



RestoRes

Research integrity in biomedical research



NASEM PANEL

“SYSTEMATIC REVIEWS AND CORRECTIONS AND RETRACTIONS”

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Conflict of Interest Disclosure



Funded by European Union



institut
universitaire
de France



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ET DE LA SANTÉ

*Liberté
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Fraternité*



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ET DE L'INNOVATION

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anr®

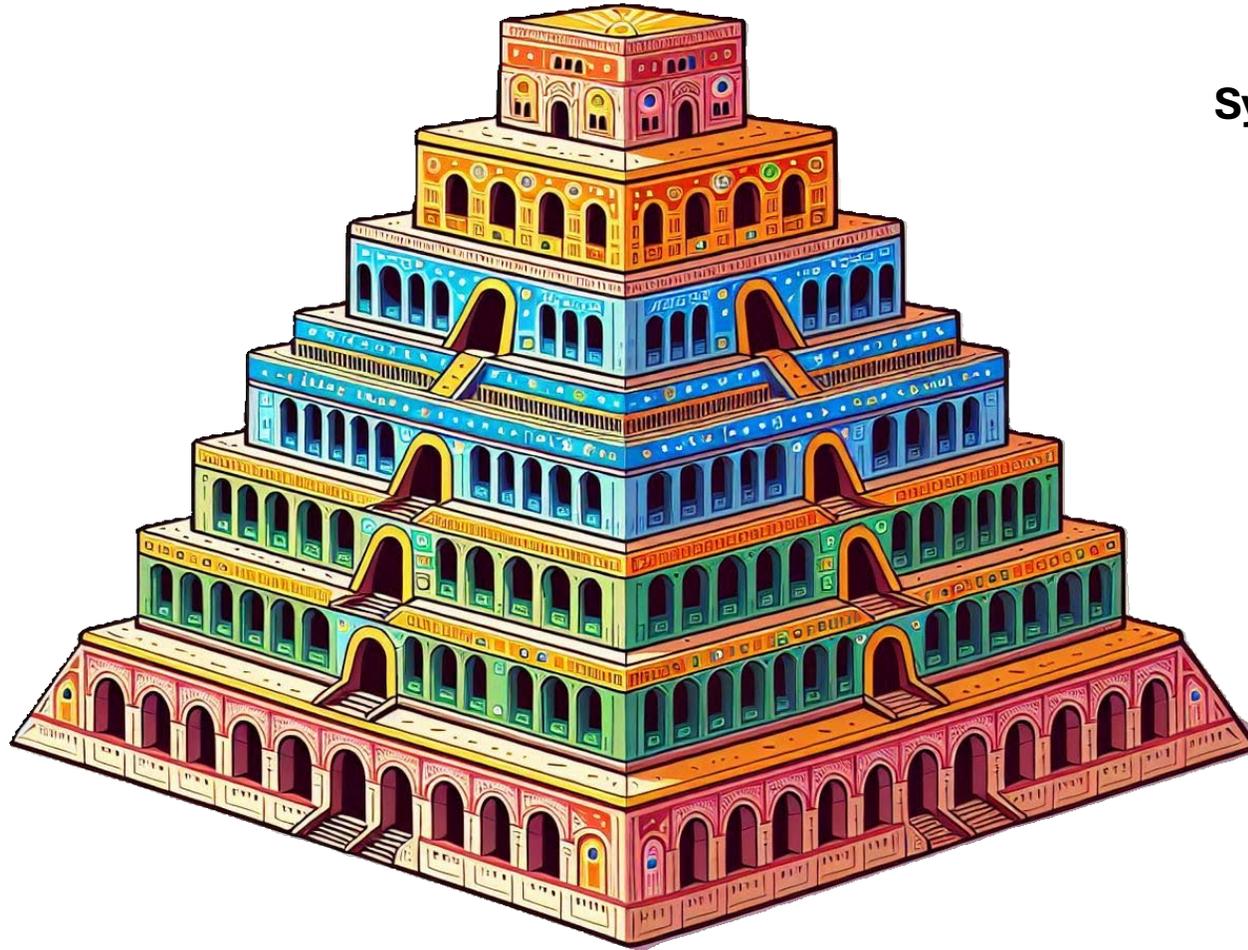


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The “evidence pyramid”



