Onlinemeta: A Web Server For Meta-Analysis Based On R-shiny

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ABSTRACT

Meta-analysis is a common statistical method used to summarize multiple studies that cover the same topic. It can provide less biased results and explain heterogeneity between studies. Although there exists a variety of meta-analysis software, they are rarely both convenient to use and capable of comprehensive analytical functions. As a result, we established a meta-analysis web tool called Meta-Analysis Online (Onlinemeta). Onlinemeta includes both risk bias analysis and meta-analysis. The risk bias analysis tool can produce heatmaps and histograms, whereas the meta-analysis tool can be used to analyze dichotomous variables, single-armed dichotomous variables, continuous variables, single-armed continuous variables, survival data, and diagnostic experiments. In addition, it can be used to generate forest plots, funnel plots, SROC curve, and crosshair plots. Onlinemeta can be found at the following address: https://smuonco.Shinyapps.io/Onlinemeta/.

Keuwords: meta analysis, Onlinemeta, shiny, web tools,

Introduction

Meta-analysis is a statistical method that synthesizes the results of independent studies covering the same topic to estimate the overall effect of the research, the stability of the results, and identify any influencing factors[1, 2] . When evidence from multiple single studies is combined, a broad meta-analysis can solve problems such as compensating for insufficient sample size, reducing the risk of single-study bias, and providing more objective and effective results. Thus, the results of this type of analysis may help explain heterogeneity among studies and provide a direction for future research[3-5]. As new research and data collection continue to accumulate, meta-analysis has provided researchers with an effective method to summarize these results and generate evidence-based medical data, becoming widely used as a result. A

search for TI = ("meta-analysis" or "meta-analysis") in Pubmed shows that between 2010 to 2021, the number of articles published using meta-analysis techniques increased rapidly from 6996 to 35085 per year.

However, existing meta-analysis software is not perfect. At present, the most commonly used meta-analysis software includes R, Stata, RevMan, and MetaXL. RevMan and MetaXL provide user-friendly interfaces, but they are limited in their statistical functions and graphic customization capabilities. In addition, the initial software setup is complicated and the software must be downloaded separately[6, 7]. Stata is one alternative, but it is paid software which can be inconvenient to use. In addition, Stata analysis struggles when outcome data is missing and small-study effects appear[8]. R is free to use and has excellent statistical and graphic customization functions, but it requires users to be familiar with programming, which limits the user population[9]. Therefore, we are in urgent need of a new tool with the following characteristics: (1) a friendly interface, requiring no specific programming knowledge; (2) no software download required; (3) non-commercial; (4) featuring a full-featured web tool, capable of multiple meta-analysis types including meta-analysis for single-arm variable and diagnostic tests; (5) highly customizable graphics.

With this in mind, we have developed the online meta-analysis web tool Onlinemeta. Onlinemeta can perform risk bias analyses that produce histograms and heatmaps, as well as perform meta-analysis for continuous variables, dichotomous variables, single-arm continuous variables, single-arm dichotomous variables, survival data, diagnostic tests, and subgroup analysis. Compared to traditional software, Onlinemeta allows for the adjustment of many more user-parameters to customize plots. It is also easy to operate, as it has a friendly interactive interface without requiring the use of coding or any software downloads. We hope that Onlinemeta can make meta-analysis more convenient to use and improve visualization of results.

Method

Onlinemeta is a web tool based on Shiny, and it includes both User Interface (UI) and Server Function (server). For the UI section, the theme uses R package ‘shinydashboard’, the data frame display uses R package ‘DT’, and the introduction interface uses R packages ‘SlickR’ and ‘ShinyLP’. For the server section, the risk bias analysis uses R packages ‘ComplexHeatmap’, ‘robvis’, ‘colourpicker’, ‘ggpubr’, and ‘RColorBrewer’, while meta-analysis uses the R packages ‘meta’, ‘metamisc’, and ‘mada’. The whole interface optimization uses R packages ‘ShinyJS’, ‘ShinyDisconnect’, ‘ShinyFeedback’, and ‘Reactable’. The images can be exported as either PDF or PNG. The web tool can be found at the address https://smuonco.Shinyapps.io/Onlinemeta/ and can be used for free without the need to log in.

Results

1. Introduction

This paper introduces the main functions of new meta-analysis tool Onlinemeta, with example output graphs of risk bias analysis and meta-analysis shown in Figure 1. The version information and manager contact information are included below, and users are invited to give feedback or ask questions if needed.

2. Histograms for risk bias analysis

This analysis tool is able to produce risk bias histograms (Figure 2). Users can click "Data Format" to view file formats, click the question mark behind parameters to view the explanation of the parameter, and click "Download Example Data" to download the sample data. Sample data is displayed by default (Figure 2A). After canceling the sample data, users can begin analysis by uploading local data to the “Upload” panel and adjusting the corresponding parameters in “Customize” panel. The histogram shows the quality of the studies being analyzed (Figure 2B). A series of parameters can be used to adjust plots, such as title, font size, color scheme, and size of output image (Figure 2C).

3. Heatmap for risk bias analysis

The software interface can also output the results of risk bias analysis as a heatmap (Figure 3). The heatmap color represents the risk, with the labels “Unclear”, “Low”, “Medium”, and “High” assigned to 0, 1, 2, and 3, respectively. The color bars in the upper right show the average risk scores of the ranks (Figure 3B). Sample data is displayed by default (Figure 3A). After canceling the sample data and uploading local data in the “Upload” panel, users can adjust the heatmap color scheme, bar color, annotation height, font size, and output image size in the “Customize” panel (Figure 3C).

4. The Meta function for different kinds of variables

The Meta function allows users to conduct a series of meta-analyses (Figure 4). Depending on the type of original data being analyzed, users can select “Meta” for dichotomous variables, continuous variables, single dichotomous variables, single continuous variables, and survival variables from the interface. Onlinemeta can then output two types of diagrams: forest plots (Figure 4A) and funnel plots (Figure 4B). In the “Customize” panel, fixed effect or random effect models can be selected. We provide "MD", "SMD", and "ROM" for continuous variables, and "RR", "OR", "RD", "ASD", and "DOR" for dichotomous variables. In addition, "PLOGIT", "PAS", "PFT", "PLN", and "PRAW" are available for single dichotomous variables, whereas "MRAW" and "MLN" are available for single continuous variables. Finally, "RD", "RR", "OR", "ASD", "HR", "MD", "SMD", and "ROM" can be used for survival variables. Users can adjust the label name, square color, CI color, and font size to beautify their forest plot (Figure 4C). After providing a group file, subgroup analysis can also be implemented.

