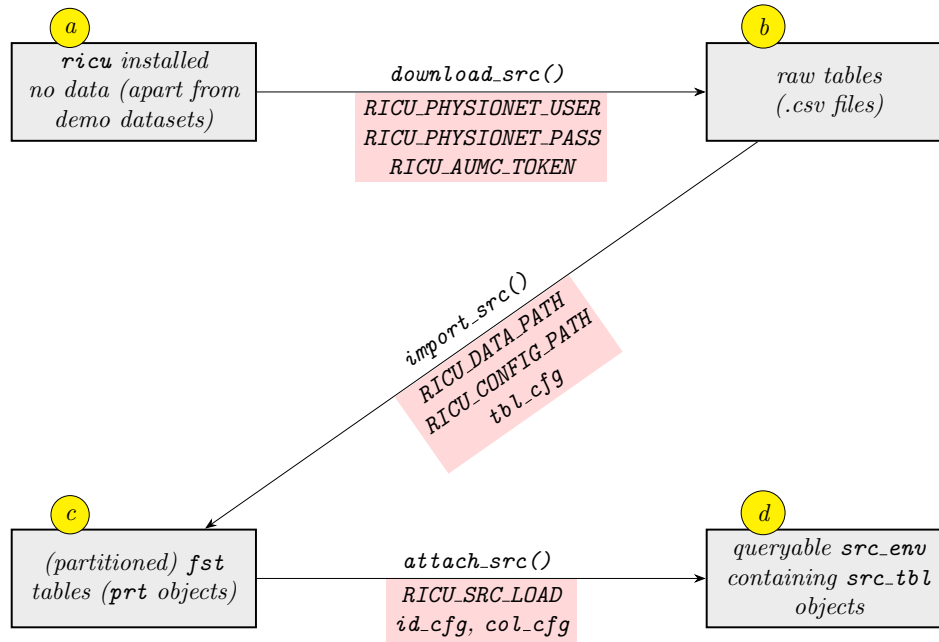


Figure 1: Making a dataset available to **ricu** involves several steps, starting with data download, followed by preparation for efficient access and finalized by instantiation of data structures containing relevant meta data. Displayed above arrows are the functions which are used for each step and below are indicated specific configuration settings or environment variables which are need for (or can be used to customize) the specific step (in red).

every time the package namespace is loaded. By default, all data sources known to **ricu** are configured to be attached and in case some data is missing for a given data source, the missing data is downloaded and imported on first access. An outline of the steps involved for data source set-up is shown in Figure 1.

Data download

The first step towards loading data is data download, taken care of the S3 generic `download_src()`. For the datasets included in **ricu**, prior to calling `download_src()`, the following environment variables can be set (indicated in red in the $a \rightarrow b$ edge in Figure 1):

- `RICU_PHYSIONET_USER`/`RICU_PHYSIONET_PASS`: PhysioNet user name and password with access to the requested dataset.
- `RICU_AUMC_TOKEN`: Download token, extracted from the download URL received when requesting data access.

If any of the required access credentials are not available as environment variables, they can be supplied as function arguments to `download_src()` or the user is queried in interactive sessions and an error is thrown otherwise.

Each of the supported datasets requires 5-10 GB disk space for permanent storage and 50-100 GB of temporary disk storage during download and import . Memory requirements are kept

low (8-16 GB) by performing all set-up operations only on subsets of rows at the time. Initial data source set up can be expected to take upwards of an hour per dataset.

Data import

After successful data download, importing prepares tables for efficient random row- and column-access, for which the raw data format (.csv) is not well suited (see edge $b \rightarrow c$ in Figure 1). Tables are read in using **readr** (Wickham and Hester 2020), potentially (re-)partitioned row-wise, and re-saved using **fst**. Environment variables that can be set to customize **ricu** data handling, relevant for import and attaching include:

- **RICU_DATA_PATH**: Optional data storage location (if unset, this defaults to a system-specific, user-specific directory). The current value used for this setting can be queried by calling **data_dir()**.
- **RICU_CONFIG_PATH**: Comma-separated paths to directories containing configuration files. The current set of paths is retrievable by calling **config_paths()** and the ordering of paths determines precedence of how configuration files are combined (if multiple files of the same name are available).

For importing, the information contained in **tbl_cfg** configuration objects is most relevant. This determines column data types, table partitioning and sanity checks like number of rows per table. Please refer to Section 5.3.3 for more information on the construction of **tbl_cfg** objects.

Data attaching

Finally, attaching a dataset creates a corresponding **src_env** object, containing several **src_tbl** objects, which together with associated meta-data is used by **ricu** to run queries against the data (edge $c \rightarrow d$ in Figure 1). The environment variable **RICU_SRC_LOAD** can contain a comma-separated list of data source names that are set up for being automatically attached on namespace loading. This defaults to all currently supported datasets and the current set of source names is available as **auto_attach_srcs()**.

Two configuration objects which are important for data loading (see the following Section 5.2) are **id_cfg** (Section 5.3.1) and **col_cfg** (Section 5.3.2), providing default values for certain types of columns, including time-stamp, measurement value and measurement unit columns, as well as defining relationships between patient identifiers (such as hospital stay ID and ICU stay ID).

5.2. Data loading

The lowest level of data access is direct subsetting of **src_tbl** objects as shown at the start of this section (5). As **src_tbl** inherits from **prt** the **subset()** implementation provided by **prt** can be used for NSE of data-expressions against on-disk, tabular data. Building on that, several S3 generic functions successively homogenize data representations as visualized in Figure 2.

The most basic layer in data loading is provided by the S3 generic function **load_src()**, which provides a string-based interface to **subset()** for all but the row-subsetting expression (see edge $a \rightarrow b$ in Figure 2).

