



**The Evidence-Based
Research Network**

Evidence-Based Research:

***Do researchers demonstrate knowledge of
earlier studies?***

Caroline Blaine

on behalf of

Karen Robinson

Johns Hopkins USA



Expert searching

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The death in June 2001 of Ellen Roche, a technician at Johns Hopkins Asthma and Allergy Center and healthy volunteer in an asthma study, had a significant impact on the medical research community far beyond the campus of Johns Hopkins University [1]. The role of literature searching as part of the development of research protocols and the subsequent internal review board reviews of these protocols became an important nationwide news story almost immediately. According to the Office for Human Research Protection (OHRP), published literature about the toxic effects of inhaling hexamethonium was readily available and should have been taken into account by the principal investigator, who decided to allow Roche to inhale the chemical that was responsible for causing her death.

News of this fatal incident created an immediate discussion among health sciences librarians around the world. Many are convinced that the inclusion of an expert searcher in the development of the research protocol at Johns Hopkins would have brought the appropriate literature to the attention of the investigators on this asthma study and may have prevented the death of the research subject.

Objective

To assess the extent of the use of prior research by measuring the citation of prior related trials in reports of randomised controlled trials (RCTs).

Specifically, do reports of RCTs cite prior similar trials?

Methods

Briefly:

1. Created groups of RCTs addressing the same question
2. Determined if RCTs in same group cite each other

Methods

For each RCT, we calculated:

Prior Research Citation Index (PRCI)

Number of RCTs cited

Total number of potential RCTs to cite

Sample Size Citation Index (SSCI)

Total number of participants in cited RCTs

Total number of participants in potential RCTs to cite

Prior Research Citation Index

Median PRCI 0.21

(95% CI 0.2 to 0.25, Mean =0.29, n=1,523 RCTs)

Publication Date	Number of RCTs	Median PRCI
2 years or earlier	1,314	0.21
5 years or earlier	747	0.11
10 years or earlier	311	0.04

PRCI = Number of RCTs cited / Total number of potential RCTs to cite

- About 80% of prior studies about the same question were NOT cited in reports of RCTs
 - About half of the RCTs cited zero or one prior trial
- Information from 76% of participants enrolled in prior trials not acknowledged

A Systematic Examination of the Citation of Prior Research in Reports of Randomized, Controlled Trials

Karen A. Robinson, PhD, and Steven N. Goodman, MD, MHS, PhD

Background: started or preceding RCT that evidence of subsequent

Objective: trials study

The New York Times

5) cited no prior RCTs and number of prior cited trials number of citable trials including trials cited by trials published with 1.5 for those published


Trial in a Vacuum: Study of Studies Shows Few Citations


By GINA KOLATA

Published: January 17, 2011


Science, so the story goes, is a meticulously built edifice. Discoveries balance on ones that preceded them. Research is stimulated by studies that went on before.

But what, then, can explain the findings by two investigators at [Johns Hopkins University](#) School of Medicine? The researchers, Karen A. Robinson and Dr. Steven N. Goodman, looked at how often