5. Onlinemeta for diagnostic tests

Users can also use this interface to conduct meta-analysis for diagnostic tests (Figure 5).

Here the results have been visualized as a forest plot (Figure 5A), SROC curve (Figure 5B), and Crosshair plot (Figure 5C), demonstrating the sensitivity and specificity of both the individual research results and the comprehensive results. A series of parameters such as line color, line width, line position, line type, and symbol can be adjusted (Figure 5D).

6. Help

Users can consult the FAQ section for solutions to common problems encountered when using this software.

Discussion

Meta-analysis can combine a large number of studies from around the world, providing less biased and more accurate results than possible from single studies for potential use in fields such as evidence-based medicine[10, 11]. However, at present, most meta-analysis is performed using programming languages or software, and some of this software is often missing several useful functions [6, 7]. To fill this gap, we developed Onlinemeta, an interactive web tool based on R-Shiny, which provides a new way to perform risk bias analysis and meta-analysis.

Onlinemeta is fully functional and accessible tool. In recent years, many online meta-analysis web tools have also been developed based on R-Shiny, such as IPD Mada[12] and MetaDTA[13]. However, we believe that Onlinemeta is the first tool capable of performing not only risk bias analysis, six kinds of meta-analysis, and subgroup analysis simultaneously. For risk bias analysis, in addition to the traditional histogram, we designed the tool to produce a risk heatmap, which calculates the average risk score of each row and column. Users can also choose whether to include ‘overall' and ‘weight' as factors in the risk bias analysis. We also enabled the use of meta-analysis for dichotomous variables, continuous variables, single dichotomous variables, single continuous variables, survival variables, and diagnostic tests. In addition, users can upload group files for subgroup analysis and select the fixed effect/random effect model by adjusting the parameters.

Onlinemeta has highly customizable analytical plots, as we provide PDF and PNG download formats for each output image. In the risk bias analysis section, we provide a variety of color schemes for histograms and heatmaps, enabling users to choose or customize colors. The title, font size, and size of output image can also be adjusted. In the meta-analysis section, we provide users with a variety of drawing methods and models. Relevant parameters such as name, line color, line type, line width, logo, and size of output image can also be adjusted to facilitate customizing pictures. As an interactive interface, Onlinemeta is easy to use regardless of whether users have any prior statistical background or programming knowledge. In addition, directly uploading the '.csv' format file avoidsthe need for complicated data preparation beforehand. Moreover, users do not need to download any software when using Onlinemeta, saving the user both time and storage space. However, as Onlinemeta is still in

version 1.0, many functions can still be improved. We welcome any user feedback to help Onlinemeta become a more mature, friendly, and widely used meta-analysis software.

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Figure legend

Figure 1: Schema describing data processing and data display for Onlinemeta.

Figure 2: Using Onlinemeta to generate histograms of risk bias analysis.

(A) Panels that show uploaded data.
(B) A histogram generated using Onlinemeta indicating literature quality.
(C) Panels for data uploading and parameter configuration to generate histograms.

Figure 3: Using Onlinemeta to generate heatmaps of risk bias analysis.

(A) Panels that show the uploaded data.
(B) A heatmap generated using Onlinemeta indicating literature quality.
(C) Panels for data uploading and parameter configuration to generate heatmaps.

Figure 4: Using Onlinemeta to conduct meta-analysis for different kinds of variables.

(A) A forest plot generated using the Onlinemeta showing the result of meta-analysis.
(B) A funnel plot generated using the Onlinemeta showing risk bias.
(C) Panels for data uploading and parameter configuration to generate forest plots and funnel plots.

Figure 5: Using Onlinemeta to conduct meta-analysis for diagnostic tests.

(A) A forest plot generated using the Onlinemeta showing the results of meta-analysis.
(B) A SROC curve generated using the Onlinemeta showing sensitivity and specificity.
(C) A crosshair plot generated using the Onlinemeta showing sensitivity and specificity.
(D) Panels for data uploading and parameter configuration to generate forest plots, SROC curves, and crosshair plots.

DATA AVAILABILITY

R studio is a language and environment for statistical computing available in https://www.r-project.org/.
Shiny is an open source collaborative initiative available in the GitHub repository (https://github.com/rstudio/shiny).

SUPPLEMENTARY DATA

None

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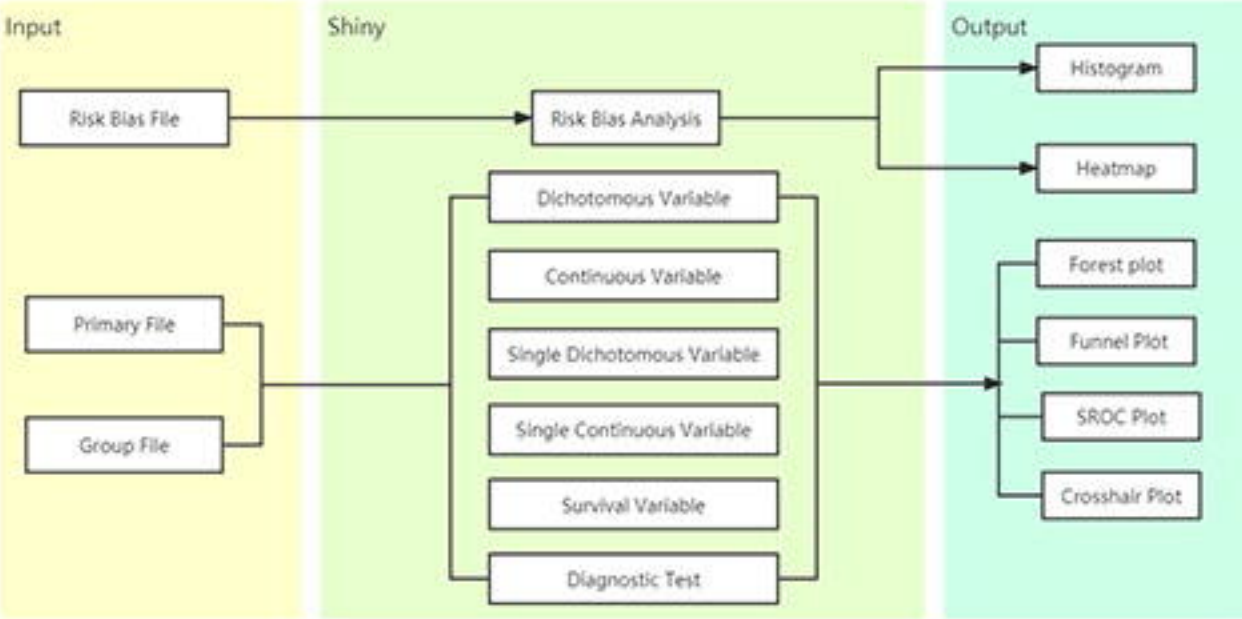
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References:

