Simplified figure to present direct and indirect comparisons: 
Revisiting the graph 10 years later

Valeria Fadda, Laura Bartoli, Elisa Ferracane, Sabrina Trippoli, Andrea Messori

ORCID number: Valeria Fadda 0000-0002-5048-8812; Laura Bartoli 0000-0002-3283-0987; Elisa Ferracane 0000-0001-6888-8040; Sabrina Trippoli 0000-0002-5762-1807; Andrea Messori 0000-0002-5829-107X.

Author contributions: Fadda V and Messori A were the main contributors of this paper; The other authors were involved in checking the manuscript, identifying inconsistencies, and generating the figure.

Conflict-of-interest statement: The authors declare no conflicts of interests.

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Manuscript source: Unsolicited manuscript

Valeria Fadda, Laura Bartoli, Elisa Ferracane, Sabrina Trippoli, Andrea Messori, HTA, ESTAR Toscana, Firenze 50132, Italy

Corresponding author: Andrea Messori, BCPS, PharmD, Academic Fellow, Associate Chief Pharmacist, Professor, HTA, ESTAR Toscana, Via San Salvi 12, Firenze 50132, Italy. andrea.messori.it@gmail.com

Abstract

A “simplified” figure was proposed in 2011 to summarize the results of controlled trials that evaluate different treatments aimed at the same disease condition. The original criteria for classifying individual binary comparisons included superiority, inferiority and no significance difference; hence, they did not differentiate between no proof of difference vs proof of no difference. We updated the criteria employed in the original “simplified” figure in order to include this differentiation. A revised version of the simplified figure is proposed and described herein. An example of application is also presented. The example is focused on first-line treatments for paroxysmal atrial fibrillation. Three treatments (medical therapy, cryoballoon ablation, radiofrequency ablation) are compared with one another through direct and indirect comparisons.

Key Words: Randomised controlled trials; Outcome research; Meta-analysis; Direct comparisons; Indirect comparison; Statistics

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Core Tip: A “simplified” figure was proposed in 2011 to summarize the results of controlled trials that evaluate different treatments aimed at the same disease condition. This graphical tool presents the network geometry along with the results of the analysis. The original criteria for classifying individual binary comparisons (direct or indirect comparisons) did not differentiate between no proof of difference vs proof of no difference. We have therefore updated the criteria employed in the original “simplified” figure to include this differentiation.

Citation: Fadda V, Bartoli L, Ferracane E, Trippoli S, Messori A. Simplified figure to present direct and indirect comparisons: Revisiting the graph 10 years later. World J Methodol 2021;
In 2011, Fadda and coworkers published in the BMJ the proposal of a simplified graph that, in the context of a network meta-analysis, presents the results of direct and indirect comparisons[1]. In 2019, another graph with very similar characteristics was proposed by De Vecchis et al[2]. Both of these graphs adopt the symbol “+” for superiority, “-” for inferiority, and “=” for the remaining cases.

Differentiating between no proof of difference (with \( P > 0.05 \)) and proof of no difference (with \( P > 0.05 \) and \( P_{\text{equivalence}} < 0.05 \)) is increasingly recognised to be important[3]; the same applies to differentiation between no proof of difference and proof of non-inferiority (with \( P > 0.05 \) and \( P_{\text{non-inferiority}} < 0.05 \), respectively). Since the two graphs of Fadda et al[1] and De Vecchis et al[2] do not include this differentiation, we propose to limit the symbol “=” to cases of equivalence and to adopt the symbol “NI” for non-inferiority or “ND” for the remaining cases. The suffix “t” remains useful because it identifies cases where the binary comparison shows a trend in favour of a treatment though in the absence of a statistically significant difference.

An example of the revisited graph is presented in Figure 1 that compares three first line treatments in paroxysmal atrial fibrillation[4-8].

In the field of network meta-analysis, the issue of graphical communication is complex, and the debate is still ongoing[9-15]. While the objective of describing the network geometry is quite straightforward[9,10], communication becomes more complex when it comes to presenting the results of the analysis[11-15]. The graphical proposal described herein is aimed at presenting the network geometry along with the results of the analysis. In our view, despite some unavoidable aspects of complexity, this tool deserves to be used particularly when the number of comparators is small.

**COMMENT:** In Figure 1, please replace “Cryoballoo” with “Cryoballoon” and “(t)RR” with “RR”.

![Figure 1 Direct and indirect comparisons across three first-line treatments for patients with paroxysmal atrial fibrillation.](image)

The comparisons of radiofrequency vs medical therapy and cryoballoon vs medical therapy are based on three[4-6] and two trials[7,8], respectively.
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