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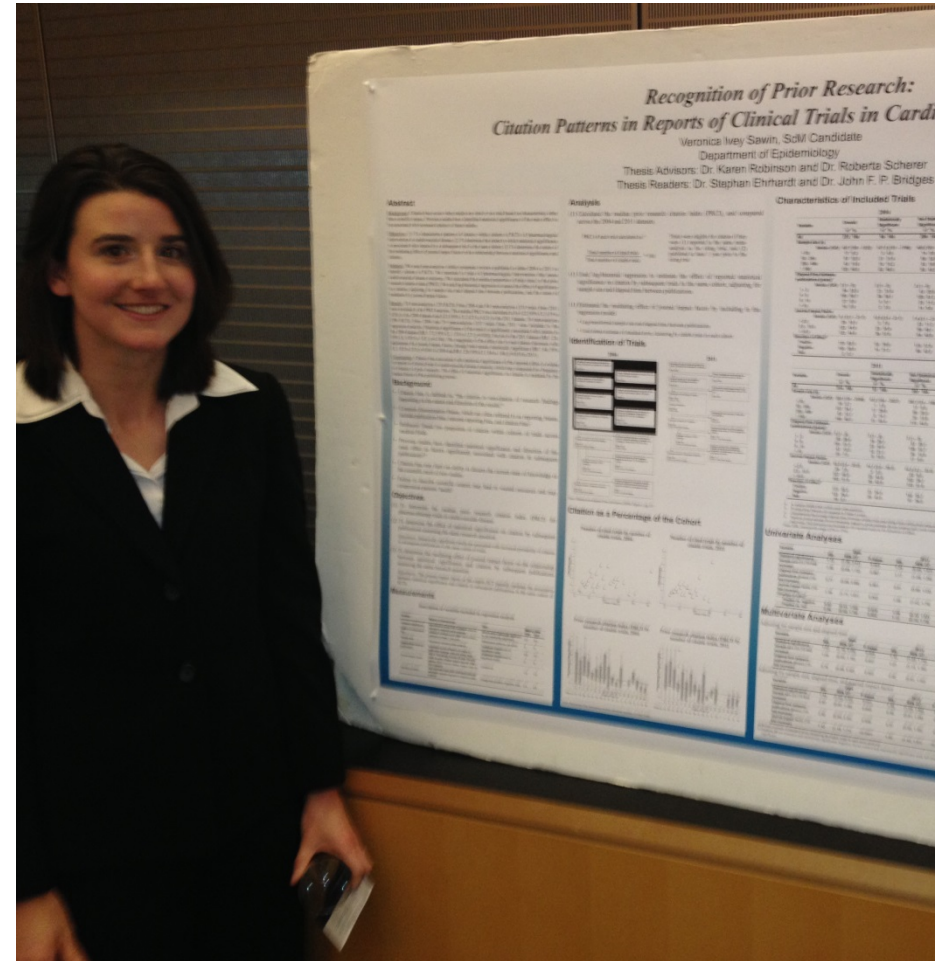
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 PRINT

 REPRINTS

Why and better now?

- Combined new search results (2011) with existing database
- Citation patterns in pharmacological CVD RCTs
- 86 meta-analyses with 580 trials



Sawin VI, Robinson KA. Biased and inadequate citation of prior research in reports of cardiovascular trials is a continuing source of waste in research. *J Clin Epidemiol.* 2016 Jan;69:174-8.

Results – Not better

Results in CVD:

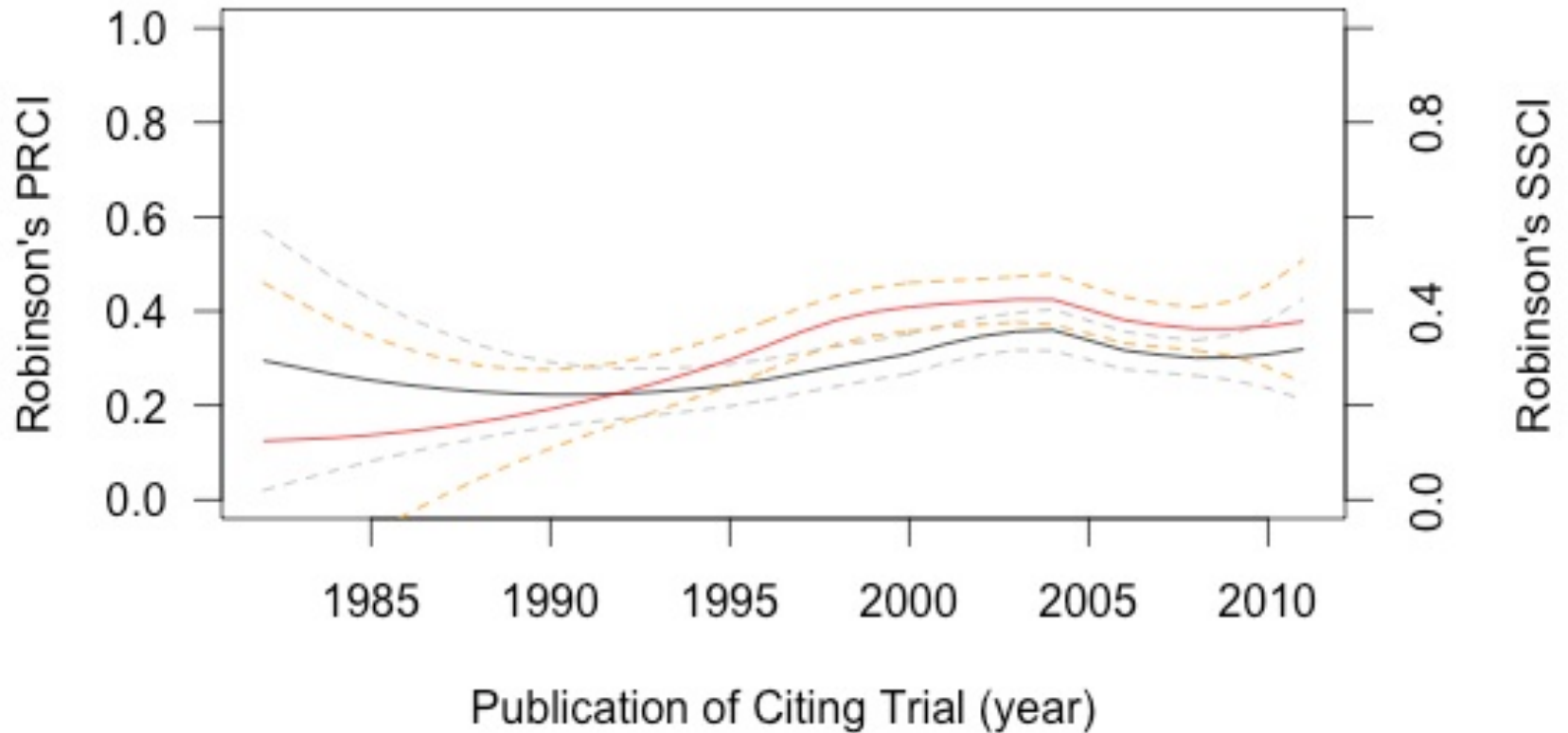
Median PRCI 0.25 (95% CI 0.23 to 0.27)

