Systematic Comparison of Meta-Analysis Software and Validation of MetaXact for Meta-Analysis of Sparse Outcomes

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Background and objectives

- While meta-analysis has become a prominent cornerstone of scientific medicine in the domain of therapeutics, there is no consensus on which software has the state-of-the-art features to be used for health technology assessment submissions.
- Each meta-analysis software has different feature sets, distinct user advantages and disadvantages, and required level of expertise.
- No systematic evaluation of software has been conducted since 2007, even though the meta-analysis software landscape has expanded dramatically.
- MetaXact has been introduced as an alternative software within the Cytel Studio platform, which focuses on expanding the available exact methodologies for conducting statistical analyses in the case of small sample sizes, rare events, and/or violations to standard distributional assumptions.

Methods: Software platforms

Two investigators compared the features of each software with respect to:

1. **Basic characteristics** (**Table 1**)
2. **Data preparation** (**Table 2**)
3. **Analysis features** (**Table 3**)

- **MetaXact**: A comprehensive meta-analysis tool within the Cytel Studio software suite; part of the Xact suite of tools, which distinguish themselves from statistical software platforms through the breadth of exact analyses
- **Review Manager 5.0** (**RevMan5**): Developed by and for the Cochrane Collaboration, it has extensive features for collaborative management of systematic reviews
- **R** (**meta package**): R is an open-source statistical software that facilitates meta-analysis through several packages
- **STATA:** A general-purpose statistical software package developed by StataCorp
- **Comprehensive Meta-analysis Software** (**CMA**): Developed in collaboration with many of the recognized experts in the field of meta-analysis

Table 1. General software features

Outcome	MetaXact	RevMan 5	R	STATA	CMA
General characteristics					
Point-and-click user interface	✓	✓	✓	✓	✓
Coding			✓	✓	
Price	-	C: 730 GBP A: Free	Free	C: 765 USD/year A: 125 USD/year S: 94 USD/year	C: 295-895 USD/year A: 195-495 USD/year S: 75-195 USD/6 months
Program size	40 MB	59 MB	85 MB	344 MB	25 MB
Last update	January 2020	September 2020	March 2021	April 2021	November 2021
License (single use/multi use)	Single user	Single user	Open source	Single user, multi user, and server available	Single user
Operating systems	Windows	Windows	Windows, Mac OS, Linux	Windows, Mac OS, Linux	Windows
Documentation					
Within-program help	✓	✓	✓	✓	✓
Printable manual	✓	✓	✓	✓	✓
Detailed methods	✓	✓	✓	✓	✓

Abbreviations: A, academic user; C, commercial user; CI, confidence interval; DPI, dots per inch; OR, odds ratio; S, student user; SD, standard deviation; SE, standard error; SMD, standardized mean difference; VAR, variation.

Table 2. Data-related features

Outcome	MetaXact	RevMan 5	R	STATA	CMA
Data import					
Manual entry	✓	✓		✓	✓
Copy and Paste	✓			✓	✓
CSV import	✓		✓	✓	
Text file import	✓		✓	✓	
Other formats	xls, xlsx, sas7bdat	Application specific format	xls, xlsx, sas7bdat, .sav	xls, xlsx, sas7bdat, .sav	Application specific format
Data structure					
Dichotomous, eg, No. of events, total	✓	✓	✓	✓	✓
Continuous, eg, No., SD	✓	✓	✓	✓	✓
Effect size, eg, theta, SE/VAR	✓	✓	✓	✓	✓
Data manipulation					
Sorting	✓	✓	✓	✓	✓
Variable creation	✓		✓	✓	
Filter (rows)	✓		✓	✓	
Select (columns)	✓		✓	✓	
Transpose	✓		✓	✓	
Merging			✓	✓	
Output options					
Copy output to clipboard	✓	✓	✓	✓	✓
Export to office application(s)	✓	✓	✓	✓	✓
Report creation	✓	✓			
Setting output file type	✓	✓ PDF, EPS, SVG, EMF, SWF	✓ PDF, JPG, PNG, BMP, TIFF	✓ PDF, EPS, SVG, EMF, SWF	✓ PDF, WMF
Ability to control the DPI of images for publications (default DPI and range of DPI)			✓	✓	✓ High-resolution, not adjustable