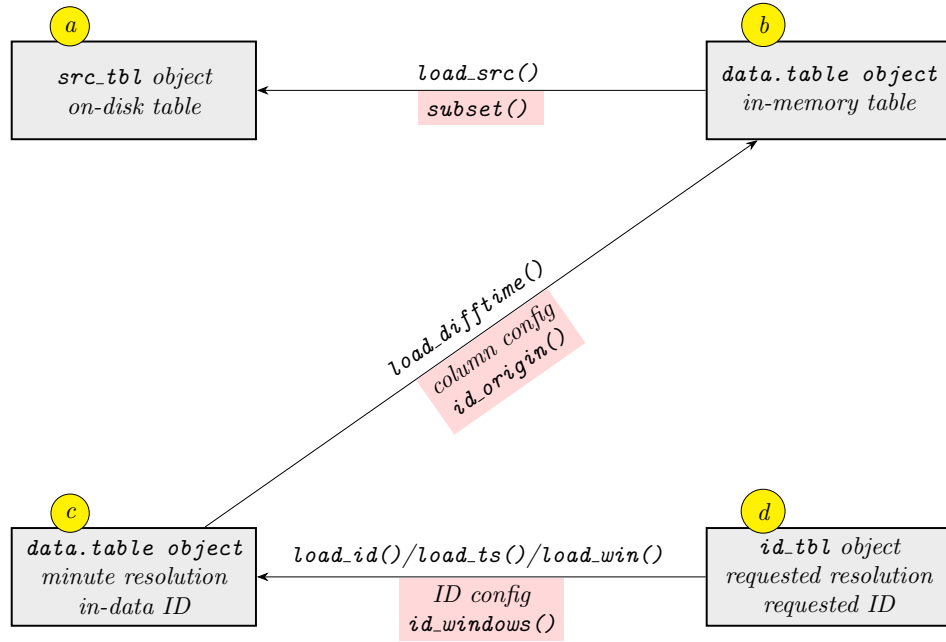


Figure 2: Data loading proceeds through several layers, each contributing a step towards harmonizing discrepancies among raw data representations provided by the different data sources. Raw data tables are represented by *ricu* as `src_tbl` objects which can be queried using `load_src()`. Absolute time-stamps in the returned `data.table` are converted to times relative to admission (in minutes) by `load_difftime()` and finally, `load_id()/load_ts()/load_win()` ensure a given ID system and time interval.

```
R> load_src(mimic_demo$admissions, subject_id > 44000,
+          cols = c("hadm_id", "admittime", "disctime"))
```

	hadm_id	admittime	disctime
1:	125157	2112-05-04 08:00:00	2112-05-11 14:15:00
2:	131048	2112-05-22 15:37:00	2112-05-25 13:30:00
3:	198330	2112-05-28 15:45:00	2112-06-07 16:50:00
4:	174245	2178-05-14 20:29:00	2178-05-15 09:45:00
5:	163189	2123-11-24 14:14:00	2123-12-30 14:31:00
6:	192189	2180-07-19 06:55:00	2180-07-20 13:00:00
7:	103379	2170-12-15 03:14:00	2170-12-24 18:00:00

As data sources differ in their representation of time-stamps, a next step in data homogenization is to converge to a common format: the time difference to the origin time-point of a given ID system (for example ICU admission).

```
R> load_difftime(mimic_demo$admissions, subject_id > 44000,
+               cols = c("hadm_id", "admittime", "disctime"))
```

```
# An 'id_tbl': 7 x 3
# Id var:      'hadm_id'
# hadm_id admittime disctime
#   <int> <drtn>    <drtn>
1  103379 0 mins    13846 mins
2  125157 0 mins    10455 mins
3  131048 0 mins     4193 mins
4  163189 0 mins    51857 mins
5  174245 0 mins     796 mins
6  192189 0 mins     1805 mins
7  198330 0 mins    14465 mins
```

The function `load_difftime()` is expected to return timestamps as base R `difftime` vectors (in minutes; edge $b \rightarrow c$ in Figure 2). The argument `id_hint` can be used to specify a preferred ID system but if not available in raw data, `load_difftime()` will return data using the ID system with highest cardinality. In the above example, if `icustay_id` were requested, data would be returned using `hadm_id`, whereas a `subject_id` request would be honored, as the corresponding ID column is available in the `admissions` table.

Building on `load_difftime()` functionality, functions `load_id()/load_ts()/load_win()` return `id_tbl/ts_tbl/win_tbl` objects with the requested ID system (passed as `id_var` argument). This uses raw data IDs if available or calls `change_id()` in order to convert to the desired ID system (edge $c \rightarrow d$ in Figure 2). Similarly, where `load_difftime()` returns data with fixed time interval of one minute, `load_id()` allows for arbitrary time intervals (using `change_interval()`; defaults to 1 hour).

```
R> load_id(mimic_demo$admissions, subject_id > 44000,
+          cols = c("admittime", "disctime"), id_var = "hadm_id")
```

```
# An 'id_tbl': 7 x 3
# Id var:      'hadm_id'
  hadm_id admittime disctime
    <int> <drtn>    <drtn>
1  103379 0 hours   230 hours
2  125157 0 hours   174 hours
3  131048 0 hours    69 hours
4  163189 0 hours   864 hours
5  174245 0 hours    13 hours
6  192189 0 hours    30 hours
7  198330 0 hours   241 hours
```

Throughout several of these functions, `col_cfg` objects are used to provide sensible defaults. In order to convert to relative times, for example, `load_difftime()` requires names of columns for which this applies (provided by the `time_vars` entry), and `load_ts()` needs to know which of the `time_vars` to use as `index_var`. For more information on the construction of `col_cfg` objects, please refer to Section 5.3.2.

