
How original should “original research” be?

The trajectory of COMET

Doug Altman

*Centre for Statistics in Medicine
University of Oxford*





“The purpose of the **original research** is to produce new knowledge”

[Wikipedia]

TABLE OF CONTENTS.

ORIGINAL PAPERS.

REMARKS on Angina Pectoris. By John Warren, M. D.	-	1
SOME Remarks on the morbid effects of Dentition. By James Jackson, M. D.	- - - - -	12, 113, 329
ACCOUNT of Bichat	- - - - -	26
CASES of apoplexy, with dissections. By John C. Warren, M. D.	34,	154
A concise view of the results of Dr. Davy's late electro-chemical researches	- - - - -	42, 130, 217, 364
OBSERVATIONS and experiments on the treatment of injuries occasioned by fire. By Jacob Bigelow, M. D.	- - - - -	52
REMARKS on Diseases resembling syphilis. By Walter Channing, M. D.		65, 139, 245, 377
CASE and dissection of a blue female child. In a letter from John H. Dorsey, M. D. of Philadelphia	- - - - -	69

Original research

- **It's *new* research**
 - It doesn't have to mean that nobody did exactly the same before
- **It does not have to use novel methods**
 - Many aspects of design and analysis are widespread
- **It does not have to collect novel data**
 - e.g. new outcome measurements; new way of grouping data values; different time points

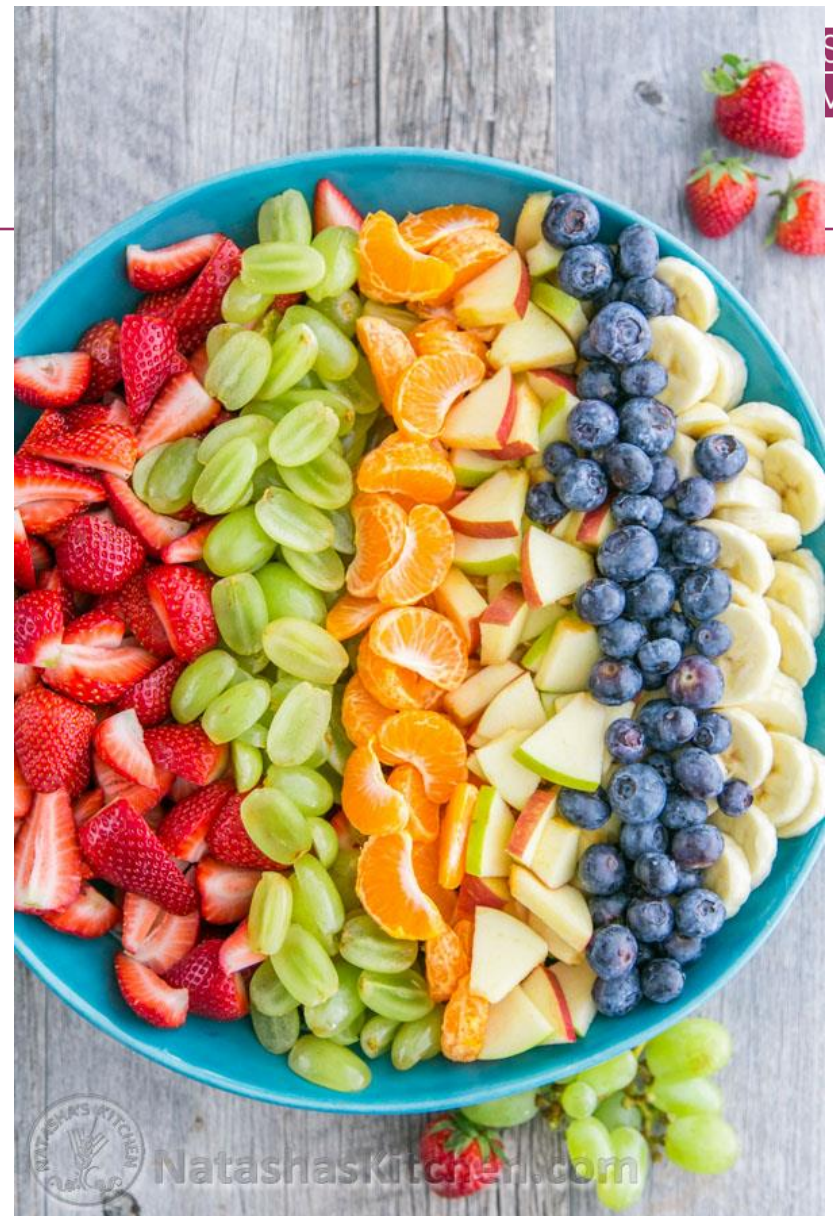
Clinical heterogeneity (PICO)