Table 3. Analysis features

Outcome	MetaXact	RevMan 5	R	STATA	CMA
Analytical Options and Settings					
Number of decimals (user-select ability)	✓	Only available for 2 or 4 decimals	✓	✓	✓
Alpha-level	✓	ü	✓	✓	✓
Transformation measures for binary outcome (Arcsin, logit, untransformed, and others)	✓	Log transform only	✓	✓	✓
Measures of SMD	Mean difference, Hedge's G	Mean difference, Hedges G	Mean difference, Hedge's G, Cohen's D,	Mean difference, Hedge's G, Cohen's D, Glass Delta 1 or 2	Mean difference, Cohen's D,
Exact method	✓		✓		
Constant continuity correction	✓	✓	✓	✓	✓
Statistical Methods					
Fixed-effect models/weighting	✓	✓	✓	✓	✓
Random-effects models/weighting	✓	✓	✓	✓	✓
Cumulative analyses			✓	✓	✓
Heterogeneity	✓	✓	✓	✓	✓
Small study effect/publication bias	✓	✓	✓	✓	✓
Prediction intervals			✓	✓	
Meta-regression			✓	✓	✓
Graphical Outputs					
Forest plot	✓	✓	✓	✓	✓
Ability to customize forest plots (study labels, event labels, scale [log vs identity],and stratified results)		Labels: study, event, strata, axis arcsine scale, stratified results, footnotes (updated version)	Labels: study, event, strata, axis arcsine scale, stratified results, footnotes (updated version)	Labels: study, event, strata, axis arcsine scale, stratified results, footnotes (updated version)	Labels: study, event, strata, axis arcsine scale, stratified results, footnotes (updated version)
Funnel plot	✓	✓	✓	✓	✓
L'Abbe plot, Galbraith plot, others	L'Abbe, Gailbraith		L'Abbe, Gailbraith, Baujat	L'Abbe, Gailbraith	
Graph formatting (any properties including color and theme for journal styles)	✓	✓	✓	✓	✓
Sensitivity Analysis					
Subgroup analyses	✓	✓	✓	✓	✓
Multi-level factors	✓	✓	✓	✓	✓
Specialized analyses	Begg-Mazumdar, fail-safe N, leave-one-out, Egger's		Trim-fill, leave-one-out	Egger, Harbord, Peters, Begg	Leave-one-out, fail-safe N, rank-correlation, trim-fill
Test for Heterogeneity	I^2, Cochrane Q, Tau^2, Chi^2	I^2, Cochrane Q, Tau^2, Chi^2	I^2, Cochrane Q, Tau^2, Chi^2	I^2, Cochrane Q, Tau^2, Chi^2	I^2, Cochrane Q, Tau^2, Chi^2

Results

- Each software produced similar numerical outputs with the standard Mantel-Haenszel odds ratio method. MetaXact and R produced similar results using the exact method, while this option was unavailable in RevMan 5. Furthermore, the exact method estimated a statistically significant difference between rosiglitazone and control, while the Mantel-Haenszel method did not (**Table 4**).
- For users desiring a point-and-click interface over a coding software, MetaXact provides a straightforward method to implement the exact method as is required in the case of rare events.

Table 4. Meta-analysis results (odds ratio)

	Fixed Effects Model			Random Effects Model			Heterogeneity			Exact Method	
Software	Pooled OR (95% CI)	Z	p	Pooled OR (95% CI)	Z	p	Q	I^2 (%)	T^2	Pooled OR (95% CI)	p
R	1.283 (0.951 to 1.733)	1.63	0.103	1.292 (0.944 to 1.767)	1.60	0.109	16.22	0	0	1.433 (1.035 to 1.984)	0.030
MetaXact	1.284 (0.951 to 1.733)	1.63	0.103	1.292 (0.944 to 1.767)	1.60	0.109	16.22	0	0	1.433 (1.022 to 2.015)	0.037
RevMan 5	1.284 (0.951 to 1.733)	1.63	0.103	1.292 (0.944 to 1.767)	1.60	0.109	16.22	0	0	N/A	N/A

Conclusion

- This study validated MetaXact against two of the most common meta-analysis statistical software platforms.
- MetaXact is well-suited for researchers without extensive experience in R coding and who prioritize a point and click interface while having more advanced features than RevMan 5, such as exact inference and calculation methods.

References

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