|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **File Name** | **File Type** | **Generated** | **Contains** | **Outputs** | **Structure page** |
| Figure2\_final\_longnames.pdf | Figure | Data\_viz.Rmd | Figure 2 |  |  |
| Figure4\_ES\_final.pdf | Figure | Data\_viz.Rmd | Figure 4 |  |  |
| Figure6\_timeline\_final\_strip.pdf | Figure | Data\_viz.Rmd | Figure 6 |  |  |
| rob\_plot\_v2.png | Figure | Data\_viz.Rmd | Figure 7 |  |  |
| AutoSTEED\_clean.R | R | In loco | The R file mines every pdf files retrieved and included in the review (list compiled in the file MS\_translation\_extraction.xlsx, sheet: “Interrater agreement+ Risk of B”, column B to G) to extract various information outlined in the description of the file mined\_rob.xlsx | mined\_rob.xlsx |  |
| Data\_Prep.Rmd | R | In loco | The R file pre-process the raw data collected and performs data cleaning and restructuring for the following analyses | HERMES\_INCLUDED.csv |  |
| Data\_viz.Rmd | R | In loco | The R file generates the figures published in the manuscript | hermes\_data.RData  Figure2\_final\_longnames.pdf  Figure6\_timeline\_final\_strip.pdf  Figure4\_ES\_final.png |  |
| HERMES-MS.Rproj | R | In loco | R Project containing the files |  |  |
| MS\_translation\_analysis-git | R | In loco | Meta analyses and survival analysis of the data. The R code performs the analysis and generates the figures | All the figures contained in Meta-Analysis, Forest plots, Survival Analysis |  |
| RoB\_Mining\_Validation\_Viz.Rmd | R | In loco | The R file performs the validation of the automated risk of bias assessment by comparing the manually extracted Risk of bias assessment (MS\_translation\_extraction.xlsx, sheet: “Interrater agreement+ Risk of B”) with the assessment that was automatically mined through the AutoSTEED\_clean.R (mined\_rob.xlsx) | rob\_plot\_v2.png |  |
| Druglist\_Multiple-sclerosis\_Mastersheet.xlsx | Sheet | In loco (Extraction file) | What is this? And is it different from Drug\_CV? |  | 4 |
| HERMES\_INCLUDED.csv | Sheet | Data\_Prep.Rmd | Data sheet from the extracted and curated data, used for any further analysis and visualizations |  |  |
| mined\_rob.xlsx | Sheet | AutoSTEED\_clean.R | Results of the automated Risk of Bias extraction |  |  |
| MS\_translation\_extraction.xlsx | Sheet | In loco | Contains sheets:   * Extraction\_sheet: raw extraction data sheet which is processed in Data\_Prep.Rmd and not further used (please refer to the metadata regarding HERMES\_INCLUDED.csv * Drug\_CV * Interrater agreement+ Risk of B |  | * Drug\_CV (page ) * Interrater agreement+ Risk of B (page ) |

Internal Use Files

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| hermes\_data.RData | R | Data\_viz.Rmd | The R data file is used for internal use in the exploratory summary statistics used for manuscript writing. |  |  |
| Exploratory Summary.Rmd | R | In loco | The R file is used to perform exploratory summary statistics used for manuscript writing and is compiled in the Exploratory-Summary.html |  |  |