Systematic reviews and meta-analyses

Randomised controlled trials

Observational studies

Case reports / Case series

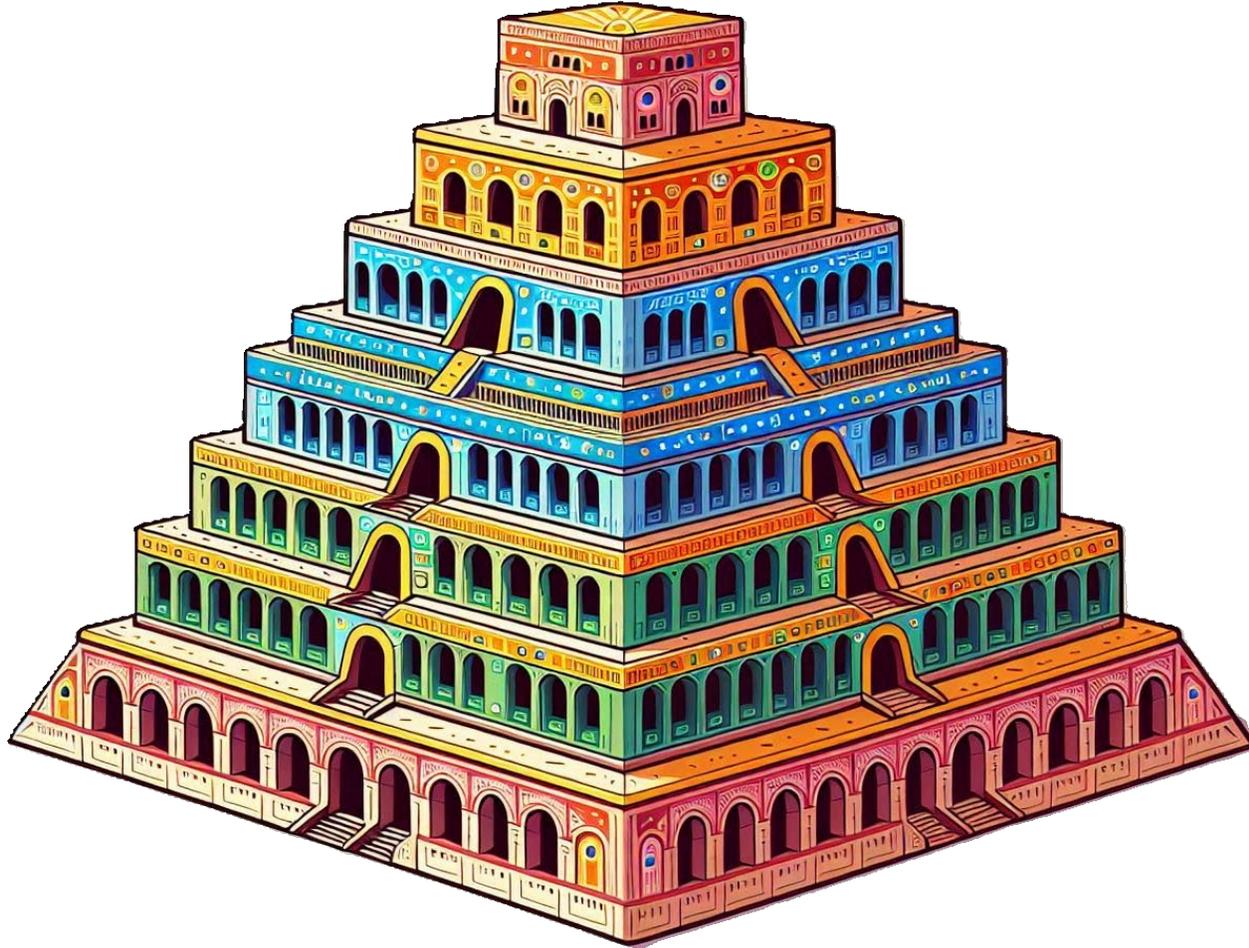
Credits:
Microsoft Designer



Another look: primary research

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Thoughtful, well-conducted
studies of any design

