Agreement of treatment effects estimates from observational studies and RCTs evaluating therapeutics for COVID-19

Main takeaway

Meta-analyses of observational studies and RCTs evaluating the same treatments for COVID-19 more often than not have summary treatment effect estimates that are in agreement, both in terms of direction and statistical significance.

Take a picture to access our full paper **in** *BMJ*

What we found

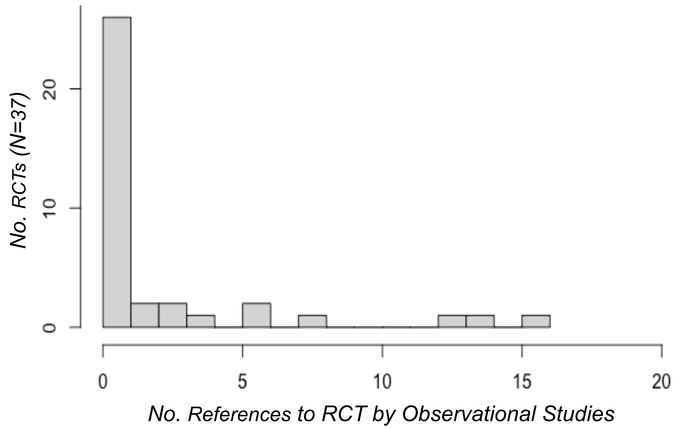
1 *21 of 27 (78%) pairs of observational studies and RCTs comparing **hydroxychloroquine, lopinavir-ritonavir**, or **dexamethasone** to an active or placebo comparator for any safety or efficacy outcomes of covid-19 had treatment effects in agreement*

Concordance between treatment effect estimates from matched observational study and RCT pairs, No=27 (pairs classified as concordant in green)				
Observational study treatment effect estimates	**RCT treatment effect estimates**			
	Increased, significantly	Decreased, significantly	Increased, but not significantly	Decreased, but not significantly
Matched pairs consisting of meta-analyses of obs. studies and meta-analyses of RCTs				
*Increased, significantly**	**0**	0	2	0
*Decreased, significantly**	0	**0**	0	0
Increased, but not significantly†	0	0	**4**	**2**
Decreased, but not significantly†	0	1	**5**	**3**
Additional matched pairs consisting of one observational study and/or one RCT				
*Increased, significantly**	**0**	0	0	1
*Decreased, significantly**	0	**0**	0	1
Increased, but not significantly†	1	0	**3**	**1**
Decreased, but not significantly†	0	0	**1**	**2**

*P<0.05.
†P ≥0.05.

- **Higher agreement** was noted in **meta-analyzed obs. studies and RCTs** (14/17 [82%] vs 7/10 [70.0%]).
- Matched obs. studies and RCTs **evaluating relative as opposed to continuous treatment effects also had higher agreement** (16/18 89% vs 5/9 (56%).

2 ***Observational studies** were **frequently referenced by matching RCTs** (39 of 46, 85%) evaluating the same interventions, comparators, and outcomes*



Distribution of RCTs referenced by individual observational studies

- **39 (85%) of the 46 individual observational studies were referenced by at least one RCT**
- 14 (38%) of the 37 individual RCTs were referenced by any observational study.

What is already known

- **RCTs** are generally **considered the gold standard** for studying clinical treatments, but have **substantial limitations**
- The **covid-19 pandemic** has **highlighted the potential role of observational studies**, although concerns have been raised about rapid dissemination of **low quality evidence**
- Little is known about the **agreement between** individual or meta-analyzed **observational studies and RCTs** evaluating the same covid-19 treatments, comparators, and outcomes

What we did

1. We identified individual RCTs or meta-analyses of RCTs from a *BMJ* living review[1], as well as **individual observational studies** from an Epistemonikos database evaluating the same interventions, comparisons, and outcomes

2. Treatment effect estimates from observational studies were identified, standardized, and meta-analyzed to match RCTs

3. The **direction and statistical significance of treatment effect estimates** from matched pairs was compared

4. Publication timing and protocol registration were compared

What does it mean

Meta-analyzed evidence from observational studies can complement, but should not replace, RCT evidence

Limitations:

- Only considered top three interventions evaluated for covid-19
- Most treatment effect estimates were null values
- Certain meta-analysis pairs had a low number of individual observational studies or RCTs included

[1]Siemieniuk RA. *BMJ*. 2020;370:m2980

Find me @osmanmoneer! Or…
1. at the symposium to discuss this paper
2. email: osman.moneer@yale.edu
3. web: www.osmanmoneer.com

Team

Presenter: Osman Moneer, Medical Student[1]

Co-authors: Garrison Daly[2], Joshua J. Skydel[3], Kate Nyhan[4, 5], Peter Lurie[2], Joseph S. Ross[6,7,8], Joshua D. Wallach[9]

[1]Yale School of Medicine. [2]Center for Science in the Public Interest. [3]Dartmouth-Hitchcock Medical Center. [4]Harvey Cushing/John Hay Whitney Medical Library, Yale University. [5]Department of Environmental Health Sciences, Yale School of Public Health.[6]Section of General Medicine and the National Clinician Scholars Program, Department of Internal Medicine, Yale School of Medicine. [7]Center for Outcomes Research and Evaluation, Yale-New Haven Health System. [8]Department of Health Policy and Management, Yale School of Public Health.[9]Department of Epidemiology, Rollins School of Public Health, Emory University