Median SSCI 0.31 (95% CI 0.25 to 0.36)

No difference between 2004 and 2011 datasets

Approximately 75% of prior trials ignored and only 30% of trial participants represented

Difference over time?



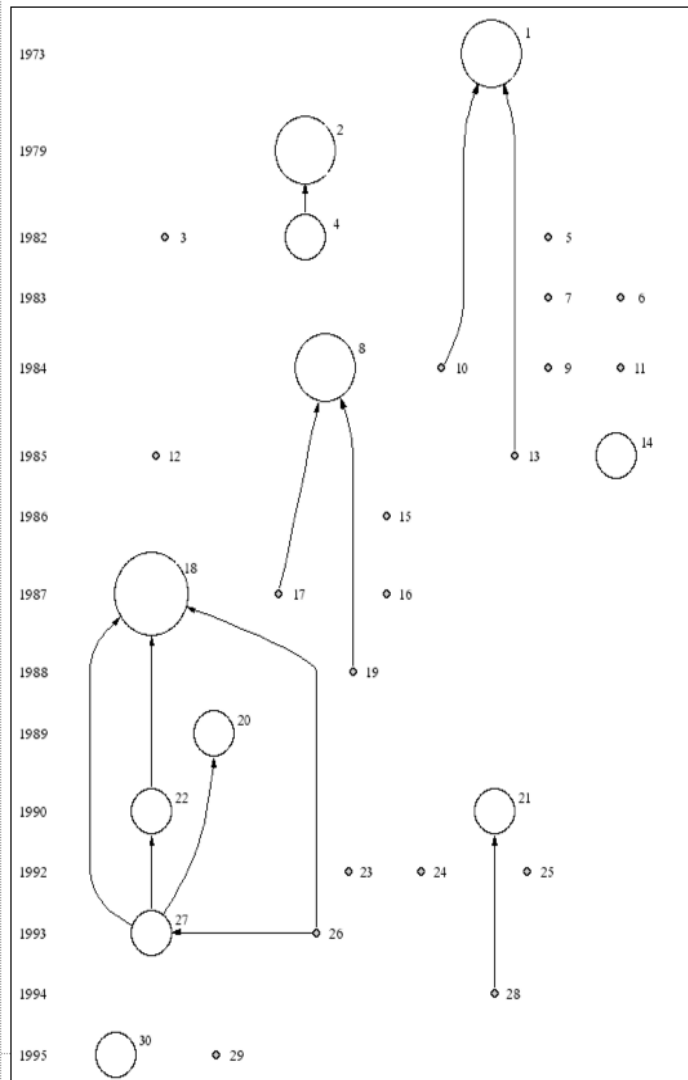
Black = PRCI Orange = SSCI

Supportive vs not?