A call to `change_id()` requires the construction of a table which contains the mapping between different ID systems, together with information about how to convert timestamps between these ID systems (edge $c \rightarrow d$ in Figure 2). The function responsible for providing the necessary information is `id_windows()` and the associated S3 generic functions `id_win_helper()`. The entry point `id_windows()` wraps `id_win_helper()`, providing memoization, as the resulting structure is expensive to compute relative to the frequency of being required.

```
R> id_windows(mimic_demo)
```

```
# An 'id_tbl': 136 x 9
# Id var:      'icustay_id'
  icustay_id hadm_id subject_id icustay_id_start hadm_id_start
    <int>    <int>    <int> <drtn>              <drtn>
1    201006  198503    10076 0 mins              -3290 mins
2    201204  114648    42321 0 mins               -2 mins
3    203766  126949    10045 0 mins             -1336 mins
4    204132  157609    40310 0 mins              -1 mins
5    204201  177678    10104 0 mins             -368 mins
...
132   295043  170883    10124 0 mins            -10413 mins
133   295741  176805    10090 0 mins              -1 mins
134   296804  110244    10035 0 mins            -1294 mins
135   297782  167612    43909 0 mins              -1 mins
136   298685  151323    42075 0 mins              -1 mins
# ... with 126 more rows, and 4 more variables: subject_id_start <drtn>,
#   icustay_id_end <drtn>, hadm_id_end <drtn>, subject_id_end <drtn>
```

Analogously, the function pair `id_origin()` and `id_orig_helper()`, with the former wrapping the latter and again providing memoization, is used for datasets where time-stamps are

represented by absolute times, returning the origin time-points for a given ID system which then can be used to calculate relative times (edge $b \rightarrow c$ in Figure 2).

```
R> id_origin(mimic_demo, "icustay_id")
```

```
# An 'id_tbl': 136 x 2
# Id var:      'icustay_id'
  icustay_id intime
      <int> <dtm>
1      201006 2107-03-24 04:06:14
2      201204 2121-12-07 20:50:36
3      203766 2129-11-24 22:46:57
4      204132 2144-12-24 16:16:41
5      204201 2120-08-24 23:47:23
...
132     295043 2192-04-24 02:29:49
133     295741 2124-01-12 14:27:16
134     296804 2129-03-04 13:40:11
135     297782 2152-10-09 19:05:36
136     298685 2166-02-12 17:57:37
# ... with 126 more rows
```

The implementations of `id_win_helper()` and `id_orig_helper()` for the included datasets use information contained in `id_cfg` objects (see Section 5.3.1) to determine which columns in which tables are used for constructing the required lookup tables. Doing so, however, is not required: an `id_win_helper()` implementation for a new dataset could forego this by hard-coding table/column names as part of the function logic, in-turn simplifying the corresponding `id_cfg` object to merely providing naming and ordering information.

5.3. Data source configuration

Data source environments (and corresponding `src_tbl` objects) are constructed using source configuration objects: list-based structures, inheriting from `src_cfg` and from any number of data source-specific class names with suffix `_cfg` appended (as discussed at the beginning of Section 5). The exported function `load_src_cfg()` reads a JSON formatted file and creates a `src_cfg` object per datasource and further therein contained objects.

```
R> cfg <- load_src_cfg("mimic_demo")
R> str(cfg, max.level = 3L, width = 70L)
```

```
List of 1
 $ mimic_demo:List of 6
  ..$ name      : chr "mimic_demo"
  ..$ prefix    : chr [1:2] "mimic_demo" "mimic"
  ..$ id_cfg    : id_cfg [1:3] 'subject_id', 'hadm_id', 'icustay_id'
  ..$ col_cfg   : col_cfg [1:25] [0, 0, 5, 0, 1], [0, 1, 6, 0, 1], [1, 0, 0...
  ..$ tbl_cfg   : tbl_cfg [1:25] [?? x 19; 1], [?? x 24; 1], [?? x 4; 1], [...
```



```

..$ extra :List of 1
.. ..$ url: chr "https://physionet.org/files/mimiciii-demo/1.4"
..- attr(*, "class")= chr [1:3] "mimic_demo_cfg" "mimic_cfg" "src_cfg"

```

```
R> mi_cfg <- cfg[["mimic_demo"]]
```

In addition to required fields **name** and **prefix** (used as class prefix), as well as further arbitrary fields contained in **extra** (**url** in this case), several additional configuration objects are part of **src_cfg**: **id_cfg**, **col_cfg** and **tbl_cfg**.

ID configuration

An **id_cfg** object contains an ordered set of key-value pairs representing patient ID systems in a dataset. An implicit assumption currently is that a given patient ID system is used consistently throughout a dataset, meaning that for example an ICU stay ID is always referred to by the same name throughout all tables containing a corresponding column. Owing to the relational origins of these datasets this has been fulfilled in all instances encountered so far. In MIMIC-III, ID systems

```
R> as_id_cfg(mi_cfg)
```

```

<id_cfg<mimic_demo[patient < hadm < icustay]>[3]>
  patient      hadm      icustay
'subject_id'   'hadm_id' 'icustay_id'

```

are available, allowing for identification of individual patients, their (potentially multiple) hospital admissions over the course of the years and their corresponding ICU admissions (as well as potential re-admissions). Ordering corresponds to cardinality: moving to larger values implies moving along a one-to-many relationship. This information is used in data-loading, whenever the target ID system is not contained in the raw data.

Default column configuration

Again used in data loading, this per-table set of key-value pairs specifies column defaults as **col_cfg** object. Each key describes a type of column with special meaning and the corresponding value specifies said column for a given table.

```
R> as_col_cfg(mi_cfg)
```

```

<col_cfg<mimic_demo[id_var, index_var, time_vars, unit_var, val_var]>[25]>
      admissions      callout      caregivers      chartevents
[0, 0, 5, 0, 1]    [0, 1, 6, 0, 1]    [1, 0, 0, 0, 1]    [0, 1, 2, 1, 1]
      cptevents      d_cpt      d_icd_diagnoses      d_icd_procedures
[0, 1, 1, 0, 1]    [1, 0, 0, 0, 1]    [1, 0, 0, 0, 1]    [1, 0, 0, 0, 1]
      d_items      d_labitems      datetimeevents      diagnoses_icd
[1, 0, 0, 0, 1]    [1, 0, 0, 0, 1]    [0, 1, 3, 0, 1]    [0, 0, 0, 0, 1]
      drgcodes      icustays      inpuvents_cv      inpuvents_mv