Others studies



Credits:
Microsoft Designer



Credits:
Darren Dahly

Another look: secondary research



Systematic reviews and meta-analyses

Credits:
Microsoft Designer





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Definition

A **meta-analysis** is...

- an **exhaustive...**
- and **reproducible...**
- **quantitative...**
- **synthesis...**

... of the results of studies addressing **the same question.**

It is more than a **systematic review**, that has no the quantitative synthesis.

It is most often conducted **retrospectively.**



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PICOS

Participants

Interventions

Comparators

Outcomes

Study design



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Different types

Head-to-head

Network meta-analyses

IPD meta-analyses

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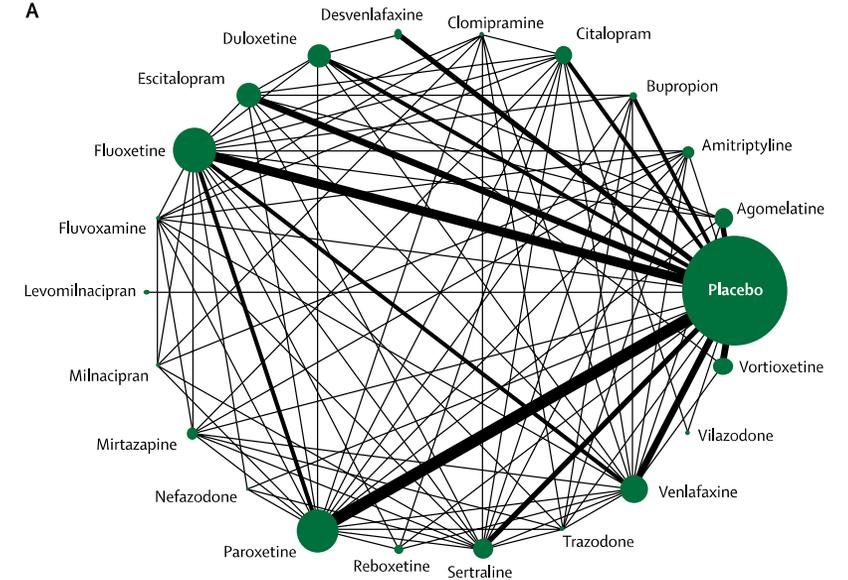
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Head-to-head
Network meta-analyses
IPD meta-analyses



Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis

Andrea Cipriani, Toshi A Furukawa, Georgia Salanti*, Anna Chaimani, Lauren Z Atkinson, Yusuke Ogawa, Stefan Leucht, Henricus G Ruhe, Erick H Turner, Julian P T Higgins, Matthias Egger, Nozomi Takeshima, Yu Hayasaka, Hissei Imai, Kiyomi Shinohara, Aran Tajika, John P A Ioannidis, John R Geddes*



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Head-to-head

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Meta-analysis of individual participant data: rationale, conduct, and reporting

