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Self-learning software tools for data analysis in meta-analysis

- Letter to the Editor –

Understanding how to conduct a meta-analysis helps clinicians in the process of making clinical decisions.¹ Researchers need additional information on software programs that are required to do a meta-analysis. In the published literature of high-impact-factor anesthesia journals, we observe the ‘RevMan 5’ as the most frequently used primary meta-analytical software package. Researchers definitely need many more other software and/or related links, but detailed information on this additional auxiliary software use is lacking. The challenge arises when multiple analyses are required, and the researcher needs to choose correctly among the software programs available. Apart from primary statistical software programs like SAS, R, STATA, SPSS, and Cochrane calculators, one needs to be aware of user-friendly auxiliary software to progress in meta-analysis. This is because primary software programs are deficient in performing additional analysis, such as meta-regressions, network plotting, etc. In general, it is believed that clinical researchers often make mistakes when they attempt to undertake their own data analysis, and not enlisting a statistician before and after undertaking a study. On the contrary, it is also true that self-learning of additional software by a researcher critically reduces the need for collaboration with a statistician and may as well improve the quality of research. In the subsequent paragraph, we effort to inform the types and representative examples of software for data management during a meta-analysis.

For data extraction from images, authors can use Engauge digitizer (Link, https://markummitchell.github.io/engauge-digitizer/) effectively and reliably. Image from an article can either be directly imported or through Microsoft Paint and need to be 'pasted as new image' to this
software. Using ‘axis point’ and curve point’ tools, one can define the graph axis and data set points of an image imported, respectively. The numerical data obtained are 'export'ed and to be saved as ‘.CSV’ files. Other softwares include WebPlotDigitizer (Link, https://automeris.io/WebPlotDigitizer/) or Plot Digitizer (Link, https://sourceforge.net/projects/plotdigitizer/files/), which have similar function. OriginPro (Link, https://www.originlab.com/) will be useful if data are in complex formats such as 2D-image or in embedded matrix sheets. Though RevMan can be used for sensitivity analysis, meta-regression necessitates a different software. The funnel plot asymmetry evaluation and derivation of Egger’s or Omnibus P-values can be easily derived from JASP (Link, https://jasp-stats.org/2017/11/15/meta-analysis-jasp/). The ‘.CSV’ data file specifically containing 'study name', 'estimate' and 'standard error' (SE) are exported from RevMan, and meta-regression factors/covariates are to be entered for each study. ‘Coefficients’, which depict the magnitude of effect from each factor/covariate on the studied outcome, ‘Omnibus’ and ‘Egger’s P-values are important outputs of this software. In addition to the images of forest and funnel plots, the ‘File-Drawer Analysis’, ‘radial’ and ‘normal Q-Q plot’s, are additional advantages of JASP. Meta-regressions are also possible in an Open-meta[analyst] (Link, http://www.cebm.brown.edu/openmeta/) with similar outcomes. Meta-correlations can be done with MedCalc (Link, https://www.medcalc.org/download.php) software, simply by entering 'study', 'sample size', and 'coefficient’ values. A forest plot with both random and mixed effect effect-estimates are depicted.

Recently, Trial Sequential Analysis (TSA, Link, https://ctu.dk/tsa/) software gained popularity for checking the power and sample sizes for each predefined meta-analytical outcome. A common question for a researcher is: ‘How many studies do I need to conduct a meta-analysis?’ Since there is no minimum limit on trials to be included for a meta-analysis, the total sample population for meta-analysis gains importance. TSA software program helps to calculate the required sample size.
information. However, one needs to operate it on a trial and error basis as non-availability of the help files (video or text forms) anywhere. The exported '.CSV' files from RevMan, needs to be converted to '.TSA' files prior to data entry in TSA. After performing sequential analysis and performing calculations, the display necessary graph with the required sample size displayed at the right upper corner. Researchers need to check whether the cumulative Z-curve surpasses the traditional or TS monitoring boundaries for statistical significance, to obtain sample size information. A short tutorial has been produced (Supplemental Video File 1A-D.mov) which may help the researcher in better understanding the previously mentioned few auxiliary software. Rarely, when multiple treatments are compared simultaneously in a single analysis, one needs to perform a network meta-analysis. A useful software program (Link, https://crsu.shinyapps.io/MetaInsight/) for undertaking network meta-analysis is ‘MetaInsight’. Further, Cochrane ‘Comparing Multiple Intervention Methods Group’ compiled a suite of online materials and software tools for conducting network meta-analysis is available in the link, https://training.cochrane.org/resource/network-meta-analysis-nma-toolkit, as a network meta-analysis tool kit.