```

[0, 0, 0, 0, 1]	[0, 1, 2, 0, 1]	[0, 1, 2, 1, 1]	[0, 1, 4, 1, 1]
labevents	microbiologyevents	outputevents	patients
[0, 1, 1, 1, 1]	[0, 1, 2, 0, 1]	[0, 1, 2, 1, 1]	[0, 0, 4, 0, 1]
prescriptions	procedureevents_mv	procedures_icd	services
[0, 1, 2, 1, 1]	[0, 1, 4, 1, 1]	[0, 0, 0, 0, 1]	[0, 1, 1, 0, 1]
transfers			
[0, 1, 2, 0, 1]			

The following column defaults are currently in use throughout **ricu** but the set of keys can be extended to arbitrary new values:

- **id_var**: In case a table does not contain at least one ID column corresponding to one of the ID systems specified as **id_cfg**, the default ID column can be set on a per-table basis as **id_var**¹⁰.
- **index_var**: A column that is used to define an ordering in time over rows, thereby providing a time series index¹¹.
- **time_vars**: Columns which will be treated as time variables (important for converting between ID systems for example), but not as time series indices¹².
- **unit_var**: Used in concept loading (more specifically for **num_cncpt** concepts, see Section 4.3) to identify columns that represent unit of measurement information.
- **val_var**: Again used when loading data concepts, this identified a default value variable in a table, representing the column of interest to be used as returned data column.

While **id_var**, **index_var** and **time_vars** are used to provide sensible defaults to functions used for general data loading (Section 5.2), **unit_var**, **val_var**, as well as potential user-defined defaults are only used in concept loading (see Section 4.2) and therefore need not be prioritized when integrating new data sources until data concepts have been mapped.

Table configuration

Finally, **tbl_cfg** objects are used during the initial set-up of a data source. In order to create a representation of a table that is accessible from **ricu** from raw data, several key pieces of information are required:

- **File name(s)**: In the simplest case, a single file corresponds to a single table. Other scenarios that have been encountered (and are therefore handled) include tables partitioned into multiple files and .tar archives containing multiple tables.
- **Column specification**: For each column, the expected data type has to be known, as well as a pair of names, one corresponding to the raw data column name and one corresponding to the column name to be used within **ricu**.

¹⁰This for example is the case for the **d_items** table in MIMIC-III, which does not contain any patient related data, but holds information on items encoding types of measurements, procedures, etc., used throughout other tables holding actual patient data for identifying the type data point, in line with the relational structure of the data source.

¹¹For the MIMIC-III table **inpuvents_mv**, one of the four available time variables lends itself to be used as index variable more than the other candidates and therefore is set as default.

¹²In case of the **admissions** table in MIMIC-III for example, a total of five columns are considered to be time variables, none of which stands out as potential **index_var**.

- (Optional) number of rows: Used as sanity check whenever available.
- (Optional) partitioning information: For very *long* tables it can be useful to specify a row-partitioning. This currently is only possible by applying a vector of breakpoints to a single numeric column, thereby defining a grouping.

Both file name and column specification are only used within the context of `download_src()` and `import_src()` and are therefore not required if download and import are carried out manually.

```
R> as_tbl_cfg(mi_cfg)
```

```
<tbl_cfg<mimic_demo[rows x cols; partitions]>[25]>
      admissions      callout      caregivers      chartevents
      [?? x 19; 1]      [?? x 24; 1]      [?? x 4; 1]      [?? x 15; 2]
      cptevents      d_cpt      d_icd_diagnoses      d_icd_procedures
      [?? x 12; 1]      [?? x 9; 1]      [?? x 4; 1]      [?? x 4; 1]
      d_items      d_labitems      datetimeevents      diagnoses_icd
      [?? x 10; 1]      [?? x 6; 1]      [?? x 14; 1]      [?? x 5; 1]
      drgcodes      icustays      inputevents_cv      inputevents_mv
      [?? x 8; 1]      [?? x 12; 1]      [?? x 22; 1]      [?? x 31; 1]
      labevents      microbiologyevents      outputevents      patients
      [?? x 9; 1]      [?? x 16; 1]      [?? x 13; 1]      [?? x 8; 1]
      prescriptions      procedureevents_mv      procedures_icd      services
      [?? x 19; 1]      [?? x 25; 1]      [?? x 5; 1]      [?? x 6; 1]
      transfers
      [?? x 13; 1]
```

For the `chartevents` table of the MIMIC-III demo dataset, for example, rows are partitioned into two groups, while all other tables are represented by a single partition. Furthermore, the expected number of rows is unknown (??) as this is missing from the corresponding `tbl_cfg` object.

5.4. Adding external datasets

In order to add a new dataset to **ricu**, several aspects outlined in the previous subsections require consideration. For illustration purposes, code for integrating AmsterdamUMCdb as external dataset is available from [Github](#). While this is no longer needed for using the `aumc` data source, the repository will remain as it might serve as template to integration of new datasets. Throughout this repository (and the following paragraphs), the AmsterdamUMCdb data treated as an **ricu**-external dataset is referred to as `aumc_ext`.

Central to adding a new dataset to **ricu** is providing some configuration information in a `data-sources.json` file pointed to by the environment variable `RICU_CONFIG_PATH`. Depending on particularities of the dataset in question, corresponding implementations of several (or none) of the S3 generic functions mentioned throughout Sections 5.1 and 5.2 might have to be provided. The amount of confirmation information required to get started also depends on the desired level of integration. As data download and import are one-time procedures,

these steps can be carried out manually, negating the need for specifying column data types in `data-sources.json` and providing data source specific methods for the `download_src()` and `import_src()` generics.