Richard D Riley,¹ Paul C Lambert,² Ghada Abo-Zaid³

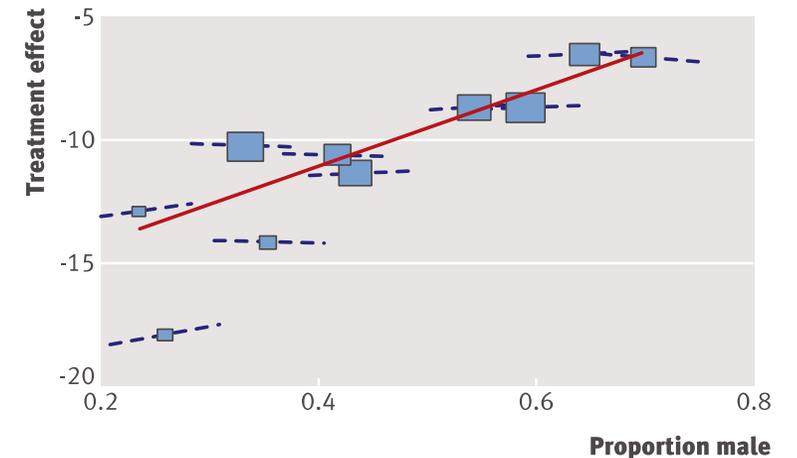


Fig 3 | An example of ecological bias within an aggregate data meta-analysis





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Reporting guidelines



Registry



Registered reports



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Overlapping network meta-analyses on psoriasis systemic treatments: an overview, quantity does not make quality

R. Guelimi ✉, S. Afach, J.-P. Régnaux, T. Bettuzzi, G. Chaby, E. Sbidian, F. Naudet, L. Le Cleach

NMA	Date of publication	ACI	CIC	FUM	MTX	ITO	EFA	ALE	BRIA	TYK2	APR	TOFA	BRO	CERT	ADA	ETA	UST	GUS	INF	IXE	RIS	SEC	TIL	BIM	GOL	MIRI
MROWIETZ 2021	2021												X	X	X	X	X	X	X	X	X	X	X			
TORRES 2020	2021			X					X				X	X	X	X	X	X	X	X	X	X	X		X	
BLAUVELT 2021	2020													X	X		X	X	X	X	X	X				
SONG 2020	2020											X				X					X	X				
DIAZ ACEDO 2020	2020												X				X				X		X			
XUJE 2020	2020												X		X	X	X	X	X	X	X		X			
MAHIL 2020	2020				X								X	X	X	X	X	X	X	X	X	X	X			
XU 2020	2020								X				X	X	X	X	X	X	X	X	X	X	X	X	X	X
TADA 2020	2020												X		X		X	X	X	X	X	X				
DU JARDIN 2020	2020																X							X		
JIANZHEN	2020																X	X				X		X		
ARMSTRONG 2020	2020	X	X	X	X					X			X	X	X	X	X	X	X	X	X	X	X	X		
SBIDIAN 2020	2020	X	X	X	X					X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
WARREN 2020a	2019												X	X	X	X	X	X	X	X	X	X	X	X		
WARREN 2020b	2019												X		X	X	X	X	X	X	X		X	X		
BAI 2019	2019												X				X	X		X	X	X	X			
XU 2019b	2019														X		X	X				X		X		
SAWYER 2019a	2019	X		X	X						X		X	X	X	X	X	X	X	X	X	X	X	X		
SAWYER 2019	2019	X		X							X		X		X	X	X		X	X		X				
XU 2019a	2018					X	X	X	X				X		X	X	X	X	X	X	X	X	X	X		
ARMSTRONG 2018	2018										X				X	X	X		X	X	X	X	X			
LV 2018	2018																X									
GENG 2018	2018		X		X											X	X	X		X						
CAMERON 2018	2018										X		X		X	X	X	X	X	X	X		X	X		
LOOS 2018	2018										X		X		X	X	X		X	X	X		X			
WARREN 2018	2017																X	X			X		X			
IMAFUKU 2018	2017														X		X			X			X			
AL SAWAH 2017	2017														X	X	X			X		X				
GOMEZ GARCIA 2017	2017														X	X	X			X			X			
JABBAR LOPEZ 2017	2017				X										X	X	X			X	X		X			
SBIDIAN 2017	2017	X	X	X	X	X		X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
FAN 2015	2015																X			X						
SIGNOROVITCH 2015	2015														X	X	X			X						
GUPTA 2014	2014				X			X							X	X	X			X						
SCHMITT 2014	2014		X	X	X			X							X	X	X			X						
IGARASHI 2013	2013						X								X	X	X			X						
GALVAN BANQUERI 2013	2013														X	X	X			X						
LIN 2012	2012							X							X	X	X			X						
REICH 2012	2012						X								X	X	X			X						
BANSBACK 2009	2009		X		X	X		X							X	X				X						
REICH 2008	2008						X	X							X					X						
WOOLACOTT 2006	2006		X	X	X		X								X					X						

Treatments cited as best in the abstract in relation to the included treatments for each NMA.