1. Strube MJ, Hartmann DP. A critical appraisal of meta-analysis, Br J Clin Psychol 1982;21 (Pt 2):129-139.
2. Walker E, Hernandez AV, Kattan MW. Meta-analysis: Its strengths and limitations, Cleve Clin J Med 2008;75:431-439.
3. Egger M, Smith GD, Phillips AN. Meta-analysis: principles and procedures, BMJ 1997;315:1533-1537.
4. Gotzsche PC. Why we need a broad perspective on meta-analysis. It may be crucially important for patients, BMJ 2000;321:585-586.
5. Lee YH. An overview of meta-analysis for clinicians, KOREAN JOURNAL OF INTERNAL MEDICINE 2018;33:277-283.
6. Bax L, Yu LM, Ikeda N et al. A systematic comparison of software dedicated to meta-analysis of causal studies, BMC Medical Research Methodology 2007;7:40.
7. Daly C, Soobiah C. Software to Conduct a Meta-Analysis and Network Meta-Analysis, Methods Mol Biol 2022;2345:223-244.
8. Chaimani A, Mavridis D, Salanti G. A hands-on practical tutorial on performing meta-analysis with Stata, Evid Based Ment Health 2014;17:111-116.
9. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial, Evid Based Ment Health 2019;22:153-160.
10. Shah A, Jones MP, Holtmann GJ. Basics of meta-analysis, Indian J Gastroenterol 2020;39:503-513.
11. Guyatt GH, Sackett DL, Sinclair JC et al. Users' guides to the medical literature. IX. A method for grading health care recommendations. Evidence-Based Medicine Working Group, JAMA 1995;274:1800-1804.
12. Wang J, Keusters WR, Wen L et al. IPDmada: An R Shiny tool for analyzing and visualizing individual patient data meta-analyses of diagnostic test accuracy, Research Synthesis Methods 2021;12:45-54.
13. Freeman SC, Kerby CR, Patel A et al. Development of an interactive web-based tool to conduct and interrogate meta-analysis of diagnostic test accuracy studies: MetaDTA, BMC Medical Research Methodology 2019;19:81.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Shiny
Output
Risk Bias File
Risk Bias Analysis
Histogram
Heatmap
Dichotomous Variable
Continuous Variable
Single Dichotomous Variable
Single Continuous Variable
Survival Variable
Diagnostic Test
Primary File
Group File
Forest plot
Funnel Plot
SROC Plot
Crosshair Plot

A

Data Format

Show 5 entries

Search:

	study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall	Weight
1	Study 1	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	0
2	Study 3	Unclear	Low	Unclear	Low	Low	Unclear	Low	Unclear	Low	Low	Medium	0
3	Study 4	Low	Low	High	Low	Low	Low	Low	High	Low	Low	High	0
4	Study 5	High	High	Unclear	Low	Low	High	High	Unclear	Low	Low	Low	0
5	Study 6	High	High	Low	Medium	Unclear	High	High	Low	Medium	Unclear	Medium	0

Showing 1 to 5 of 15 entries

Previous 1 2 3 Next

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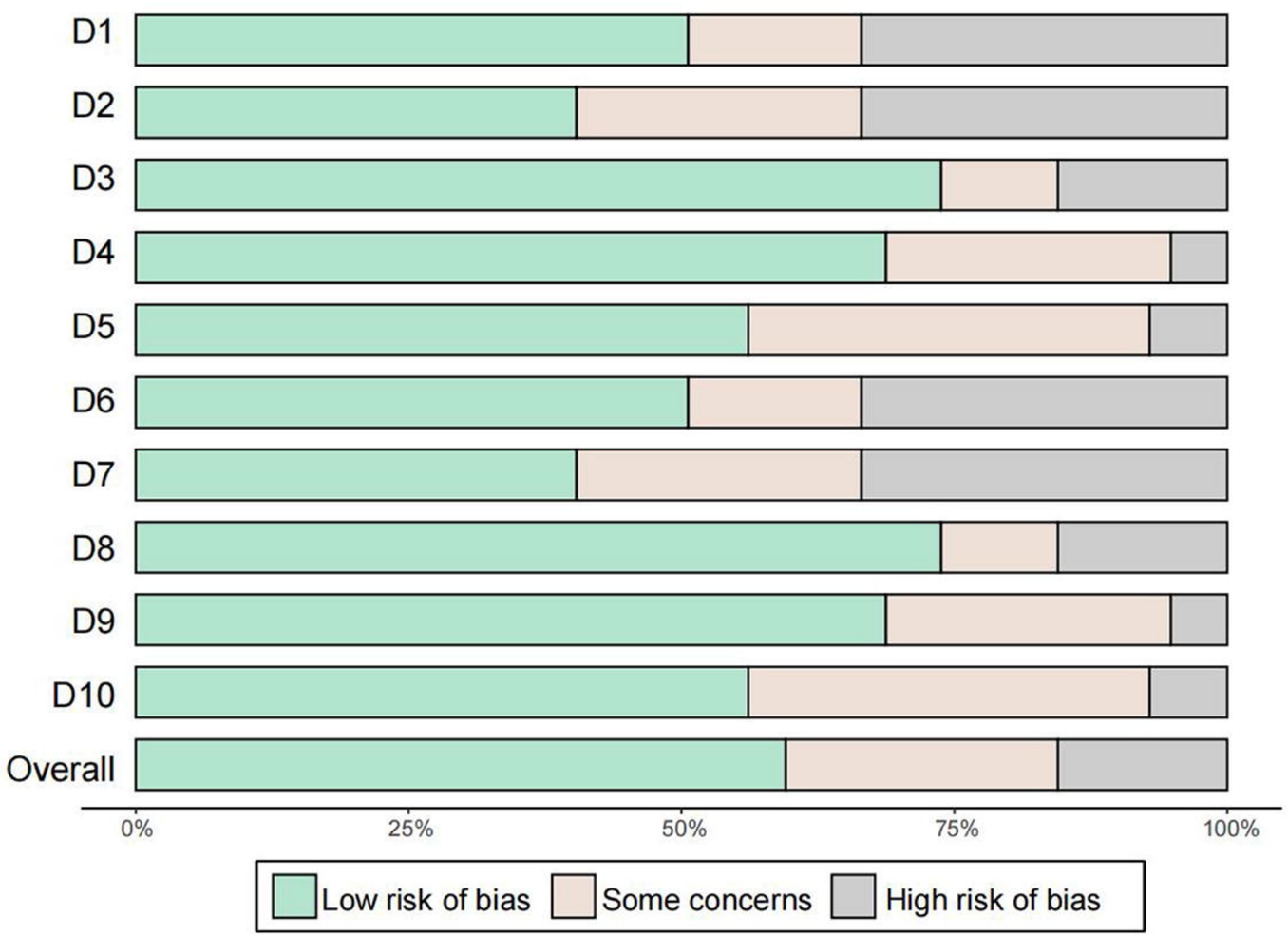