“This question of lumping versus splitting is difficult to answer objectively for clinical heterogeneity ... different reviewers, readers, and clinicians may disagree on the (dis)similarity of interventions, **outcomes, designs, participant characteristics, and settings.”**

[Ioannidis *et al*, *BMJ* 2008]





Trials in schizophrenia



10000 RCTs of schizophrenia (Miyar and Adams 2012)

- 1940 different interventions
- 2194 different instruments
 - every 5th trial introduced a new rating scale
- 1142 scales used only once
 - Most common: 36% used Brief Psychiatric Rating Scale

“Trials were more likely to report that a treatment was superior to control when an unpublished scale was used to make the comparison (RR 1.94; 95% CI 1.35 to 2.79)”

[Marshall et al., *Br J Psychiatry* 2000]

Problems with outcomes

How to measure an outcome?

- the specific measurement variable (eg, Beck Depression Inventory score, all cause mortality);
- the participant-level analysis metric (eg, change from baseline, final value, time to event);
- the method of aggregation (eg, mean, proportion with score > p);
- the specific measurement time point

Which outcomes to measure ?

- Variation hampers systematic reviews

Conclusions

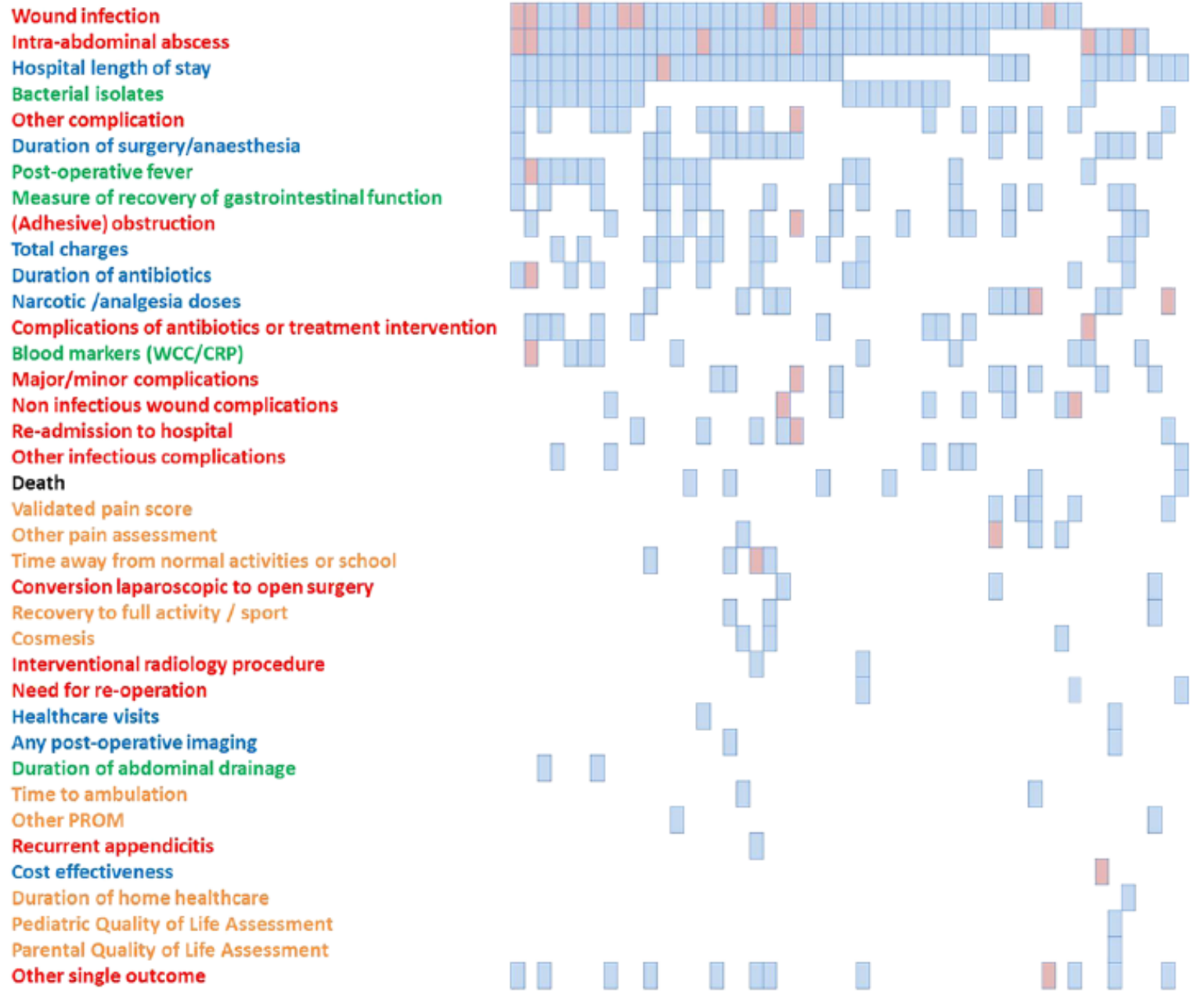
There is a wide heterogeneity in the selection and definition of outcomes in RCTs and SRs of paediatric appendicitis with little overlap in outcomes used across studies. A paucity of studies report patient relevant outcomes within the 'Life Impact' core area. These factors impair meaningful evidence synthesis and pose challenges to those designing prospective clinical trials and cohort studies. The commitment to develop a COS for paediatric appendicitis is justified.