Each “X” represents the included treatments, squares filled in green represent the treatments cited as best, red squares represent the treatment of the funding pharmaceutical company





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Handling risk of bias



Thoughtful, well-conducted studies of any design

Others studies

Credits:
Microsoft Designer







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Definition

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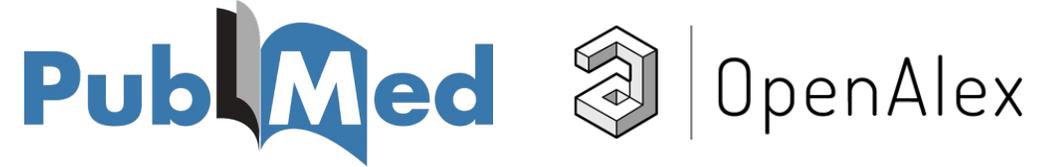
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Published studies



Unpublished studies



Regulatory documents



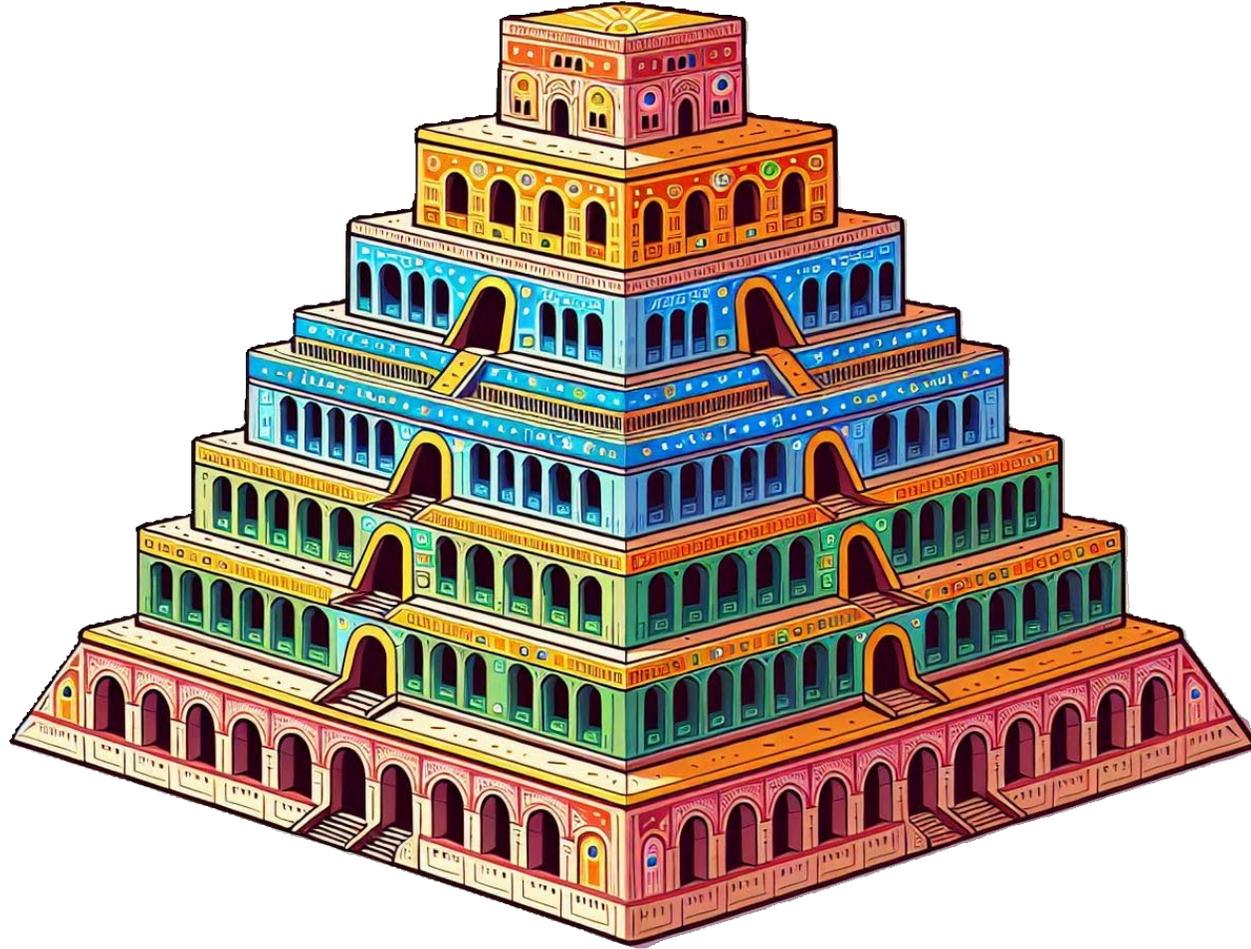


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Beneath the Evidence Floor



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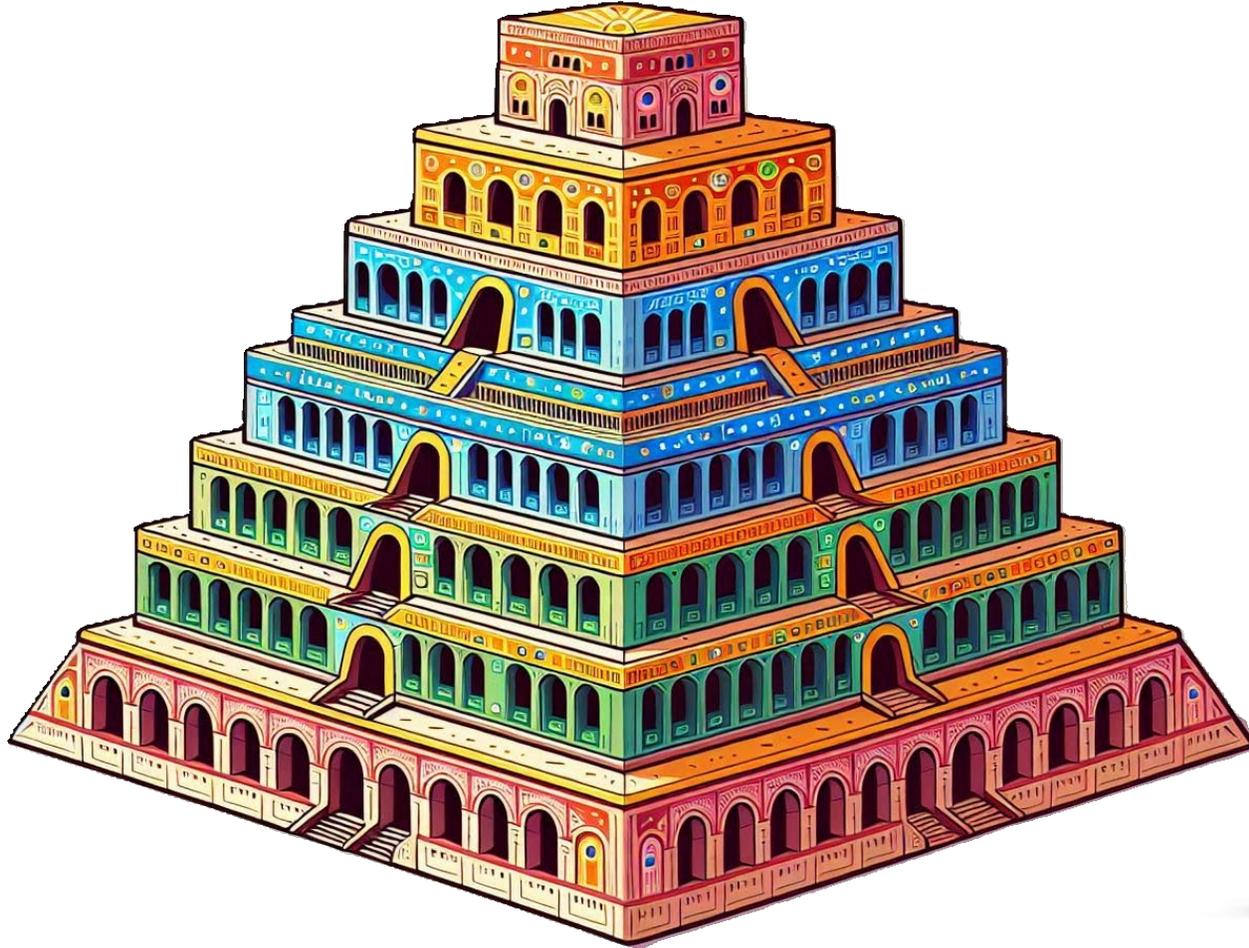