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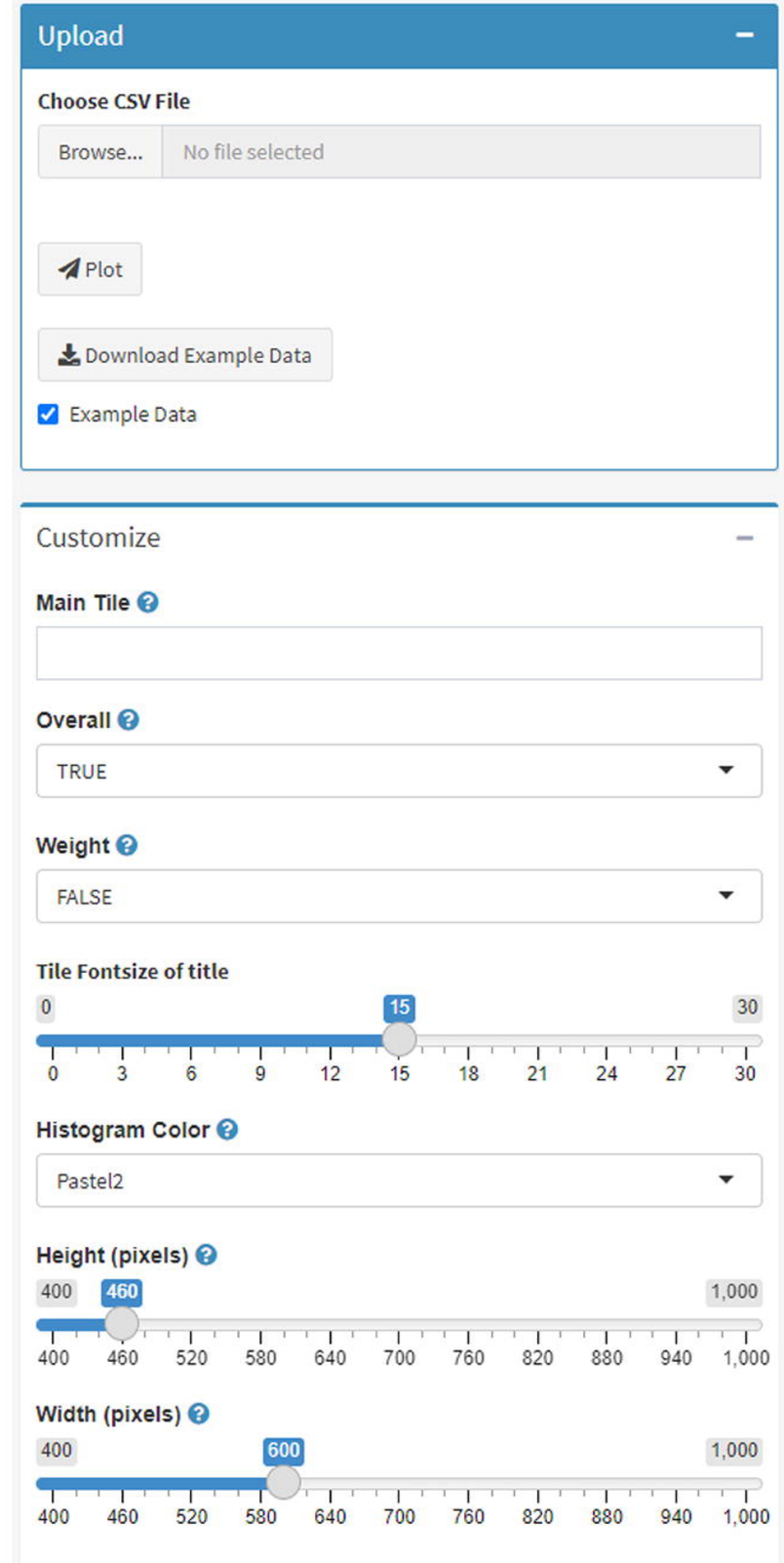

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Data Format

Show 5 entries

Search:

	study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall	Weight
1	Study 1	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	0
2	Study 3	Unclear	Low	Unclear	Low	Low	Unclear	Low	Unclear	Low	Low	Medium	0
3	Study 4	Low	Low	High	Low	Low	Low	Low	High	Low	Low	High	0
4	Study 5	High	High	Unclear	Low	Low	High	High	Unclear	Low	Low	Low	0
5	Study 6	High	High	Low	Medium	Unclear	High	High	Low	Medium	Unclear	Medium	0

