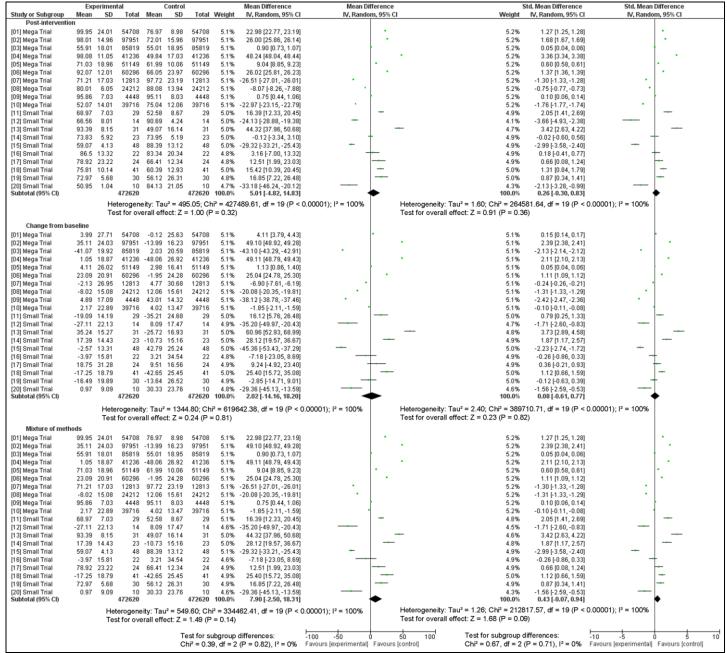**Figure 1**. Data extraction options (a) to perform meta-analysis and function (b) for produced theoretical randomized controlled trials by statistical simulation in Software R.

Post-intervention

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Weight	Std. Mean Difference IV, Random, 95% CI
[01] Mega Trial	99.95	24.01	54708	76.97	8.98	54708	5.1%	22.98 [22.77, 23.19]	5.2%	1.27 [1.25, 1.28]
[02] Mega Trial	98.01	14.96	97951	72.01	15.96	97951	5.1%	26.00 [25.86, 26.14]	5.2%	1.68 [1.67, 1.69]
[03] Mega Trial	55.91	18.01	85819	55.01	18.95	85819	5.1%	0.90 [0.73, 1.07]	5.2%	0.05 [0.04, 0.06]
[04] Mega Trial	98.08	11.05	41236	49.84	17.03	41236	5.1%	48.24 [48.04, 48.44]	5.2%	3.36 [3.34, 3.38]
[05] Mega Trial	71.03	18.96	51149	61.99	10.06	51149	5.1%	9.04 [8.85, 9.23]	5.2%	0.60 [0.58, 0.61]
[06] Mega Trial	92.07	12.01	60296	66.05	23.97	60296	5.1%	26.02 [25.81, 26.23]	5.2%	1.37 [1.36, 1.39]
[07] Mega Trial	71.21	17.03	12813	97.72	23.19	12813	5.1%	-26.51 [-27.01, -26.01]	5.2%	-1.30 [-1.33, -1.28]
[08] Mega Trial	80.01	6.05	24212	88.08	13.94	24212	5.1%	-8.07 [-8.26, -7.88]	5.2%	-0.75 [-0.77, -0.73]
[09] Mega Trial	95.86	7.03	4448	95.11	8.03	4448	5.1%	0.75 [0.44, 1.06]	5.2%	0.10 [0.06, 0.14]
[10] Mega Trial	52.07	14.01	39716	75.04	12.06	39716	5.1%	-22.97 [-23.15, -22.79]	5.2%	-1.76 [-1.77, -1.74]
[11] Small Trial	68.97	7.03	29	52.58	8.67	29	5.0%	16.39 [12.33, 20.45]	4.9%	2.05 [1.41, 2.69]
[12] Small Trial	66.56	8.01	14	90.69	4.24	14	5.0%	-24.13 [-28.88, -19.38]	4.1%	-3.66 [-4.93, -2.38]
[13] Small Trial	93.39	8.15	31	49.07	16.14	31	5.0%	44.32 [37.96, 50.68]	4.7%	3.42 [2.63, 4.22]
[14] Small Trial	73.83	5.92	23	73.95	5.19	23	5.0%	-0.12 [-3.34, 3.10]	4.9%	-0.02 [-0.60, 0.56]
[15] Small Trial	59.07	4.13	48	88.39	13.12	48	5.0%	-29.32 [-33.21, -25.43]	4.9%	-2.99 [-3.58, -2.40]
[16] Small Trial	86.5	13.32	22	83.34	20.34	22	4.8%	3.16 [-7.00, 13.32]	4.9%	0.18 [-0.41, 0.77]
[17] Small Trial	78.92	23.22	24	66.41	12.34	24	4.8%	12.51 [1.99, 23.03]	4.9%	0.66 [0.08, 1.24]
[18] Small Trial	75.81	10.14	41	60.39	12.93	41	5.0%	15.42 [10.39, 20.45]	5.0%	1.31 [0.84, 1.79]
[19] Small Trial	72.97	5.68	30	56.12	26.31	30	4.8%	16.85 [7.22, 26.48]	5.0%	0.87 [0.34, 1.41]
[20] Small Trial	50.95	1.04	10	84.13	21.05	10	4.7%	-33.18 [-46.24, -20.12]	4.3%	-2.13 [-3.28, -0.99]
Subtotal (95% CI)			472620			472620	100.0%	5.01 [-4.82, 14.83]	100.0%	0.26 [-0.30, 0.83]