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Zombie studie

Credits:
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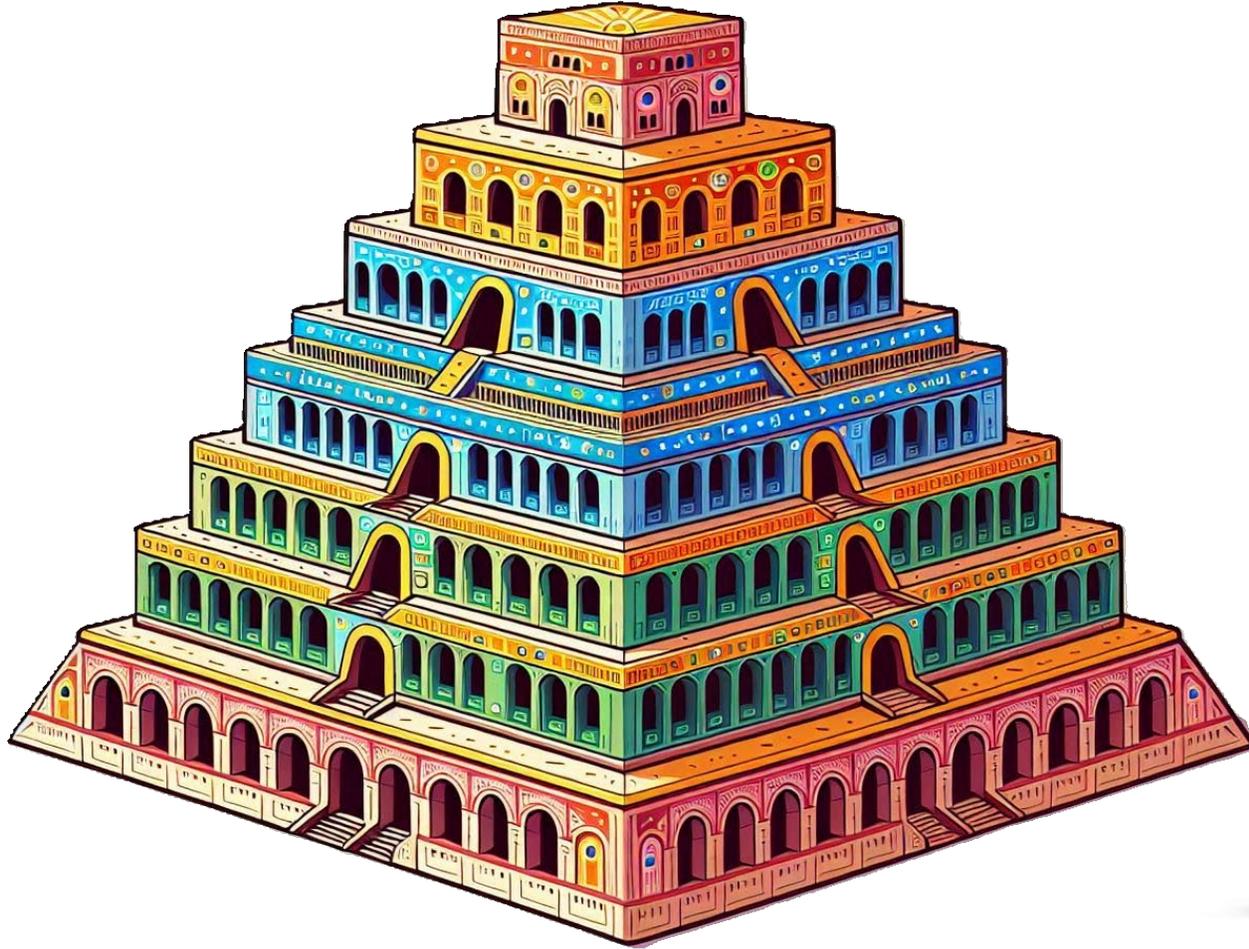