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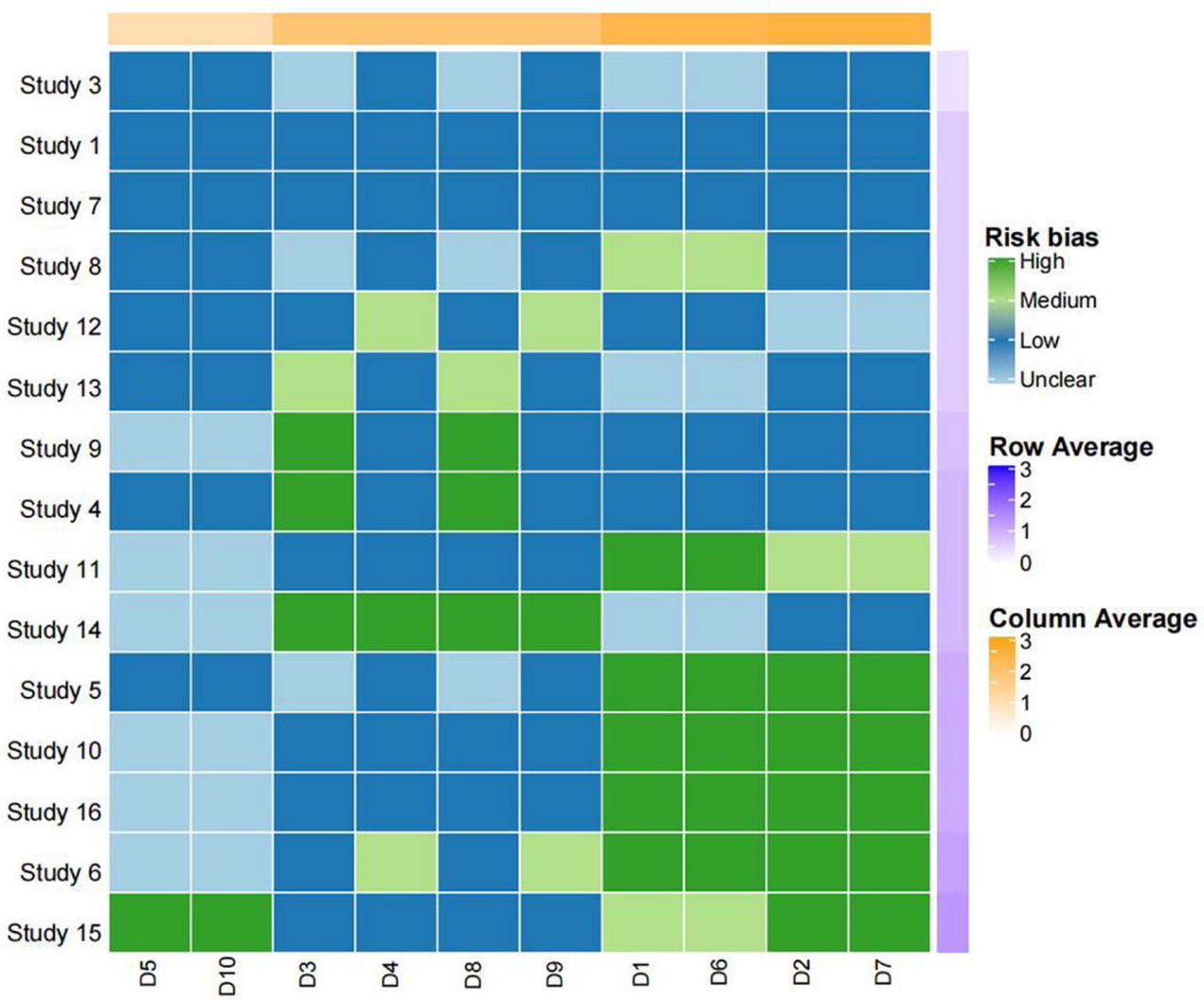

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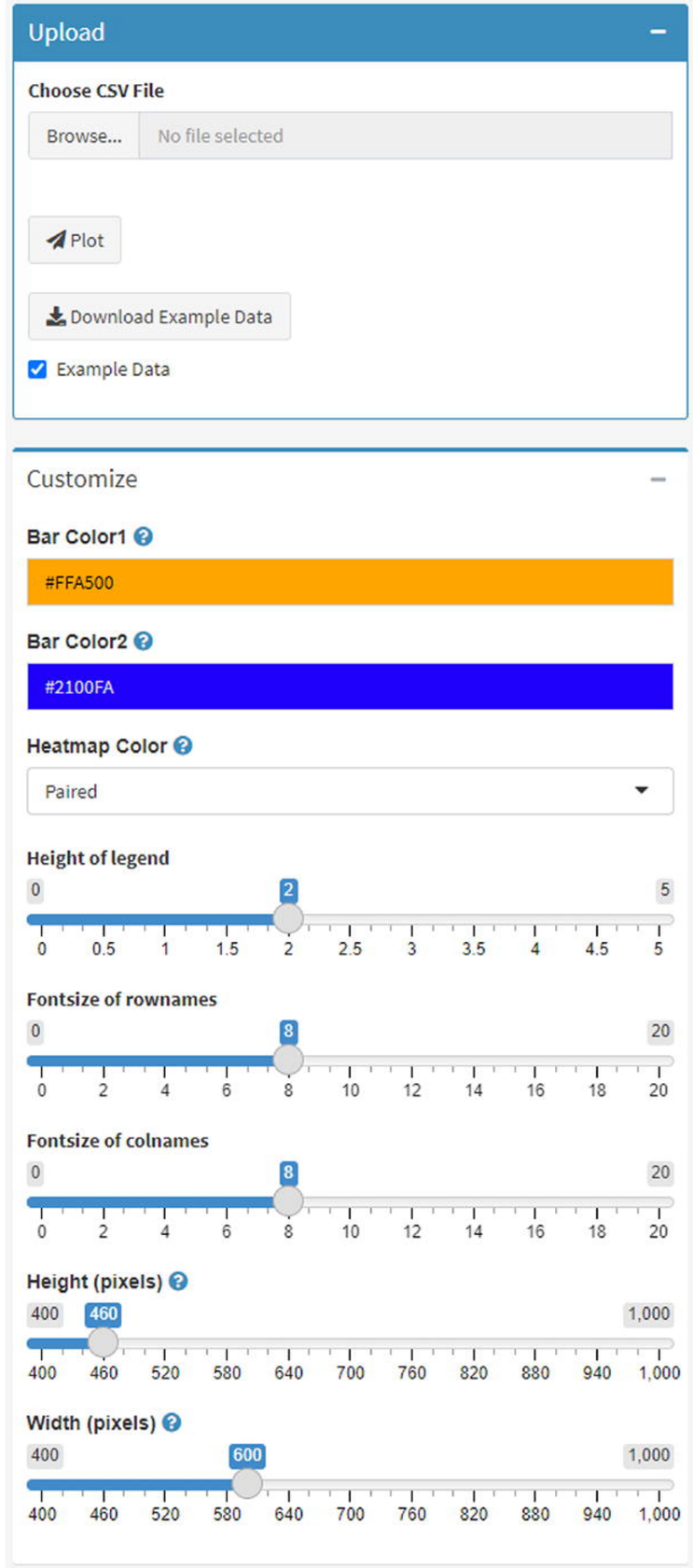
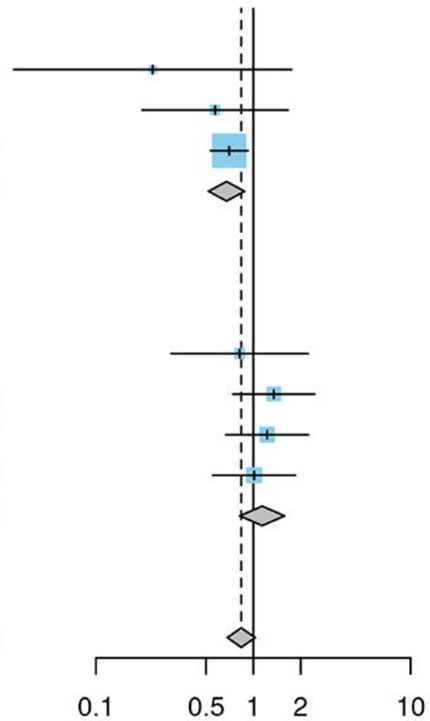