The basic organization of a data source configuration entry, as it could be used for `aumc_ext`, specified as JSON is as follows:

```
{
  "name": "aumc_ext",
  "id_cfg": {
    "patient": {
      "id": "patientid",
      "position": 1
    },
    "icustay": {
      "id": "admissionid",
      "position": 2
    }
  },
  "tables": {
    ...
  }
}
```

The shown `id_cfg` entry represents the minimally required set of entries, where for each ID specification, `start`, `end` and `table` are omitted (when compared to the `aumc` configuration provided by `ricu`). The `tables` entry expands to something like the following:

```
"tables": {
  "freetextitems": {
  },
  "drugitems": {
    "defaults": {
      "index_var": "start",
      "val_var": "dose",
      "unit_var": "doseunit",
      "time_vars": ["start", "stop"]
    }
  },
  "numericitems": {
    "defaults": {
      "index_var": "measuredat",
      "val_var": "value",
      "unit_var": "unit",
      "time_vars": ["measuredat", "registeredat", "updatedat"]
    },
    "partitioning": {
```

```

    "col": "",
    "breaks": [
      0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
      0, 0, 0, 0, 0
    ]
  },
  ...
}

```

Minimally required is simply an entry indicating the data source membership of a table (if not partitioned; c.f. `freetextitems`). This does slightly complicate data exploration, as if no `defaults` are specified, no default values can be provided to calls to `load_ts()` and related functions. For partitioned tables, the basic structure of a `partitioning` entry is required, but the content itself is irrelevant, as this is only used for set-up (c.f. `numericitems`). The length of `breaks`, however, is required to match the number of partitions (i.e. a length 23 `breaks` specification corresponds to a partitioning into 24 row-groups.)¹³ The directory containing such a `data-sources.json` can then be pointed to by the environment variable `RICU_CONFIG_PATH`, making it available to `ricu`.

As for functions that are required, currently there is no default method available for the loading step provided by `load_difftime()` and most likely an implementation of `id_win_helper()` will be required as well. For `aumc_ext`, `load_difftime()` could be implemented as

```

R> ms_as_min <- function(x) as.difftime(as.integer(x / 6e4), units = "mins")
R>
R> aumc_difftime <- function(x, rows, cols = colnames(x),
+                             id_hint = id_vars(x),
+                             time_vars = ricu::time_vars(x), ...) {
+
+   if (id_hint %in% colnames(x)) {
+     id_sel <- id_hint
+   } else {
+     id_opt <- id_var_opts(sort(as_id_cfg(x), decreasing = TRUE))
+     id_sel <- intersect(id_opt, colnames(x))[1L]
+   }
+
+   stopifnot(is.character(id_sel), length(id_sel) == 1L)
+
+   if (!id_sel %in% cols) {
+     cols <- c(id_sel, cols)
+   }
+
+   time_vars <- intersect(time_vars, cols)
+
+

```

¹³Originally it was intended to use partitioning information during data loading in order to narrow down the set of partitions that have to be accessed. So far, this optimization has not been implemented.

```

+   dat <- load_src(x, {{ rows }}, cols)
+   dat <- dat[, c(time_vars) := lapply(.SD, ms_as_min), .SDcols = time_vars]
+
+   as_id_tbl(dat, id_vars = id_sel, by_ref = TRUE)
+ }

```

Such a function attempts to use the ID as requested but falls back to the best possible alternative (using the ordering as previously specified in the `id_cfg` JSON configuration) if not provided by the data. Both row-subsetting expression and column selection are passed on to `load_src()` and all columns specified as `time_vars` are converted to `difftime` vectors in minutes. Operations can safely be carried out using by-reference semantics, as intermediate objects are not exposed to the user.

For a possible implementation of the `id_win_helper()` generic, column and table names to assemble the desired lookup table are hard coded instead of provided by the corresponding `id_cfg` object.

```

R> aumc_windows <- function(x) {
+
+   ids <- c("admissionid", "patientid")
+   sta <- c("admittedat", "firstadmittedat")
+   end <- c("dischargedat", "dateofdeath")
+
+   tbl <- as_src_tbl(x, "admissions")
+
+   res <- tbl[, c(ids, sta[1L], end)]
+   res <- res[, c(sta[2L]) := 0L]
+   res <- res[, c(sta, end) := lapply(.SD, ms_as_min), .SDcols = c(sta, end)]
+
+   res <- data.table::setcolorder(res, c(ids, sta, end))
+   res <- rename_cols(res, c(ids, paste0(ids, "_start"),
+                               paste0(ids, "_end")), by_ref = TRUE)
+
+   as_id_tbl(res, ids[2L], by_ref = TRUE)
+ }

```

As all the required information is available from the `admissions` table, `aumc_windows()` simply loads the corresponding columns, converts them to minute resolution, followed by some renaming. ICU admissions and discharges in this table are relative to initial hospital admissions and therefore an all-zero column `firstadmittedat` is added and the `id_var` of the resulting `id_tbl` is marked as `patientid`¹⁴.

A final step in making a new dataset accessible to **ricu** lies in specifying concept items. To this end, a file `concept-dict.json` can be added to the directory pointed to by `RICU_CONFIG_PATH`,

¹⁴The patient ID created in this way is limited to what is possible in MIMIC-III, for example, where patient data of birth is available. An approximate data of birth could be constructed if ages were reported more precisely, but given the rough binning available here, this might be considered an acceptable limitation of resulting patient IDs. Nevertheless awareness of such differences in data presentation is important.

containing entries like the following:, which will make it possible to use the `hr` concept across both datasets included with **ricu**, alongside the newly added dataset.

```
{
  "hr": {
    "sources": {
      "aumc_ext": [
        {
          "ids": 6640,
          "table": "numericitems",
          "sub_var": "itemid"
        }
      ]
    }
  }
}
```

The above outline serves only as an example on how to proceed when adding new data to **ricu**. Aspects like having multiple patient IDs, for example, could be further simplified. Also, owing to the extensive use of S3 generic functions, **ricu** offers considerable flexibility for customizing certain behavior to specifics of a given data source, while providing fallback procedures whenever more general treatment can be applied.

6. Examples

In order to briefly illustrate how **ricu** could be applied to real-world clinical questions, two toy examples are provided in the following sections. While the first example fully relies on data concepts that are included with **ricu**, the second one explores both how some data pre-processing can be added to an existing concept by creating a new `rec_cncpt` and how to create a new data concept altogether.

