Considering the methodological limitations in the evidence base of antidepressants for depression: A reanalysis of a network meta-analysis

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S2 Appendix

Trial duration and long-term effect estimates

Overall trial length

According to the trial characteristics by Cipriani et al.[1] 492 (94%) of the 522 included trials lasted between four and 12 weeks (figure 1), 28 trials (5%) lasted more than 12 weeks, and the trial duration was unclear for two trials (table 3).

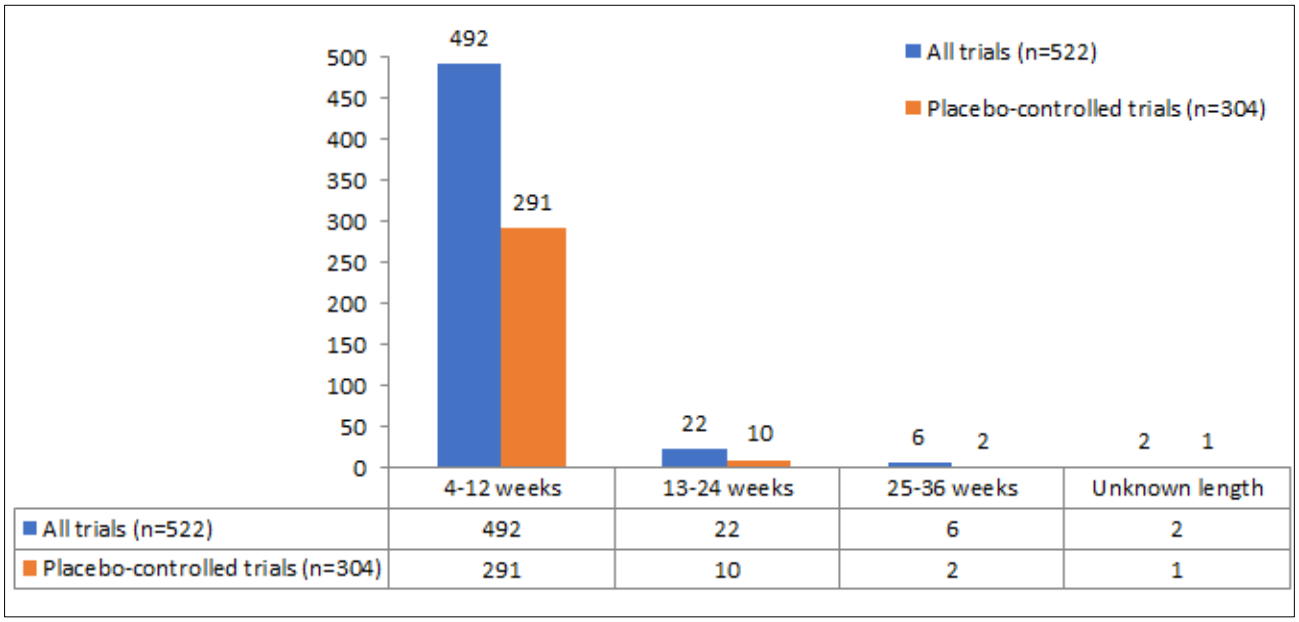

Figure 1. All 522 trials arranged into three follow-up periods according to Cipriani et al.'s trial characteristics: Four to 12 weeks (the period used by Cipriani et al.), 13 to 24 weeks, and 25 to 36 weeks [1].

Longer-term placebo-controlled trials

Of the 28 trials lasting more than 12 weeks, 12 trials had a placebo-controlled arm (table 3) and 16 were head-to-head trials. However, upon closer examination, eight of the 12 placebo-controlled trials consisted of several 'phases' and only four trials contained a continuous randomised placebo-controlled phase of more than 12 weeks (table 4). It is unclear why Cipriani et al.[1] did not list the correct trial length characteristics, since the various extension phases were described in the available documents, also for the unpublished trials.

Table 1. All 522 trials arranged according to the trial length characteristics by Cipriani et al.[1]

Trial length according to Cipriani et al.[1] (N = 522)	Trials without a placebo arm (N)	Placebo-controlled trials (N)
4 weeks	9	39
5 weeks	11	4
6 weeks	92	100
7 weeks	9	0
8 weeks	59	118
9 weeks	3	2
10 weeks	4	10
12 weeks	14	18
13 weeks	1	1
16 weeks	2	2
20 weeks	0	1
24 weeks	9	6

25 weeks	2	0
26 weeks	1	0
36 weeks	0	2
Trial length unknown	2	1
Total	218	304

Table 2. Longer-term placebo-controlled trials (trial length of more than 12 weeks).

Trial	Drug arm 1	Drug arm 2	Trial length according to Cipriani et al. (weeks)	Actual trial length (weeks)	Study design and phases
Oakes 2012a [2]	duloxetine	-	36	36	-
Oakes 2012b [2]	duloxetine	-	36	36	-
CL3-20098-022 [3]	agomelatine	fluoxetine	24	6 + 18	"Optional double-blind placebo-controlled extension" (page 24) for "responders to treatment" (page 26)
CL3-20098-023 [3]	agomelatine	paroxetine	24	6 + 18	"Optional double-blind placebo-controlled extension" (page 24) for "W6 responders" (page 26)
CL3-20098-024 [3]	agomelatine	fluoxetine	24	6 + 18	"Optional double-blind placebo-controlled extension" (page 24) for "responders to treatment at W6" (page 26)
CL3-20098-026 [3]	agomelatine	-	24	6 + 18	"18-week extension period" of "responders at W6" (page 42)
CL3-20098-070 [4]	agomelatine	-	24	8 + 16	16-week extension period for responders
Robinson 2014 [5]	duloxetine	-	24	12 + 12	From week 12 to 20 placebo rescue or dose increase were available
Lopez-Rodriguez 2004 [6]	fluoxetine	-	20	20	-
Barber 2011 [7]	sertraline	-	16	8 + 8	Non-responders on sertraline were switched to venlafaxin ER at week 8
Dimidjian 2006 [8]	paroxetine	-	16	8 + 8	The blind was broken at week 8 and the placebo arm was offered other treatments
Lecrubier 1997 [9]	venlafaxine	-	13	13	-

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