A

Study	Events	Total	Events	Total	RR	95%-CI	Weight
group = A							
MRC-1	1	12	4	11	0.23	[0.03; 1.75]	2.5%
CDP	4	21	7	21	0.57	[0.20; 1.66]	4.2%
PARIS	69	373	94	357	0.70	[0.53; 0.92]	58.2%
Common effect model		406		389	0.68	[0.52; 0.88]	64.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.53							
group = B							
MRC-2	6	43	7	41	0.82	[0.30; 2.23]	4.3%
GASP	20	83	15	84	1.35	[0.74; 2.45]	9.0%
AMIS	22	219	17	207	1.22	[0.67; 2.24]	10.6%
ISIS-2	19	164	18	157	1.01	[0.55; 1.85]	11.1%
Common effect model		509		489	1.14	[0.82; 1.58]	35.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82							
Common effect model		**915**		**878**	**0.84**	**[0.68; 1.03]**	**100.0%**

Heterogeneity: I^2 = 25%, τ^2 = 0.0374, p = 0.24

Test for subgroup differences: χ^2_1 = 5.91, df = 1 (p = 0.02)



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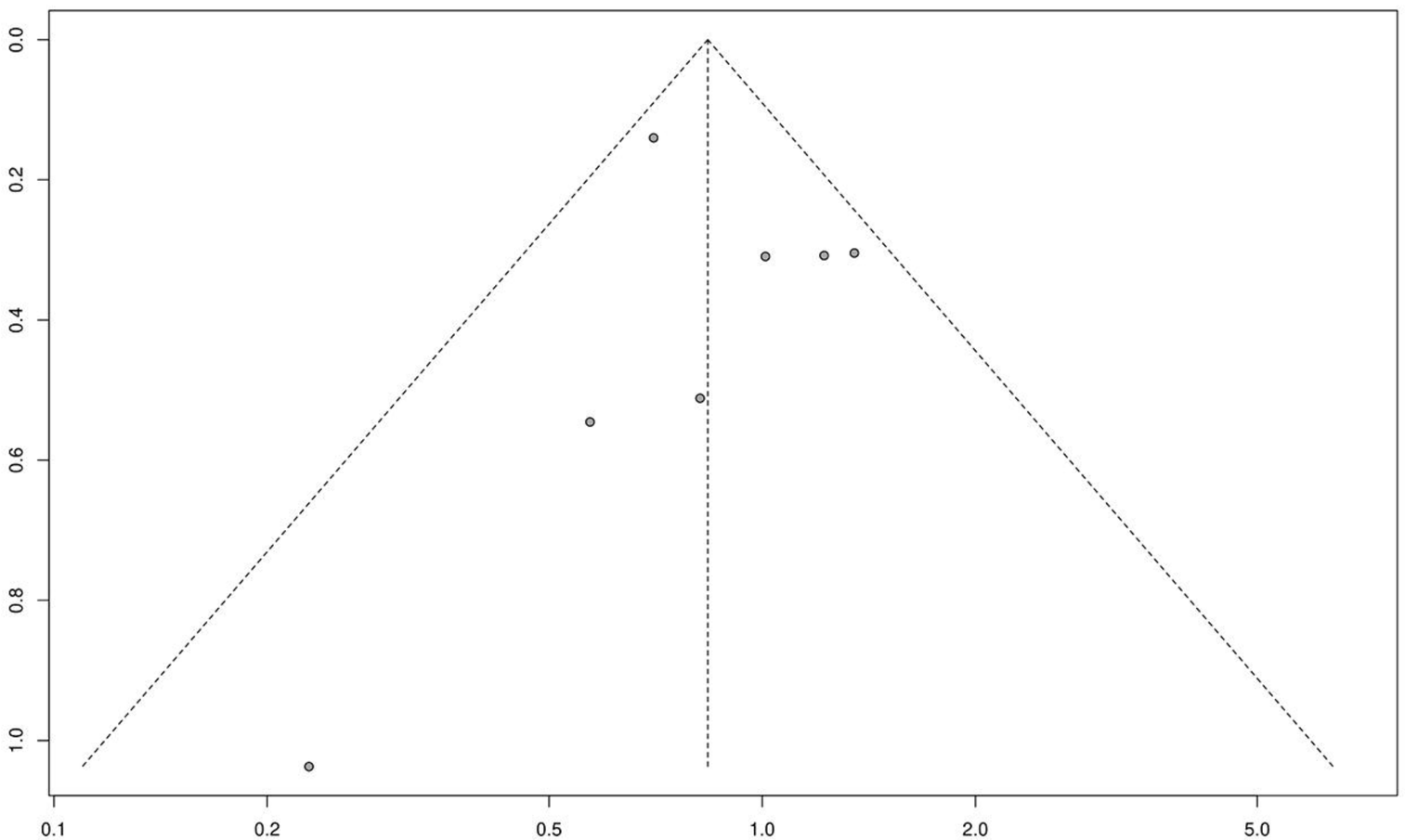