6.1. Lactate and mortality

First, we investigate the association of lactate levels and mortality. This problem has been studied before and it is widely accepted that both static and dynamic lactate indices are associated with increased mortality (Haas, Lange, Saugel, Petzoldt, Fuhrmann, Metschke, and Kluge 2016; Nichol, Bailey, Egi, Pettila, French, Stachowski, Reade, Cooper, and Bellomo 2011; Van Beest, Brander, Jansen, Rommes, Kuiper, and Spronk 2013). In order to model this relationship, we fit a time-varying proportional hazards Cox model (Therneau and Grambsch 2000; Therneau and Lumley 2015), which includes the SOFA score as a general predictor of illness severity, using MIMIC-III data. Furthermore, for the sake of this example, we are only interested in patients admitted from 2008 onwards (corresponding to the MetaVision database) of ages 20 to 90 years old.

```
R> src <- "mimic_demo"
R>
```

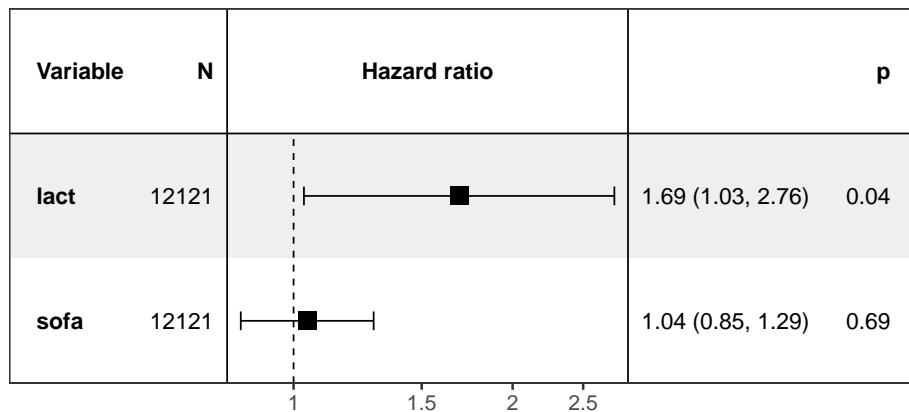


```

R> cohort <- load_id("icustays", src, dbsource == "metavision",
+                   cols = NULL)
R> cohort <- load_concepts("age", src, patient_ids = cohort,
+                         verbose = FALSE)
R>
R> dat <- load_concepts(c("lact", "death", "sofa"), src,
+                     patient_ids = cohort[age > 20 & age < 90, ],
+                     verbose = FALSE)
R>
R> dat <- dat[, head(.SD, n = match(TRUE, death, .N)), by = c(id_vars(dat))]
R> dat <- fill_gaps(dat)
R>
R> dat <- replace_na(dat, c(NA, FALSE), type = c("locf", "const"),
+                       by_ref = TRUE, vars = c("lact", "death"),
+                       by = id_vars(dat))
R>
R> cox_mod <- coxph(
+   Surv(charttime - 1L, charttime, death) ~ lact + sofa,
+   data = dat
+ )

```

After loading the data, some minor pre-processing is still required before modeling: first, we want to make sure we only use data up to (and including) the hour in which the **death** flag switches to **TRUE**. After that we impute missing values for **lact** using a last observation carry forward (locf) scheme (observing the patient grouping) and we simply replace missing **death** values with the value **FALSE**. The resulting model fit can be visualized as:



A simple exploration already shows that the increased values of lactate are associated with mortality, even after adjusting for the SOFA score.

6.2. Diabetes and insulin treatment

For the next example, again using MIMIC-III data, we turn to the usage of co-morbidities and treatment related information. We look at the amount of insulin administered to patients in

the first 24 hours from their ICU admission. In particular, we investigate if diabetic patients receive more insulin in the first day of their stay compared to non-diabetic patients. For this we create two concepts: `ins24`, a binned variable representing the cumulative amount of insulin administered within the first 24 hours of an ICU admission, and `diab`, a logical variable encoding diabetes co-morbidity.

As there already is an insulin concept available, `ins24` can be implemented as `rec_cncpt`, loading `ins` with aggregation set to `sum()` instead of the default `median()` and inserting the callback function `ins_cb()` into the loading process. The callback function takes care of the pre-processing steps outlined above: first data is subsetting to fall into the the first 24 hours of ICU admissions, followed by binning of summed values.

```
R> ins_breaks <- c(0, 1, 10, 20, 40, Inf)
R>
R> ins_cb <- function(ins, ...) {
+
+   day_one <- function(x) x >= hours(0L) & x <= hours(24L)
+
+   idx_var <- index_var(ins)
+   ids_var <- id_vars(ins)
+
+   ins <- ins[
+     day_one(get(idx_var)), list(ins24 = sum(ins)), by = c(ids_var)
+   ]
+
+   ins <- ins[,
+     ins24 := list(cut(ins24, breaks = ins_breaks, right = FALSE))
+   ]
+
+   ins
+ }
R>
R> ins24 <- load_dictionary(src, "ins")
R> ins24 <- concept("ins24", ins24, "insulin in first 24h", aggregate = "sum",
+   callback = ins_cb, target = "id_tbl", class = "rec_cncpt")
```

The binary diabetes concept can be implemented as `lgl_cncpt`, for which ICD-9 codes are matched using a regular expression. As we're not only interested in retrieving diabetic patients, a `col_itm` is more suited for data retrieval over an `rgx_itm` and for creating the required callback function that produces a logical vector we can use `transform_fun()` coupled with a function like `grep_diab()`. The two concepts are then combined using `c()` and loaded via `load_concepts()`.