Druglist\_Multiple-sclerosis\_Mastersheet.xlsx

HERMES\_INCLUDED.csv

|  |  |  |
| --- | --- | --- |
| **Item** | **Description** | **Type of data** |
| **Author** | Author(s) of the paper | text |
| **Year** | Paper year publication | text |
| **Journal** | Journal of publication | text |
| **Title** | Title of paper | text |
| **Abstract** | Abstract text of the paper | text |
| **DOI** | DOI of the paper | text |
| **exclude\_duplicate\_study** | is the paper to be excluded because of duplication study | binary (yes/no) |
| **Extracted by** | reviewer who performed the data extraction | text |
| **Included** | was the paper included in the analysis? - because this file went through processing and cleaning, only the included papers are present. | binary (1/0) |
| **Reason for exclusion** | Reason for paper exclusion - because this file went through processing and cleaning, only the included papers are present. | text |
| **Animal model** | Animal model used in the paper | categorical |
| **Species** | species (multiple possible) used in the study | text/categorical |
| **Strain** | strain of the animal used in the study | text/categorical |
| **Sex** | sex of the animals used in the study | text/categorical |
| **Age** | age of the animals used in the study | text/categorical |
| **Tested drug(s)** | drugs that have been tested in the study | text/categorical |
| **Comparator** | Comparator/control used in the study | text/categorical |
| **Outcome** |  |  |
| **Total number of animals** | Total number of animals used in the entire publication | |
| **Treatment regimen** | |  |
| **EAE\_\*\_drug\_mean** | mean score for the treatment group in EAE | numeric |
| **EAE\_\*\_drug\_n** | sample size for the treatment group in EAE | numeric |
| **EAE\_\*\_drug\_var** | variance measure for the treatment group in EAE | numeric |
| **EAE\_\*\_con\_mean** | mean score for the control group in EAE | numeric |
| **EAE\_\*\_con\_n** | sample size for the control group in EAE | numeric |
| **EAE\_\*\_con\_var** | variance measure for the control group in EAE | numeric |
| **EAE\_\*\_data\_type** | data type for the control group in EAE | text/categorical |
| **MRI\_\*\_drug\_mean** | mean score for the treatment group in MRI | numeric |
| **MRI\_\*\_drug\_n** | sample size for the treatment group in MRI | numeric |
| **MRI\_\*\_drug\_var** | variance measure for the treatment group in MRI | numeric |
| **MRI\_\*\_con\_mean** | mean score for the control group in MRI | numeric |
| **MRI\_\*\_con\_n** | sample size for the control group in MRI | numeric |
| **MRI\_\*\_con\_var** | variance measure for the control group in MRI | numeric |
| **MRI\_\*\_data\_type** | data type for the control group in MRI | text/categorical |
| **MRI Outcome\_\*** | |  |
| **Comment** |  |  |
| **label** |  |  |
| **type** |  |  |
| **issue** |  |  |
| **keywords** |  |  |
| **language** |  |  |
| **issn** |  |  |
| **pages** |  |  |
| **volume** |  |  |
| **accession** |  |  |
| **address** |  |  |
| **url** |  |  |
| **c1** |  |  |
| **c2** |  |  |
| **DA** |  |  |
| **DP** |  |  |
| **ID** |  |  |
| **n1** |  |  |
| **ST** |  |  |
| **DB** |  |  |
| **m3** |  |  |
| **ET** |  |  |
| **c5** |  |  |
| **j2** |  |  |
| **m1** |  |  |
| **c6** |  |  |
| **OP** |  |  |
| **Tested drug 2** | |  |
| **Outcome drug 2** | |  |
| **Treatment regimen drug 2...67** | | |
| **Tested drug 3** | |  |
| **Species\_in\_study** | species that was used in relation to the extracted data | |
| **status** | status of the drug 1 | |
| **status2** | status of the drug 2 | |