Intravenous and nebulised magnesium for treating asthma

	function	admission	pressure	score	score	potassium/ magnesium	frequency or rate	length of hospital stay	rate
Dadhich, 2003 [17]	X	X	X	X	X	X	X	X	X
Santana, 2001 [18] (children)	X	X	o	X	X	✓	✓	✓	✓
Bijani, 2002 [22] (adults)	✓	X	X	X	X	X	X	X	X
Bessmertny, 2002 [21] (adults)	✓	X	o	X	X	o	o	X	o
Gurkan, 1999 [24] (children)	✓	X	o	X	X	X	X	X	o
Devi, 1997 [23] (children)	✓	X	X	X	X	X	X	X	✓
Tiffany, 1993 [26] (adults)	✓	X	X	X	X	✓	X	X	X
Meral, 1996 [25] (children)	✓	X	o	X	✓	X	o	X	o
Boonyavorakul, 2000 [19] (adults)	X	✓	X	✓	X	X	X	X	X
Scarfone, 2000 [20] (children)	X	✓	X	X	X	X	X	X	X

- ✓ indicates full reporting of results for treatment comparison of interest
- X indicates no reporting
- o indicates partial reporting (i.e. only the *p-value* is given for the comparison)

**Hall et al,
Trials 2015**



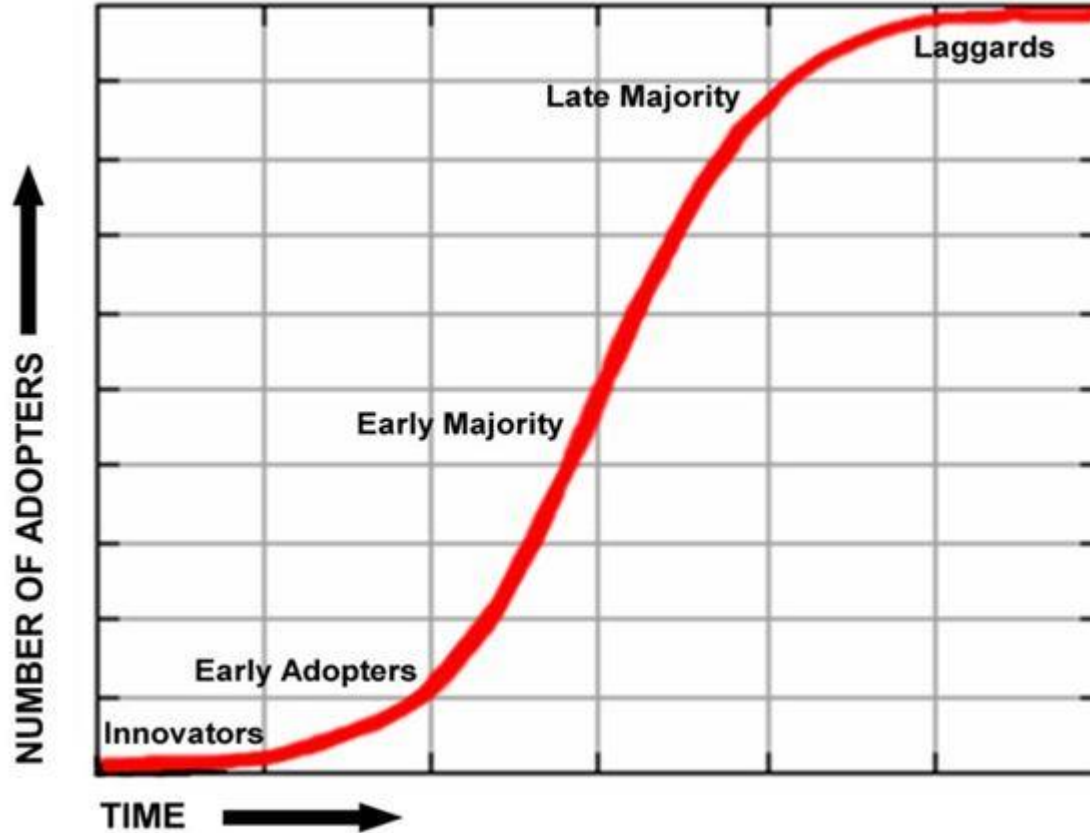
■ signifies included as a primary outcome ■ signifies included as a secondary outcome