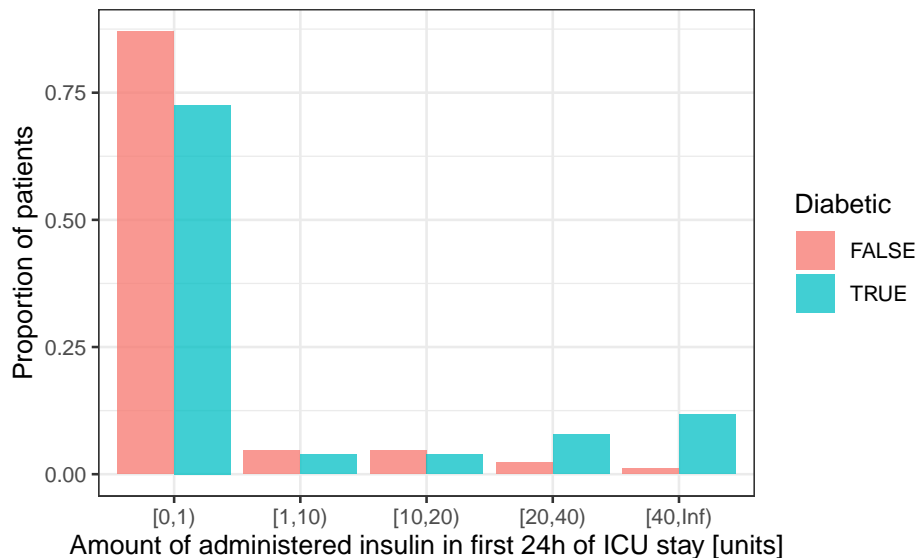
```
R> grep_diab <- function(x) grepl("^250\\.?.?[0-9]{2}$", x)
R>
R> diab <- item(src, table = "diagnoses_icd",
+   callback = transform_fun(grep_diab), class = "col_itm")
```

```

R> diab <- concept("diab", diab, "diabetes", target = "id_tbl",
+               class = "lgl_cncpt")
R>
R> dat <- load_concepts(c(ins24, diab), id_type = "icustay", verbose = FALSE)
R> dat <- replace_na(dat, "[0,1]", vars = "ins24")
R>
R> dat

```

After this, we can visualize the difference between the two groups with a histogram:



The plot suggests that for the cohort defined in the previous example and during the first day of ICU stay, perhaps unsurprisingly, with increasing insulin dosage, diabetic patients receive more insulin compared to non-diabetic patients. This effect is more pronounced when looking at the full MINIC-III data instead of the demo subset which includes only data corresponding to 136 ICU stays.

7. Acknowledgments

Nicolas Bennett, Drago Plečko, Nicolai Meinshausen and Peter Bühlmann were supported by grant #2017-110 of the Strategic Focal Area “Personalized Health and Related Technologies (PHRT)” of the ETH Domain for the SPHN/PHRT Driver Project “Personalized Swiss Sepsis Study”.

References

Adibuzzaman M, Musselman K, Johnson A, Brown P, Pitluk Z, Grama A (2016). “Closing the data loop: An integrated open access analysis platform for the mimic database.” In *2016 Computing in Cardiology Conference (CinC)*, pp. 137–140. IEEE.

- Bennett N (2021). *prt: Tabular Data Backed by Partitioned 'fst' Files*. R package version 0.1.3, URL <https://CRAN.R-project.org/package=prt>.
- Bone RC, Sibbald WJ, Sprung CL (1992). “The ACCP-SCCM Consensus Conference on Sepsis and Organ Failure.” *Chest*, **101**(6), 1481 – 1483. ISSN 0012-3692.
- Desautels T, Calvert J, Hoffman J, Jay M, Kerem Y, Shieh L, Shimabukuro D, Chettipally U, Feldman MD, Barton C, *et al.* (2016). “Prediction of sepsis in the intensive care unit with minimal electronic health record data: a machine learning approach.” *JMIR medical informatics*, **4**(3), e28.
- Evans R (2016). “Electronic health records: then, now, and in the future.” *Yearbook of medical informatics*, **25**(S 01), S48–S61.
- Faltys M, Zimmermann M, Lyu X, Hüser M, Hyland SL, Rätsch G, Merz TM (2021). “HiRID, a high time-resolution ICU dataset (version 1.1.1).” *PhysioNet*.
- Fleuren LM, Klausch TLT, Zwager CL, Schoonmade LJ, Guo T, Roggeveen LF, Swart EL, Girbes ARJ, Thorat P, Ercole A, Hoogendoorn M, Elbers PWG (2020). “Machine learning for the prediction of sepsis: a systematic review and meta-analysis of diagnostic test accuracy.” *Intensive Care Medicine*, **46**(3), 383–400.
- Futoma J, Hariharan S, Sendak M, Brajer N, Clement M, Bedoya A, O’Brien C, Heller K (2017). “An improved multi-output gaussian process rnn with real-time validation for early sepsis detection.” *arXiv preprint arXiv:1708.05894*.
- Goldberger AL, Amaral LAN, Glass L, Hausdorff JM, Ivanov PC, Mark RG, Mietus JE, Moody GB, Peng CK, Stanley HE (2000). “PhysioBank, PhysioToolkit, and PhysioNet.” *Circulation*, **101**(23), e215–e220.
- Haas SA, Lange T, Saugel B, Petzoldt M, Fuhrmann V, Metschke M, Kluge S (2016). “Severe hyperlactatemia, lactate clearance and mortality in unselected critically ill patients.” *Intensive care medicine*, **42**(2), 202–210.
- Henry L, Wickham H (2020). *rlang: Functions for Base Types and Core R and 'Tidyverse' Features*. R package version 0.4.9, URL <https://CRAN.R-project.org/package=rlang>.
- Hyland SL, Faltys M, Hüser M, Lyu X, Gumbsch T, Esteban C, Bock C, Horn M, Moor M, Rieck B, Zimmermann M, Bodenham D, Borgwardt K, Rätsch G, Merz TM (2020). “Early prediction of circulatory failure in the intensive care unit using machine learning.” *Nature Medicine*, **26**(3), 364–373.
- Jiang F, Jiang Y, Zhi H, Dong Y, Li H, Ma S, Wang Y, Dong Q, Shen H, Wang Y (2017). “Artificial intelligence in healthcare: past, present and future.” *Stroke and vascular neurology*, **2**(4), 230–243.
- Johnson A, Bulgarelli L, Pollard T, Horng S, Celi LA, Mark R (2021). “MIMIC-IV (version 1.0).” *PhysioNet*.
- Johnson AE, Pollard TJ, Shen L, Li-wei HL, Feng M, Ghassemi M, Moody B, Szolovits P, Celi LA, Mark RG (2016). “MIMIC-III, a freely accessible critical care database.” *Scientific data*, **3**, 160035.

