

## 15 ExpoMeta module

### 15.1 Application domain

Meta-analyses can be performed when there are multiple scientific studies addressing the same question, with each individual study reporting measurements that are expected to have some degree of error. The aim then is to use approaches from statistics to derive a pooled estimate closest to the unknown common truth based on how this error is perceived. Meta-analytic results are considered the most trustworthy source of evidence by the evidence-based medicine literature.

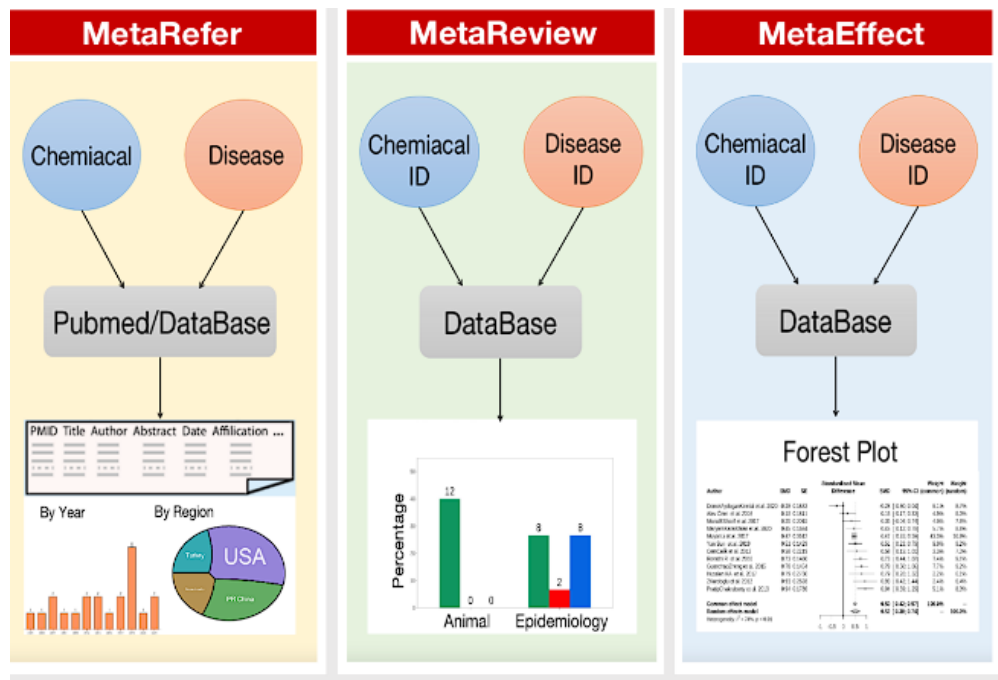
The ExpoMeta module mainly provides users preliminary information retrieval and screening for meta-analysis. It can also summarize the conclusions and effect values of previous studies (available in our meta database), which can help users form a preliminary view of the research topic and further validate the result from the present study. It provides four main functions for users : MetaRefer, VizRef, MetaReview, and MetaEffect.

- MetaRefer: Auto-search all the relative publications from the our meta database and PubMed based on the defined keyword, which has been summarized by the machine learning method and further conveyed to the users.
- VizRefer: VizRefer provides the visual function of papers information searched or downloaded by **MetaRefer**, showing the year and region distribution directly.
- MetaReview: We have been building a standardized database to summarize the up-to-now knowledge about the relationship between environmental exposure and specific diseases. For each topic, the viewpoint from the animal and epidemiological studies are comprehensively summarized by well-trained researchers.
- MetaEffect: For some issues, if their epidemiological studies have been well-conducted, e.g. association between PM2.5 exposure and mortality, the meta-analysis can be conducted to summarize the effect value [e.g. odds ratio (OR), relative risk (RR), hazardous risk (HR)]. The related publications are also summarized in the same database with the “MetaReiew”.

### 15.2 Theory

The “ExpoMeta” module is based on “A 24-step guide on how to design, conduct, and successfully publish a systematic review and meta-analysis in medical research”, which can be summarized by the flow chart below.

```
knitr::include_graphics("@Figures/exmeta1.png")
```



Muka T, Glisic M, Milic J, Verhoog S, Bohlius J, Bramer W, Chowdhury R, Franco OH. A 24-step guide on how to design, conduct, and successfully publish a systematic review and meta-analysis in medical research. *Eur J Epidemiol.* 2020 Jan;35(1):49-60. doi: 10.1007/s10654-019-00576-5. Epub 2019 Nov 13. PMID: 31720912.

