|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **File Name** | **File Type** | **Generated** | **Contains** | **Outputs** | **Structure on 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) | Contains all the included drugs  Used to select the included drugs in the study, includes the search string for pubmed and embase |  | 9 |
| HERMES\_INCLUDED.csv | Sheet | Data\_Prep.Rmd | Data sheet from the extracted and curated data, used for any further analysis and visualizations |  | 4 |
| mined\_rob.xlsx | Sheet | AutoSTEED\_clean.R | Results of the automated Risk of Bias extraction |  | 6 |
| 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: used for the survival analysis, manually extracted year of first animal study, human study, FDA approval * Interrater agreement+ Risk of B |  | * Drug\_CV (page 8) * Interrater agreement+ Risk of B (page 9) |

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 |  |  |

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) (n\*)** | drugs that have been tested in the study. Numbers indicate the nth drug used. This index is also in reference of the other numbers used in the file (for instance, “EAE\_2\_drug\_mean” is in reference to “Tested drug 2”). | text/categorical |
| **Comparator** | Comparator/control used in the study | text/categorical |
| **Outcome\_\*** | Main outcome of the study- 0 = neutral, 1 = positive, 2 = negative, 3 = mixed | Categorical |
| **Total number of animals** | Total number of animals used in the entire publication | numeric |
| **Treatment regimen** | profilactic or therapeutic, 0=pre-induction, 1=prophylactic (d=0 bis Disease onset), 2=therapeutic, 3=different schemes, if different regimens are available, we use primarily therapeutic, then prophylactic and lastly pre-inducted; starting point of drug administration is relevant; Cuprizone: 0=before initiating feeding, 2= after feeding started (similar for lysolecithin) | Categorical |
| **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\_\*** | What the MRI measured T1, T2, T2\*, brain volume, ADC/DWI, gadolinium enhancement measure, MTI/MTR |  |
| **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** | **Description** | **Type of data** |
| **Drug** | official drug name | text |
| **Source** | literature source for highest development phase | text |
| **Reason** | failed or approved drug | categorical |
| **First\_animal\_overall** | Year of first animal experimentation with specific drug | Date |
| **Source\_first\_animal\_overall** | Literature source for year of first animal experimentation | text |
| **First\_human** | Year of first human trial with specific drug | Date |
| **Source** | Literature source for year of first human trial | text |
| **Year of failure** | Year in which the drug has failed clinical trial | Date |
| **Source for year of failure** | Literature source for year in which the drug has failed clinical trial | text |
| **Comment on failure** | Comments | text |
| **Year when last clinical study was finished** | Year when last clinical study with specific drug was finished | Date |
| **comment on year of last trial** | Comments | text |
| **FDA\_approval** | Year in which the drug received FDA approval | date |

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

Druglist\_Multiple-sclerosis\_Mastersheet.xlsx

|  |  |  |
| --- | --- | --- |
| **Item** | **Description** | **Type of data** |
| **Name** | Name of the drug | text |
| **Reason\_class** | Whether the drug is currently marketed (therefore approved for treatment) or has failed during clinical trials | categorical |