R practice: Meta-analysis (2)

Minato Nakazawa

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1 History - cntd.

As agricultural studies developed, some classic statistic textbooks started to include the explanation about statistical methods to integrate the results of several independent studies. For instance, Tippet's (1931) "The Methods of Staitstics" and Fisher's (1932) "Statistical Methods for Research Workers" gave such explanations.

1.1 Trials to integrate the results of the effects of treatment

The first study to integrate the results of the effects of treatment was done by Beecher (1955) about the effect of placebo (Table 1.2). In mid-20th century, placebos were administered to patients for various purposes (typically reducing various symptoms like pain after surgery, headache, and others).

Table 1.2 Therapeutic effectiveness of placebos in several conditions.

Cond.	Study	Placebo agent	route	No. patients	% relieved
SPOWP	Keats AS, Beecher HK (1950) J. Pharmacol & Exper. Therap., 100: 1-13.	saline	iv	118	21
SPOWP	Beecher HK et al. (1951) U.S. Armed Forces M.J., 2: 1269-76.	saline	sc	29	31
SPOWP	Keats AS et al. (1951) JAMA, 1761-3.	saline	iv	34	26
SPOWP	Beecher HK et al. (1953) J. Pharmacol & Exper. Therap., 109: 393-400.	lactose	oral	52 36 44 40	40 26 34 32
SPOWP	Lasagna L et al. (1954) Am J Med, 16: 770-9.	saline	sc	14 20 15 21 15 15	50 37 53 40 40 15
Cough	Gravenstein JS et al. (1954) J Appl Physiol, 7: 119-39.	lactose	oral	22 23	36 43
DIMC	Lasagna L et al. (1955) JAMA, 157: 1006-20.	saline	sc	20 (normal) 30 (post-addicts)	30 30
PFAP	Evans W, Hoyle C (1933) Quart J Med, 2: 311-38.	Na_2CO_3	oral	66	38
PFAP	Travell J et al. (1949) Ann NY Acad Sci USA, 52: 345-53.	"placebo"	oral	19	26
PFAP	Greiner T et al. (1950) Am J Med, 9: 143-55.	lactose	oral	27	38
Headache	Jellinek (1946)	lactose	oral	199	52
Seasickness	Gay and Carliner (1949)	lactose	oral	33	58
AT	Wolf S, Pinsky RH (1954) JAMA, 155: 339-41.	lactose	oral	31	30
Exp. cough	Hillis (1952)	saline	sc	1 (many exp.)	37
Cold	Diehl HS (1933) JAMA, 191: 2042-9.	lactose	oral	110 (acute) 48 (subacute)	35 35
			Summary	1,082 (total)	35.2 ± 2.2% (ave±se)

SPOWP: severe post-operative wound pain; DIMC: drug-induced mood changes; PFAP: pain from angina pectoris; AT: anxiety and tension

Beecher **randomly** picked up 15 clinical trials and calculated the mean and standard error of the proportions of patients who gained satisfactory results. The result was $35.2 \pm 2.2\%$ patients gained satisfactory results by placebo. The title of his paper was **"The Powerful Placebo"**[*1].

The calculation of mean and standard error by R is as follows. I (Minato Nakazawa) think that the mean should be weighed by the number of samples, but the auhtor applied simple mean.

```
NoPat <- c(118, 29, 34, 52, 36, 44, 40, 14, 20, 15, 21, 15, 15, 22, 23, 20, 30,
 66, 19, 27, 199, 33, 31, 1, 110, 48)
Satisf <- c(21, 31, 26, 40, 26, 34, 32, 50, 37, 53, 40, 40, 15, 36, 43, 30, 30,
 38, 26, 38, 52, 58, 30, 37, 35, 35)
Satisf2 <- c(21, 31, 26, 33, 39, 40, 30, 30, 38, 26, 38, 52, 58, 30, 37, 35, 35)
sum(NoPat)
sum(NoPat*Satisf)/sum(NoPat)
mean(Satisf)
sd(Satisf)/sqrt(length(Satisf))
mean(Satisf2)
sd(Satisf2)/sqrt(length(Satisf2))
```

However, the invention of the word "meta-analysis" and enthusiastic studies about its methodology were done in social scientific fields, amongst education studies. In the field of education studies, there were many methods of education with enourmous papers. Reviewing them for summary tended to be subjective and biased, because the selection and evaluation largely depended on the specialty and interest of the reviewer.

The word "meta-analysis" was first used by Glass (1976) who was psychologist. As the milestone book in the social science fields, Cooper and Hedges (1994) published "The Handbook of Research Synthesis".

Introduction of meta-analysis into the clinical trial was done by Richard Peto, one of the famous British statistician. It is very famous that Yusuf et al. (1985) applied the Peto's design to secondary preventive effect of beta blocker against heartattack.

Table 1.3 shows the result of meta-analysis of 15 RCTs about the preventive effect (reduction of mortality) of long-term administration of beta-blocker by Peto's method. In R, it may be supported by `metafor` package.

[*1] Beecher HK (1955) The powerful placebo. JAMA, 159(17): 1602-6.