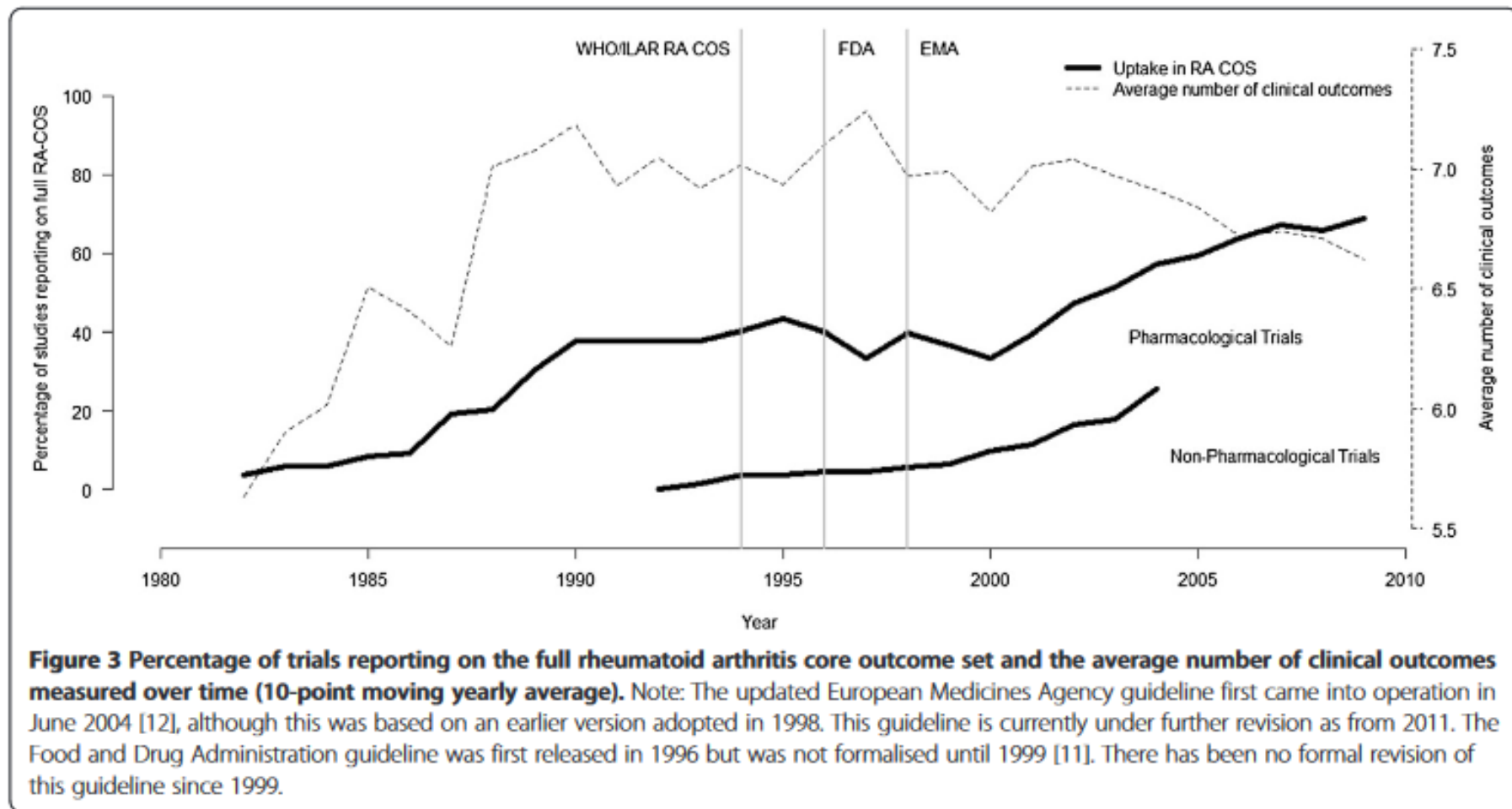
-
- **We need more Core Outcome Sets**
 - **We need (much) more uptake of COS in trial protocols**

