



JOHNS HOPKINS
BLOOMBERG
SCHOOL of PUBLIC HEALTH

Department of Epidemiology
Johns Hopkins Bloomberg School of Public Health
415 N. Washington Street, 2nd Floor
Baltimore, Maryland 21231

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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: Clinical trials versus meta-analyses

The title reminds me of Ford v Ferrari, the movie, set around the 24-hour Le Mans in France in 1966. Ford won the race, but car racing for me is like watching paint dry with noise.

Meta-analysis defined by Last (4th edition; 2001 **Dictionary of Epidemiology**) as *The statistical synthesis of the data from separate but similar, i.e. comparable studies, leading to a quantitative summary of the pooled results.* Distinct from systematic review, defined by Last as *The application of strategies that limit bias in the assembly, critical appraisal, and synthesis of all relevant studies on a specific topic. Meta-analysis may be, but is not necessarily, used as part of this process.*

The term *meta-analysis* was coined by Gene Glass in his presidential address to the American Educational Research Association in 1976 to denote statistical synthesis of results of similar studies. “*My subject is data analysis at three levels. **Primary analysis** is the original analysis of data in a research study. It is what one typically imagines as the application of statistical methods. **Secondary analysis** is the re-analysis of data for the purpose of answering the original research question with better statistical techniques, or answering new questions with old data. . . . My major interest currently is in what we have come to call . . . meta-analysis of research. . . . **Meta-analysis** refers to the analysis of analyses. I use it to refer to the statistical analysis of a large collection of analysis results from individual studies for the purpose of integrating the findings.*”

The term was new, but not the concept. Karl Pearson (BMJ, 1904) published a “meta analysis” in his “Report on certain enteric fever inoculation statistics”. RA Fisher, during his work at the Agricultural Research Station in Rothamstead, performed numerous “meta-analyses” of results from like experiments. In his 1935 textbook, he gives examples of combined analysis of like agriculture studies to identify the real and probable fertilizer effects.

The term was introduced as a publication type in Medline in 1993; denoted in the table below as [MA]. Counts are for full length publications indexed in Medline from 2000 through 2019.

The publication type [MA] was the fastest growing category among the three, increasing from 0.29% of publications in 2000 to 2.30% in 2019 compared to modest decreases in percentages of publications indexed to [CT] and [RZT] over the same time period.

Year	PubMed Pubs	[CT]	[RZT]	[MA]	% [CT]	%[RZT]	%[MA]
2000	258,817	19,883	10,108	757	7.68%	3.91%	0.29%
2001	268,714	19,302	10,988	859	7.18%	4.09%	0.32%
2002	279,446	19,917	11,271	998	7.13%	4.03%	0.36%
2003	296,439	22,714	12,289	1,194	7.66%	4.15%	0.40%
2004	316,787	25,274	13,857	1,504	7.98%	4.37%	0.47%
2005	347,513	27,616	14,835	1,995	7.95%	4.27%	0.57%
2006	373,737	26,773	15,630	2,319	7.16%	4.18%	0.62%
2007	397,608	27,829	17,226	2,615	7.00%	4.33%	0.66%
2008	422,424	27,775	17,873	2,910	6.58%	4.23%	0.69%
2009	446,295	28,399	18,893	3,451	6.36%	4.23%	0.77%
2010	482,894	30,346	20,658	4,319	6.28%	4.28%	0.89%
2011	525,894	34,398	23,297	5,608	6.54%	4.43%	1.07%
2012	557,456	37,494	25,173	7,432	6.73%	4.52%	1.33%
2013	587,666	40,460	27,489	9,207	6.88%	4.68%	1.57%
2014	607,644	39,923	27,898	10,821	6.57%	4.59%	1.78%
2015	624,055	38,442	27,642	12,110	6.16%	4.43%	1.94%
2016	634,157	36,200	26,761	12,732	5.71%	4.22%	2.01%
2017	643,544	35,891	26,784	13,507	5.58%	4.16%	2.10%
2018	658,029	35,457	26,049	14,383	5.39%	3.96%	2.19%
2019	649,669	33,810	24,461	14,943	5.20%	3.77%	2.30%
	9,378,788	607,903	399,182	123,664	6.48%	4.26%	1.32%