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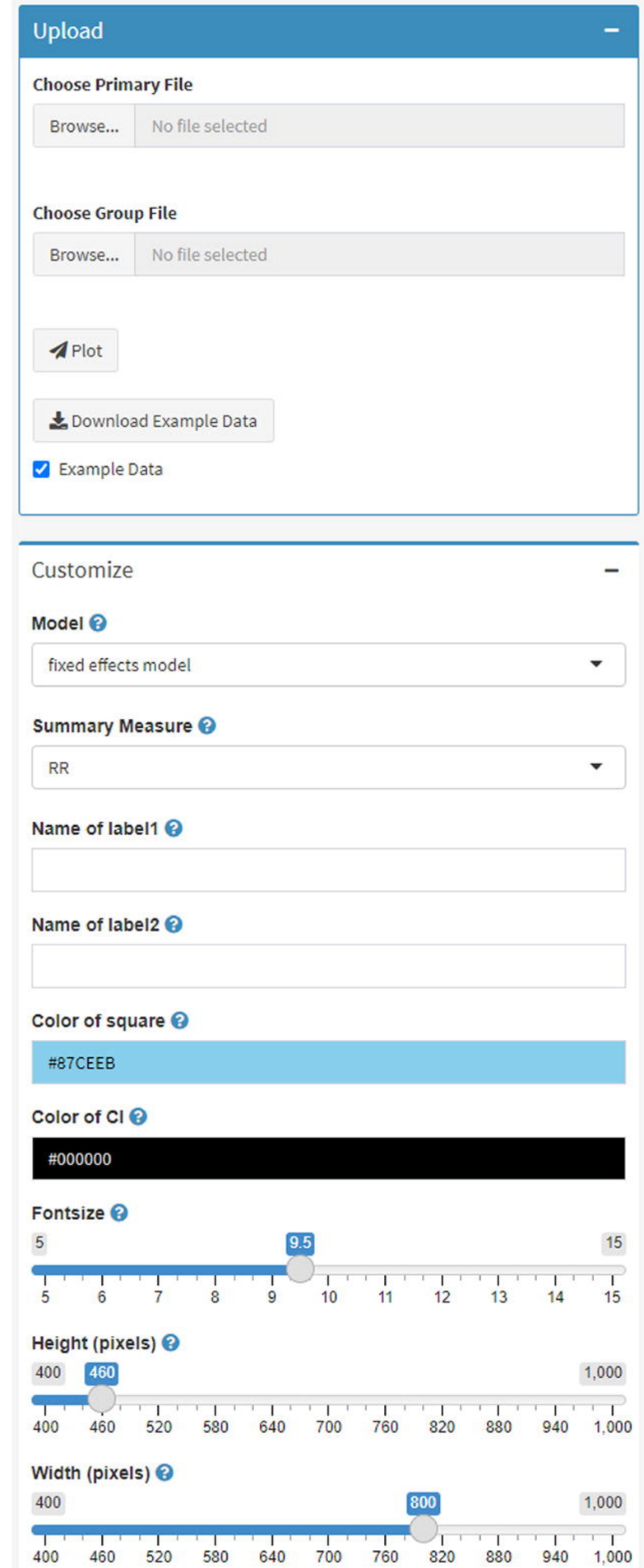

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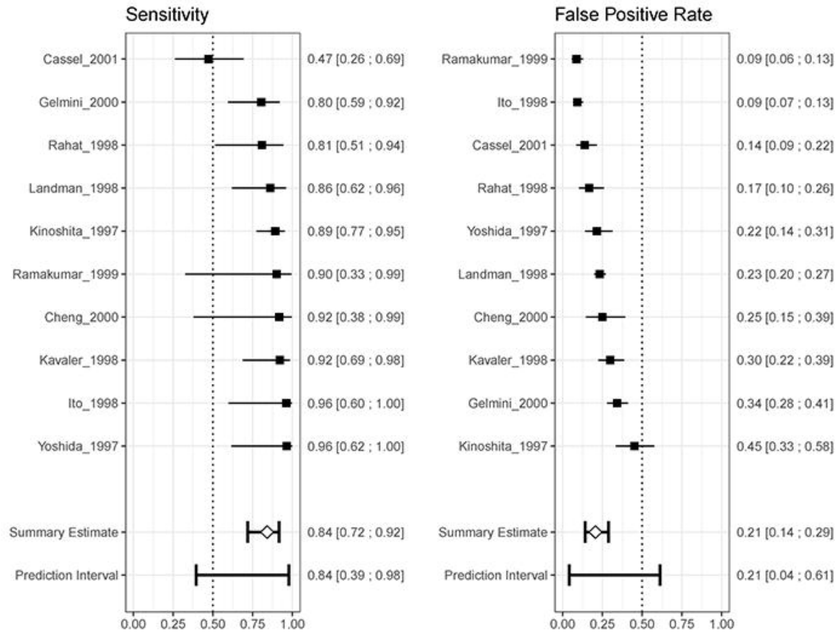
Sensitivity
Cassel_2001 0.47 [0.26 ; 0.69]
Gelmini_2000 0.80 [0.59 ; 0.92]
Rahat_1998 0.81 [0.51 ; 0.94]
Landman_1998 0.86 [0.62 ; 0.96]
Kinoshita_1997 0.89 [0.77 ; 0.95]
Ramakumar_1999 0.90 [0.33 ; 0.99]
Cheng_2000 0.92 [0.38 ; 0.99]
Kavaler_1998 0.92 [0.69 ; 0.98]
Ito_1998 0.96 [0.60 ; 1.00]
Yoshida_1997 0.96 [0.62 ; 1.00]
Summary Estimate 0.84 [0.72 ; 0.92]
Prediction Interval 0.84 [0.39 ; 0.98]
0.00 0.25 0.50 0.75 1.00
False Positive Rate
Ramakumar_1999 0.09 [0.06 ; 0.13]
Ito_1998 0.09 [0.07 ; 0.13]
Cassel_2001 0.14 [0.09 ; 0.22]
Rahat_1998 0.17 [0.10 ; 0.26]
Yoshida_1997 0.22 [0.14 ; 0.31]
Landman_1998 0.23 [0.20 ; 0.27]
Cheng_2000 0.25 [0.15 ; 0.39]
Kavaler_1998 0.30 [0.22 ; 0.39]
Gelmini_2000 0.34 [0.28 ; 0.41]
Kinoshita_1997 0.45 [0.33 ; 0.58]
Summary Estimate 0.21 [0.14 ; 0.29]
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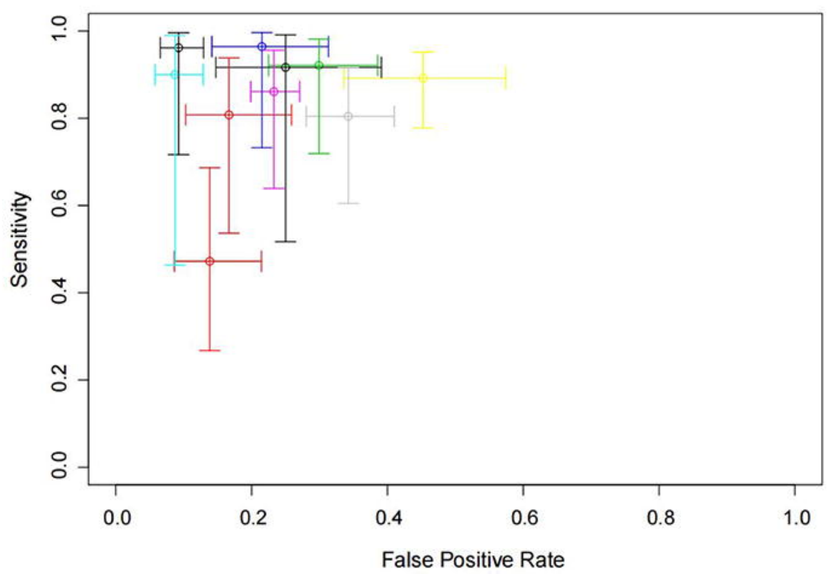
0.00 0.25 0.50 0.75 1.00