- Johnson AEW, Aboab J, Raffa JD, Pollard TJ, Deliberato RO, Celi LA, Stone DJ (2018). “A Comparative Analysis of Sepsis Identification Methods in an Electronic Database.” *Critical care medicine*, **46**(4), 494–499.
- Jones M (2012). “NEWSDIG: The National Early Warning Score Development and Implementation Group.” *Clinical Medicine*, **12**(6), 501–503. doi:[10.7861/clinmedicine.12-6-501](https://doi.org/10.7861/clinmedicine.12-6-501).
- Kam HJ, Kim HY (2017). “Learning representations for the early detection of sepsis with deep neural networks.” *Computers in biology and medicine*, **89**, 248–255.
- Klik M (2020). *fst: Lightning Fast Serialization of Data Frames*. R package version 0.9.4, URL <https://CRAN.R-project.org/package=fst>.
- Lee J, Scott D, Villarroel M, Clifford G, Saeed M, Mark R (2011). “Open-access MIMIC-II database for intensive care research.” In *Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference*, volume 2011, pp. 8315–8.
- Moody GB, Mark RG (1996). “A database to support development and evaluation of intelligent intensive care monitoring.” In *Computers in Cardiology*, pp. 657–660.
- Nemati S, Holder A, Razmi F, Stanley MD, Clifford GD, Buchman TG (2018). “An interpretable machine learning model for accurate prediction of sepsis in the ICU.” *Critical care medicine*, **46**(4), 547–553.
- Nichol A, Bailey M, Egi M, Pettila V, French C, Stachowski E, Reade MC, Cooper DJ, Bellomo R (2011). “Dynamic lactate indices as predictors of outcome in critically ill patients.” *Critical Care*, **15**(5), R242.
- Ooms J (2014). “The jsonlite Package: A Practical and Consistent Mapping Between JSON Data and R Objects.” *arXiv preprint arXiv:1403.2805*.
- Pebesma E, Mailund T, Hiebert J (2016). “Measurement Units in R.” *R Journal*, **8**(2), 486–494. doi:[10.32614/RJ-2016-061](https://doi.org/10.32614/RJ-2016-061).
- Pollard TJ, Johnson AE, Raffa JD, Celi LA, Mark RG, Badawi O (2018). “The eICU Collaborative Research Database, a freely available multi-center database for critical care research.” *Scientific data*, **5**, 180178.
- Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC (2016). “The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).” *JAMA*, **315**(8), 801–810.
- Subbe C, Kruger M, Rutherford P, Gemmel L (2001). “Validation of a modified Early Warning Score in medical admissions.” *QJM: An International Journal of Medicine*, **94**(10), 521–526.
- Therneau TM, Grambsch PM (2000). *Modeling survival data: extending the Cox model*. Springer, New York.
- Therneau TM, Lumley T (2015). “Package ‘survival’.” *R Top Doc*, **128**, 112.

Thoral PJ, Peppink JM, Driessen RH, Sijbrands EJG, Kompanje EJO, Kaplan L, Bailey H, Kesecioglu J, Cecconi M, Churpek M, Clermont G, van der Schaar M, Ercole A, Girbes ARJ, Elbers PWG, Force obotAUMCDAC, the SCCM/ESICM Joint Data Science Task (2021). “Sharing ICU Patient Data Responsibly Under the Society of Critical Care Medicine/European Society of Intensive Care Medicine Joint Data Science Collaboration: The Amsterdam University Medical Centers Database (AmsterdamUMCdb) Example.” *Critical Care Medicine*, **Latest Articles**.

Van Beest PA, Brander L, Jansen SP, Rommes JH, Kuiper MA, Spronk PE (2013). “Cumulative lactate and hospital mortality in ICU patients.” *Annals of intensive care*, **3**(1), 6.

Villar J, Pérez-Méndez L, Blanco J, Añón JM, Blanch L, Belda J, Santos-Bouza A, Fernández RL, Kacmarek RM, Spanish Initiative for Epidemiology and Therapies for ARDS (SIESTA) Network S (2013). “A universal definition of ARDS: the PaO₂/FiO₂ ratio under a standard ventilatory setting—a prospective, multicenter validation study.” *Intensive Care Medicine*, **39**(4), 583–592.

Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, Reinhart C, Suter P, Thijs LG (1996). “The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure.”

Wang RZ, Sun CH, Schroeder PH, Ameko MK, Moore CC, Barnes LE (2018). “Predictive Models of Sepsis in Adult ICU Patients.” In *2018 IEEE International Conference on Healthcare Informatics (ICHI)*, pp. 390–391.

Wang S, McDermott MB, Chauhan G, Ghassemi M, Hughes MC, Naumann T (2020). “Mimic-extract: A data extraction, preprocessing, and representation pipeline for mimic-iii.” In *Proceedings of the ACM Conference on Health, Inference, and Learning*, pp. 222–235.

Wickham H, Hester J (2020). *readr: Read Rectangular Text Data*. R package version 1.4.0, URL <https://CRAN.R-project.org/package=readr>.

Affiliation:

Nicolas Bennett¹
 ETH Zürich
 Seminar for Statistics
 Rämistrasse 101
 CH-8092 Zurich
 E-mail: nicolas.bennett@stat.math.ethz.ch

Drago Plečko¹
ETH Zürich
Seminar for Statistics
Rämistrasse 101
CH-8092 Zürich
E-mail: drago.plecko@stat.math.ethz.ch

Ida-Fong Ukor
Monash Health
Department of Anaesthesiology and Perioperative Medicine
246 Clayton Road
Clayton VIC 3168
E-mail: ida-fong.ukor@monashhealth.org

Nicolai Meinshausen
ETH Zürich
Seminar for Statistics
Rämistrasse 101
CH-8092 Zürich
E-mail: meinshausen@stat.math.ethz.ch

Peter Bühlmann
ETH Zürich
Seminar for Statistics
Rämistrasse 101
CH-8092 Zürich
E-mail: peter.buehlmann@stat.math.ethz.ch

¹These authors contributed equally.