Online tools are often required, that help in the measurements of collected data. Simultaneous to Cochrane calculators, data synthesis, and conversions of measures of dispersion, one may need alternatives for assorted analysis. For a pooled data conversion, statsdo.com (Link, https://www.statstodo.com/CombineMeansSDs_Pgm.php11) often found as user-friendly. In the A to Z 'Index(subject) link' of home menu bar, necessary 'program' tab can be identified. For example, conversion of data into a pooled data, one needs to search on the 'C' index (C for Conversion). Bookdown.org (Link, https://bookdown.org/MathiasHarrer/Doing_Meta_Analysis_in_R/power-calculator-tool.html) has a good power calculator available for meta-analysis. With effect size mentioned as standardized mean difference, a power plot is displayed once the number of studies and
participants are entered in the calculator. Practical-meta-analysis-effect-size-calculator (Link, https://campbellcollaboration.org/escalc/html/EffectSizeCalculator-OR-main.php) is a comprehensible tool. GRADEpro (Link, https://gradepro.org/) is used provide GRADE evidence. A Microsoft Publisher is of considerable help to combine images or adjust the large tables (such as a table of study characteristics) and conversion of files to a different format such as .pdf, as per the author’s desire. In the end, one can choose Adobe Illustrator CC (Link, https://www.adobe.com/in/products/illustrator.html) for converting the images into high-resolution publication quality.

The Korean Journal of Anesthesiology is currently publishing a special issue devoted to the topic of ‘Systematic review and Meta-Analysis’. This special issue will feature applications of systematic reviews and meta-analyses that will show evidence-based knowledge that will contribute significantly to the field of anesthesiology. We believe such contextual thinking by the editorial team definitely helps the readers to crack their research visions into a reality. Using as examples the meta-analyses published in previous issues of high impact factor anesthesia journals, prospective researchers can answer their similar study goals. User help-guides in Cochrane articles and RevMan teach us meta-analysis methodologies from the scratch. To complete the task, however, knowledge of auxiliary software is unequivocally essential. Self-learning of above-mentioned software tools are not only easy and interesting but also vital for academic anesthesia teaching faculty.
Reference


Video legends

Supplemental Video File 1A.mov: Tutorial on software for data extraction using Engauge Digitizer.
Supplemental Video File 1B.mov: Tutorial on software for meta-regression analysis using JASP.
Supplemental Video File 1C.mov: Tutorial on software for meta-correlation analysis using MedCalc.
Supplemental Video File 1D.mov: Tutorial on software for performing Trial Sequential Analysis using TSA. The exported .CSV files from RevMan, need to be converted to .TSA files prior to data entry in TSA. This can be achieved using 'Review Manager' of 'RM5 converter' at the menu bar of TSA. These .TSA files, later, directly can be imported to begin the analysis. After effect measure and model are entered, the 'Trial' tab is used for editing risk of bias of included studies. The ‘TSA’ tab has to be used to ‘Add’ and ‘Edit’ the information of conventional and alpha-spending boundaries. The 'conventional test boundary' once selected, the dialog box opens for the name of boundary to be entered (author's choice) along with chosen alpha-error. The more important 'alpha-spending boundaries' is to be selected for sample size information and additional steps are necessary. ‘In the 'Information axis' section, clicking on 'sample size', and in the 'Required Information Size' section, the buttons for 'estimate', 'empirical' and ‘Model variance based' options are essential selections. The model is ready to estimate sample size when researcher clicks on 'Add' button, displayed at the bottom of window. At all levels, the alpha and beta-spending function of O'Brien-Fleming is opted. In the final step, clicking the
'Perform calculation’ button is essential to obtain the TSA graph; subsequent selection of ‘Graph’s’ tab, will display the necessary graph with required sample size displayed at the right upper corner.