B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False Positive Rate
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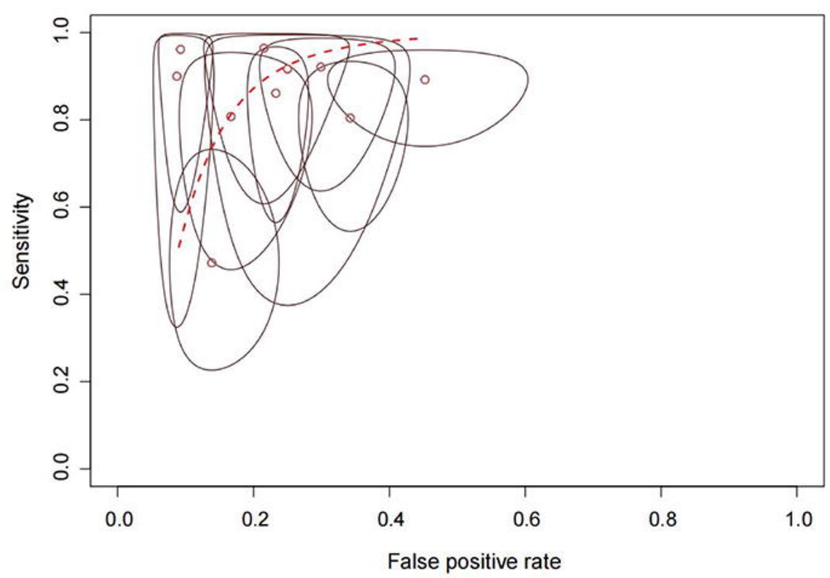
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False positive rate
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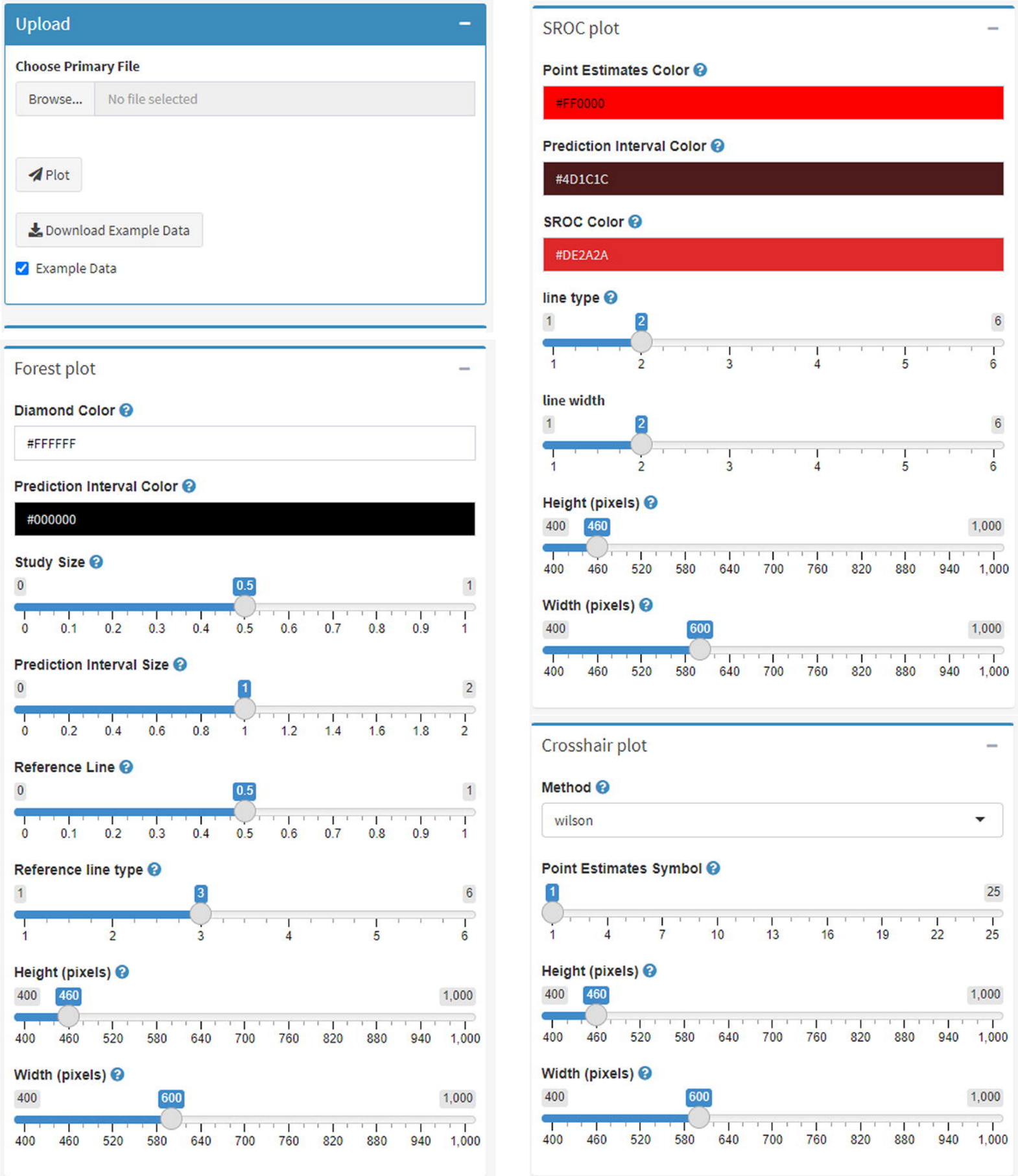
D


Upload
Choose Primary File
Browse... No file selected
Plot
Download Example Data
Example Data
Forest plot
Diamond Color
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Prediction Interval Color
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Study Size
Prediction Interval Size
Reference Line
Reference line type
Height (pixels)
Width (pixels)
SROC plot
Point Estimates Color
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Prediction Interval Color
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SROC Color
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line type
line width
Height (pixels)
Width (pixels)
Crosshair plot
Method
wilson
Point Estimates Symbol
Height (pixels)
Width (pixels)