Rogers' S curve

(Diffusion of innovations)

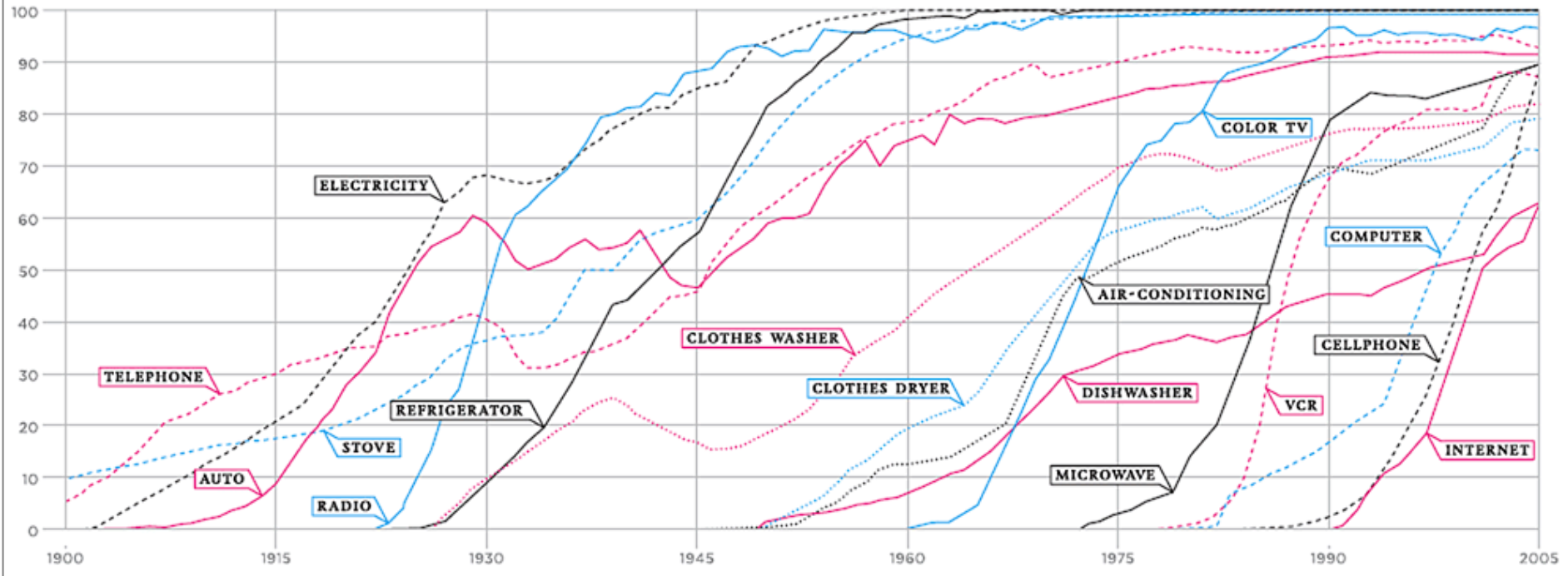


Rheumatoid Arthritis COS

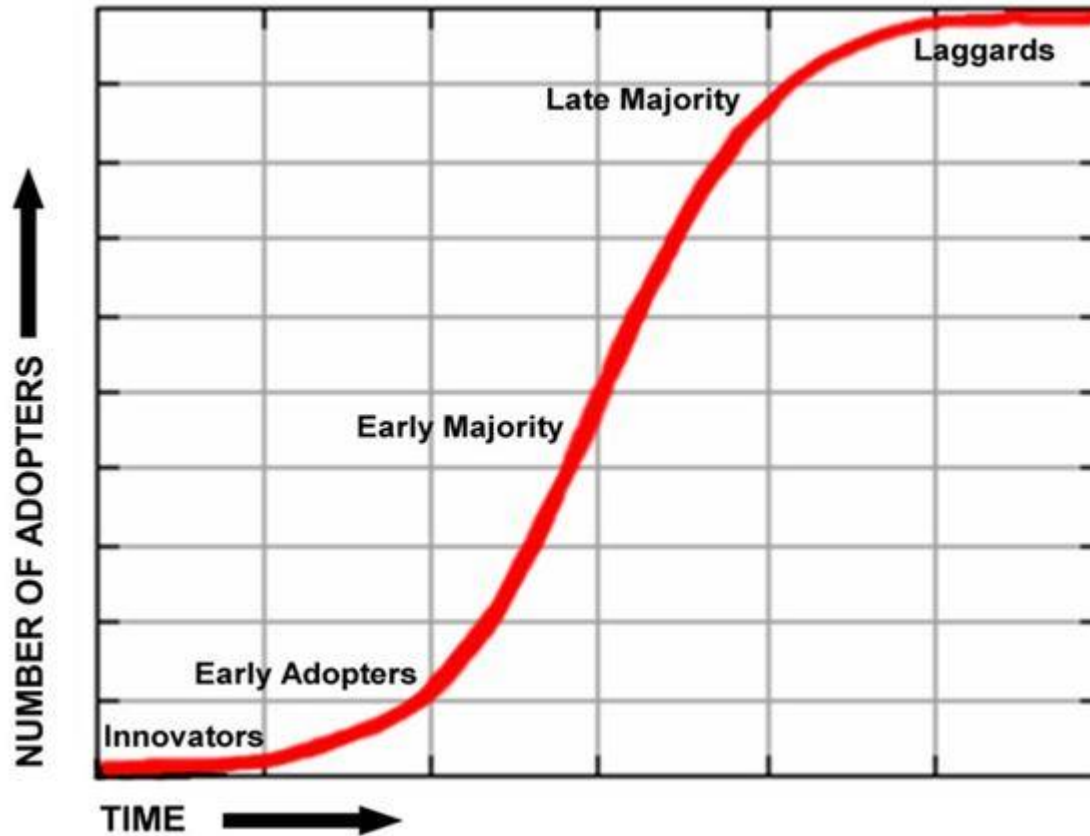


PERCENT OF
U.S. HOUSEHOLDS

CONSUMPTION SPREADS FASTER TODAY



Rogers' S curve



Where is COMET?

Google

"core outcome set"

Scholar

About 762 results (0.09 sec)

Resuscitation 88 (2015) 150–157



ELSEVIER

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation



Review article

A systematic review of the outcomes reported in cardiac arrest clinical trials: The need for a core outcome set[☆]

L. Whitehead^{a,b}, G.D. Perkins^{a,b}, A. Clarey^c, K.L. Haywood^{d,*}



How original should “original research” be?

Trials should build on what’s already been done

It’s not the place to be too novel

Use a Core Outcome Set if it exists

Too much originality won’t help patients



“In the early days of meta-analysis (at least in its current incarnation) Robert Rosenthal was asked if it makes sense to perform a meta-analysis, given that the studies differ in various ways, and the analysis amounts to combining apples and oranges. Rosenthal answered that combining apples and oranges makes sense if your goal is to produce a fruit salad.”

[Borenstein et al. *Introduction to meta-analysis* 2009]

Table 1 | Example of a review outcome matrix displaying the information available in trial reports

Trial ID (author, year of publication)	Review primary outcome	Other review outcomes		Additional outcomes (reported in any of the eligible trials)		
		Chemical pregnancy rate	Clinical pregnancy rate	Ectopic pregnancy rate	Birth weight of baby	Reason for exclusion
12345678.1 (Smith, 1999)	o	x	v	x	x	—
12345678.2 (Lowe, 2001)	v	o	x	v	x	—
12345678.3 (Biggs, 2004)	x	v	v	x	v	—
...						
Excluded trials						
1234578.9 (Johns, 2006)	x	x	x	x	x	No relevant outcome data
...						

v Full reporting of results for treatment comparison of interest.

x No reporting of results for treatment comparison of interest.

o Partial reporting of results for treatment comparison of interest.