## 15.3 Work pipeline

### Initialize package

Make sure that the required packages is already installed.

```
# The following two packages should be installed in advance
# devtools::install_github("ExposomeX/exmeta", force = TRUE)
# devtools::install_github("ExposomeX/extidy", force = TRUE)

# library(exmeta)
# library(extidy)
library(tidyverse)

# devtools::install_github("ExposomeX/exposomex", force = TRUE)
library(exposomex)
```

At first, you need to initialize the calculation environment using a series of initialization functions, e.g., `InitCros`, `InitMo`, `InitTidy`, `InitViz`, `InitBiolink`, etc. Here, we use the package “exmeta” for meta analysis for example. The detailed information about the functions and returned value will be introduced in the following chapters.

```
res <- InitMeta()
res

## <eSet>
##   Public:
##     AddCommand: function (x)
##     AddLog: function (x)
```

```
##      clone: function (deep = FALSE)
##      ExcecutionLog: Complete initializing the ExpoMeta module.2022.12.14 15. ...
##      Expo: list
##      FileDirIn: NULL
##      FileDirOut: /home/ubuntu/@changxin/R_Exposome_1.0/output_150303TKYFFP
##      PID: 150303TKYFFP
##      RCommandLog: eSet <- InitMeta(PID = Any ID your like, FileDirOut = An ...
```

Here, we can see that the returned value “res” is an R6 object. It contains an unique program ID of res\$PID (e.g., “100737GJMWJA”), which is random generated by the system. Users need to use it in the following step for further data process.

## Upload data

After initializing the calculation environment, the second step is to load upload local data file for ExpoMeta Module. `LoadMeta` is provided for this. It has three parameters, PID, UseExample and DataPath. PID is Program ID, which must be the same with the PID generated by `InitMeta`. UseExample is a character indicates whether uses example data for analyses, available option include “example#1” for using example data1 and “default” for using data uploaded. DataPath refer to the input file directory, e.g. “D:/test/eg\_meta.xlsx”. It should be noted that the slash symbol is /, not \. For convenience, here we use example data one for the following step.

```
res1 <- LoadMeta(res$PID,
                  UseExample = "example#1")
```

## MetaRefer

MetaRefer provides the functions of paper retrieval and relevance sorting, returning the information to the user based on keywords. Please attention, PID must be got from the return result of `InitMeta()`. MetaRefer can only run successfully after successfully running `InitMeta` and `LoadMeta` functions.

Two modes are provided in MetaRefer. “Search” for paper retrieval by keywords VarX/VarY/VarM/YearFrom/YearEnd, and “Download” for downloading information (main information only) for specified PMID. Set the Mode parameter as you like. OutPath refers to the output file directory, e.g. “D:/output”. If “default”, the current working directory will be set. It should be noted that the slash symbol is /, not \.

VarX/VarY/VarM/YearFrom/YearEnd/PMID parameters can be default” or a character, run `?MetaRefer` to see more details. For convenience, we set them “default” in this example.

```
res2 <- MetaRefer(PID = res$PID,
                  OutPath = "default",
                  Mode = "search",
                  VarX = "default",
                  VarY = "default",
                  VarM = "default",
                  YearFrom = "default",
                  YearEnd = "default",
                  PMID = "default")
```

## VizRefer

VizRefer function can visualize the articles’ main information after MetaRefer function. Which has only two parameters, PID and OutPath. PID is Program ID, which must be the same with the PID generated by `InitMeta` and OutPath refers to the output file directory.

```
res3 <- VizRefer(PID = res$PID,
                 OutPath = "default")
```

## MetaReview

MetaReview provides the functions of literature review. In the published papers, how many recorded that X is a protective/risky factor for Y? This questions can be solved by MetaReview function. (It can only search the papers available in our database).

MetaReview has four parameters, PID, CID, DID and OutPath. PID and OutPath are the same as introduced above. CID can be "default" or a chemical ID character (separate different values by ","). If "default", the function will use the Chemical\_ID values in the file loaded by LoadMeta. If a character (separate different values by ","), the function will use the chemical ID in the character instead. Chemical\_ID refers to the target chemical ID which can be inchikey (eg. JIAARYAFYJHUJI-UHFFFAOYSA-L ), cas.rn (eg. 7784-42-1) or our EXC ID (eg. EX:C01631). DID can be "default" or a disease ID character (separate different values by ","). If "default", the function will use the Disease\_ID values in the file loaded by LoadMeta. If a character (separate different values by ","), the function will use the disease ID in the character instead. Disease\_ID refers to the target disease ID which can be MESH ID (format like MESH:D006973), OMIM ID (format like OMIM:182940) or our EXD ID (eg. EX:D16243).

```
res2 <- MetaReview(PID = res$PID,
                  OutPath = "default",
                  CID = "default",
                  DID = "default")
```

## MetaEffect

MetaEffect provides the functions of effect value pooling. In the published papers, what is the effect value between X and Y? This questions can be solved by MetaEffect function. It can provide the combined results of fixed effect model and random effect model. (It can only search the papers available in ExpoMeta database DB\_Meta).

MetaEffect has four parameters, PID, CID, DID and OutPath, which are all the same as MetaReview.

```
res2 <- MetaEffect(PID = res$PID,
                  OutPath = "default",
                  CID = "default",
                  DID = "default")
```

```
## [[1]]
## TableGrob (2 x 1) "arrange": 2 grobs
##   z      cells      name      grob
## 1 1 (2-2,1-1) arrange gTree[GRID.gTree.580]
## 2 2 (1-1,1-1) arrange  text[GRID.text.581]
##
## attr("class")
## [1] "arrangelist" "list"
```

After all the analysis is done, please run the "FuncExit()" function to delete the data uploaded to the server.

```
FuncExit(PID = res$PID)
```

```
## [1] "Success to exit. Thanks for using ExposomeX platform!"
```