

Meta-analysis: the method of systematic review

- Very difficult. It requires very sophisticated manner of statistical thinking. You must pay substantial effort to learn. In this lecture, just a overview is given.
- The recommendable textbook (in Japanese) “メタアナリシス入門:エビデンスの統合を目指す統計手法” (Introduction to meta-analysis: the statistical technique to integrate various evidences), written by Dr. Toshiro Tango, Asakura-Shoten Pub., 2002.

Definition and history

- What “meta” means?
 - Something occurring later, more comprehensive, and is often used to name a new but related discipline designated to deal critically with the original one. (Egger et al., 1997)
- A statistical analysis to integrate the results of various previous studies found by systematic review. It should fulfill PRISMA statement [<http://www.prisma-statement.org/>]
 - Using academic literature database such as PubMed, Google Scholar and Web of Science, systematic keywords search enables to find the all appropriate papers.
 - By setting rigid inclusion and exclusion criteria, select all appropriate papers to get them in hand.
 - Read carefully all those papers, extract the data based on common criteria (all those processes have to be clearly described)
 - Conduct meta-analysis (such as forest plot, common odds ratio, funnel plot, ...) for the data, and find the common feature over all those studies (evaluation of heterogeneity is also needed)
- The trials to integrate or summarize the previously conducted studies are not new.
 - Sir Wright (1896) developed a new vaccine against typhoid fever and tested the effectiveness of the same vaccine in several different groups.
 - Karl Pearson (1904) re-evaluated the effectiveness of that vaccine ever used.

Karl Pearson's calculation

- Data: <http://minato.sip21c.org/Pearson1.txt>

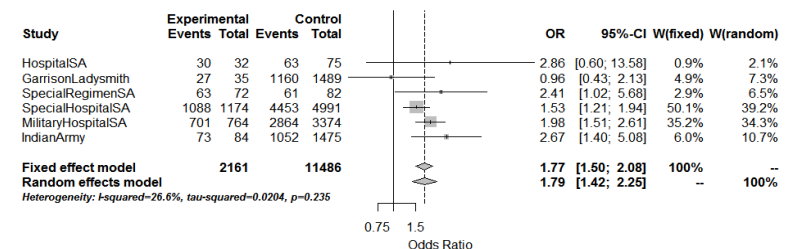
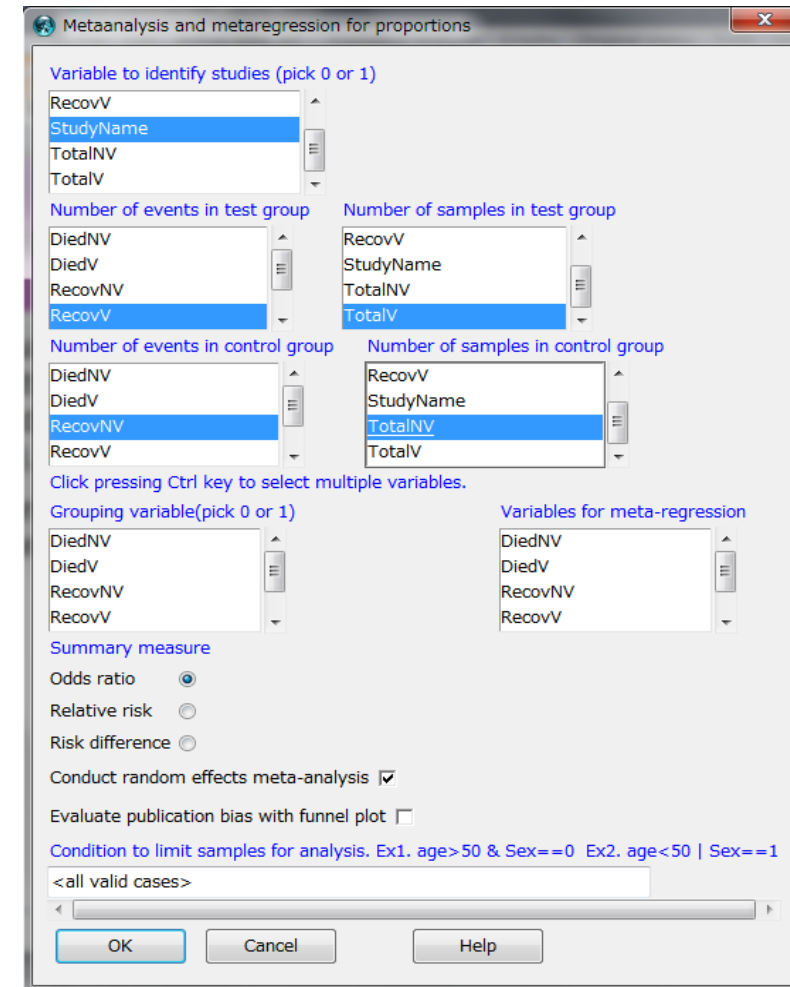
StudyName	RecovV	DiedV	TotalV	RecovNV	DiedNV	TotalNV
HospitalSA	30	2	32	63	12	75
GarrisonLadysmith	27	8	35	1160	329	1489
SpecialRegimenSA	63	9	72	61	21	82
SpecialHospitalSA	1088	86	1174	4453	538	4991
MilitaryHospitalSA	701	63	764	2864	510	3374
IndianArmy	73	11	84	1052	423	1475

- Calculate the tetrachoric correlation coefficients for each study (cf. <http://www.personality-project.org/r/psych/R/tetrachor.R> [File] -> [Load script file] -> select all and submit)
- `tetrachoric(matrix(c(30,2,63,12),2,2))` gives 0.307
- Taking mean of 6 studies by `mean(c(0.307,-0.010,0.300,0.119,0.194,0.248))` gives 0.193
Pearson concluded “The effects is too small to recommend the vaccine”.

Using Odds Ratios for meta-analysis

- Each result can also be evaluated using odds ratio. For example, $(30/2)/(63/12)$ gives 2.86. It means vaccination raised the viability 2.86 times at the first study. Using `fisher.test(matrix(c(30,2,63,12),2,2))`, the odds ratio is 2.83.
- [Statistical analysis], [Metaanalysis and metaregression], [Metaanalysis and metaregression for proportions]
- Estimated combined odds ratio is 1.77 in fixed effect model and 1.79 in random effect model (both statistically significant at 5% level). “No heterogeneity” is not rejected ($p=0.235$).

- Forest plot is very convenient to see.



Meta-analysis for covid-19

- <http://dx.doi.org/10.1136/bmjopen-2020-039652>
- Using metafor package of R, estimating the latent period of covid-19 from 2 parameters of log-normal distribution.
- The method is implemented as Shiny application <https://mcaloon-ucd.shinyapps.io/shiny2/>
- [https://doi.org/10.1016/S0140-6736\(20\)31142-9](https://doi.org/10.1016/S0140-6736(20)31142-9)