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medRxiv

THE PREPRINT SERVER FOR HEALTH SCIENCES



BMJ Yale





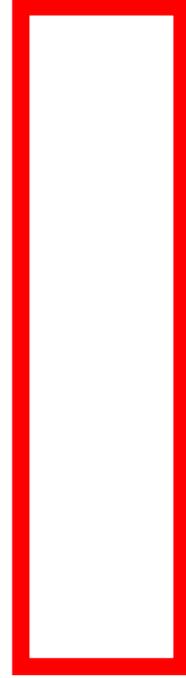
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BMJ Yale





Original Article

Comparison of Efficacy of Fluoxetine with Nortriptyline in Treatment of Major Depression in Children and Adolescents: a double-blind study

A. Attari MD*, F. Yadollah Moghaddam MD**, A. Hasanzadeh MS***,
 M. Soltani MS****, M. Mahmoodi MS*****

Table 1. Baseline data of groups A and B.

	Nortriptyline group	Fluoxetine group
Girls	9	11
Boys	11	9
Age (mean±SD)	12.5±2.5	13.2±2.3
Mean depression score before intervention	28.4±8.7	28.9±8.4

Independent t-test showed a significant difference in after treatment mean depression scores of two groups ($t=2.97$, $df=38$, $P=0.004$). The changes at the endpoint compared with baseline were -10.9 ± 2.6 and -2.6 ± 0.8 for fluoxetine and nortriptyline respectively (Table 2).

Table 2. Comparison of mean depression scores based on CDI before and after treatment in both studied groups.

Group	Before treatment		After treatment		P- value
	Max	SD	Mean	SD	
Fluoxetine	28.9	8.4	17.9	8.1	0.0000
Nortriptyline	28.4	8.7	25.8	8.5	0.3422

t- paired test showed a significant decrease in mean depression score in group of fluoxetine ($P\leq 0.0001$) while that was not significant in group of nortriptyline ($P=0.34$).



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SMD= 4.89

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SMD= 0.95

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- Attari 2006 was problematic but met all inclusion criteria
- Little evidence that Attari was « made up »
- Inconsistency was explicitly acknowledged
- The discussion emphasised substantial uncertainty in effect estimates
- Clarification of the issues surrounding Attari 2006 should be undertaken by the editor of the journal that originally published the study, who can review the peer-review record and contact the authors or institution.

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Exhaustivity...

Lack of IPD

But the reason was not disclosed

**Low evidence/modest effect VS
Moderate evidence/small effect**

Nothing happened

Editors do not see a need to change either of the papers published in The Lancet and The Lancet Psychiatry.







Conclusion

A meta-analysis is... **... is not fit for purpose** to deal with “zombie”...
... studies within our current research ecosystem...

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+



Grant agreement
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Grant Agreement
HORIZON-MSCA.2022-DN 101120360





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