Trials were about 45% more likely to be cited by subsequent trials if results supportive. [RR 1.45 (95% CI 1.303 to 1.612)]

Inadequate, and biased, consideration of prior research remains – implications include ethically unjustifiable trials, wasted research and unnecessary risk for trial participants.

Rich get Richer



If trial cited, 60% probability it will be cited again

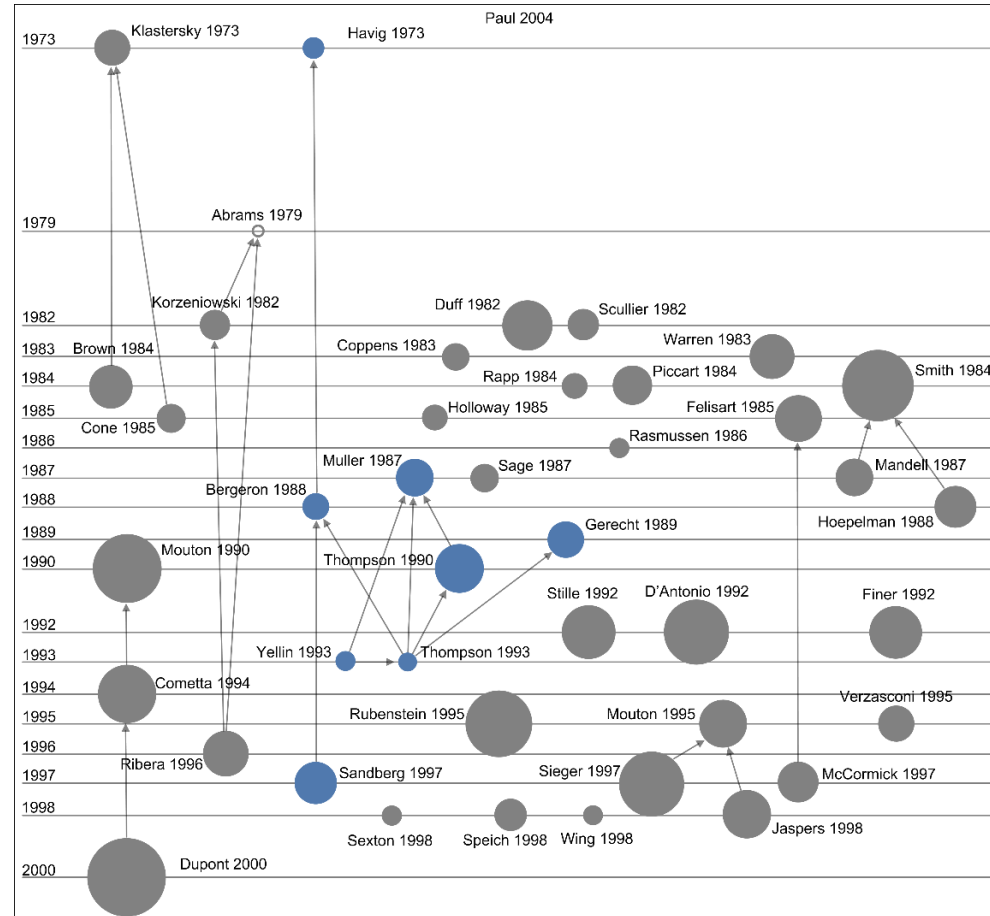
If trial NOT cited – more than 60% probability that it will remain uncited

*“No trial is an island, entire of itself;
every trial is a piece of the continent, a part of the
main.”*

- Clarke and Chalmers, 1998

54% of groups of studies
did not form a single
connected network:

- 39% two islands
- 4% 10 or more separate islands



Robinson KA, Dunn AG, Tsafnat G, Glasziou P. Citation networks of trials: Feasibility of iterative bidirectional citation searching. *Journal of Clinical Epidemiology* 2014;67(7):793-9.

All scientific work is incomplete...that does not confer upon us a freedom to ignore the knowledge we already have...

-Sir Austin Bradford Hill

Hill AB. The reasons for writing. BMJ. 1965;4:870



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