mined\_rob.xlsx

|  |  |  |
| --- | --- | --- |
| **Item** | **Description** | **Type of data** |
| **File.title** | Title of the file for which mining was conducted | text |
| **First.author** | First author of the paper | text |
| **Year** | Year of publication of the paper | numeric |
| **Paper.title** | Title of the Paper | text |
| **Model.1** | Animal model used in the paper | text |
| **Model.count.1** | How many times the model was mentioned in the paper | numeric |
| **Model.2** | Additional animal model used in the paper | text |
| **Model.count.2** | How many times the additional model was mentioned in the paper | numeric |
| **Species.1** | Species used in the paper | text |
| **Species.count.1** | How many times the species was mentioned in the paper | numeric |
| **Species.2** | Additional animal species used in the paper | text |
| **Species.count.2** | How many times the additional species was mentioned in the paper | numeric |
| **Sex** | Animal sex used in the paper | text |
| **Outcome.histology** | Was a histological outcome reported in the study? | text |
| **Outcome.behaviour** | Was a behavioural outcome reported in the study? | text |
| **Outcome.imaging** | Was a imaging outcome reported in the study? | text |
| **Randomization** | Was randomization of the experimental animal described? | text |
| **Randomization\_QC** | is a manual check of the item advised? | text |
| **Blinding** | Was blinding of the experimenters described? | text |
| **Blinding\_QC** | is a manual check of the item advised? | text |
| **Welfare** | Was an animal welfare compliance statement present in the study? | text |
| **Welfare\_QC** | is a manual check of the item advised? | text |
| **Conflict** | Was a conflict of interest statement present in the study? | text |
| **Conflict\_QC** | is a manual check of the item advised? | text |
| **Samplesize** | Was the sample size adequately calculated? | text |
| **Sample\_QC** | is a manual check of the item advised? | text |
| **ARRIVE** | Did the study adhere to the ARRIVE guidelines? | text |
| **ARRIVE\_QC** | is a manual check of the item advised? | text |
| **Data\_availability\_statement** | Was a data availability statement present in the study? | text |
| **doi** | DOI of the paper | text |
| **email** | email of the authors | text |
| **Abstract.start** | line at which the abstract section begins | numeric |
| **Introduction.start** | line at which the introduction section begins | numeric |
| **Methods.start** | line at which the method section begins | numeric |
| **Results.start** | line at which the results section begins | numeric |
| **Discussion.start** | line at which the discussion section begins | numeric |
| **Methods.range** | lines range of the method section | numeric |
| **Paper.range** | lines range of the entire paper | numeric |

MS\_translation\_extraction.xlsx – Drug\_CV

|  |
| --- |
| **Item** |
| **Synonyms** |
| **Drug** |
| **Class** |
| **Mechanism of action** |
| **Orphan drug status** |
| **Orphan drug status MS** |
| **Highest development phase MS** |
| **Highest development phase non-MS** |
| **Source** |
| **Reason** |
| **Reason (short)** |
| **Eligible (drug, discontinued in clinical trial phase for efficacy or safety reason)** |
| **Comment** |
| **Final decision** |
| **Reason** |
| **Clinical\_phenotype** |
| **DMT** |
| **Drug block** |
| **MS block** |
| **Search\_string\_pubmed\_formula** |
| **Search\_string\_pubmed** |
| **Pubmed Hits (March 26, 2023)** |
| **Search\_string\_embase** |
| **Embase Hits (March 26, 2023)** |
| **Total hits** |
| **No MS block preclinical** |
| **Preclinical block no MS** |
| **Pubmed hits** |
| **First\_animal** |
| **First\_animal\_overall** |
| **Source\_first\_animal\_overall** |
| **First\_human** |
| **Source** |
| **year of failure** |
| **source for year of failure** |
| **comment on failure** |
| **Year when last clinical study was finished** |
| **comment on year of last trial** |
| **FDA\_approval** |

MS\_translation\_extraction.xlsx – Interrater agreement+ Risk of B

The majority of the columns here, are a copy of the file “HERMES\_INCLUDED.csv”) with the addition of the following items:

|  |  |  |
| --- | --- | --- |
| **Item** | **Description** | **Type of data** |
| **Randomization** | Was randomization of the experimental animal described? | categorical |
| **Blinding** | Was blinding of the experimenters described? | categorical |
| **ARRIVE guidelines** | Did the study adhere to the ARRIVE guidelines? | categorical |
| **Animal welfare statement** | Was an animal welfare compliance statement present in the study? | categorical |
| **Sample size calculation** | Was the sample size adequately calculated? | categorical |
| **Conflict of interest** | Was a conflict of interest statement present in the study? | categorical |
| **Dedicated statistical analysis section** | was the statistical analysis adequately described? | categorical |

Categories: 0 = no, 1 = yes, 2 = not reported; E.g., for conflict of interest 0 = no conflict of interest, 1 = there is a conflict of interest, 2 = no section about COI