Heterogeneity: Tau² = 495.05; Chi² = 427489.61, df = 19 (P < 0.00001); I² = 100%
Test for overall effect: Z = 1.00 (P = 0.32)

Heterogeneity: Tau² = 1.60; Chi² = 264581.64, df = 19 (P < 0.00001); I² = 100%
Test for overall effect: Z = 0.91 (P = 0.36)

Change from baseline

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Weight	Std. Mean Difference IV, Random, 95% CI
[01] Mega Trial	3.99	27.71	54708	-0.12	25.63	54708	5.1%	4.11 [3.79, 4.43]	5.1%	0.15 [0.14, 0.17]
[02] Mega Trial	35.11	24.03	97951	-13.99	16.23	97951	5.1%	49.10 [48.92, 49.28]	5.1%	2.39 [2.38, 2.41]
[03] Mega Trial	-41.07	19.92	85819	2.03	20.59	85819	5.1%	-43.10 [-43.29, -42.91]	5.1%	-2.13 [-2.14, -2.12]
[04] Mega Trial	1.05	18.87	41236	-48.06	26.92	41236	5.1%	49.11 [48.79, 49.43]	5.1%	2.11 [2.10, 2.13]
[05] Mega Trial	4.11	26.02	51149	2.98	16.41	51149	5.1%	1.13 [0.86, 1.40]	5.1%	0.05 [0.04, 0.06]
[06] Mega Trial	23.09	20.91	60296	-1.95	24.28	60296	5.1%	25.04 [24.78, 25.30]	5.1%	1.11 [1.09, 1.12]
[07] Mega Trial	-2.13	26.95	12813	4.77	30.68	12813	5.1%	-6.90 [-7.61, -6.19]	5.1%	-0.24 [-0.26, -0.21]
[08] Mega Trial	-8.02	15.08	24212	12.06	15.61	24212	5.1%	-20.08 [-20.35, -19.81]	5.1%	-1.31 [-1.33, -1.29]
[09] Mega Trial	4.89	17.09	4448	43.01	14.32	4448	5.1%	-38.12 [-38.78, -37.46]	5.1%	-2.42 [-2.47, -2.36]
[10] Mega Trial	2.17	22.89	39716	4.02	13.47	39716	5.1%	-1.85 [-2.11, -1.59]	5.1%	-0.10 [-0.11, -0.08]
[11] Small Trial	-19.09	14.19	29	-35.21	24.68	29	5.0%	16.12 [5.76, 26.48]	5.0%	0.79 [0.25, 1.33]
[12] Small Trial	-27.11	22.13	14	8.09	17.47	14	4.9%	-35.20 [-49.97, -20.43]	4.7%	-1.71 [-2.60, -0.83]
[13] Small Trial	35.24	15.27	31	-25.72	16.93	31	5.0%	60.96 [52.93, 68.99]	4.8%	3.73 [2.89, 4.58]
[14] Small Trial	17.39	14.43	23	-10.73	15.16	23	5.0%	28.12 [19.57, 36.67]	4.9%	1.87 [1.17, 2.57]
[15] Small Trial	-2.57	13.31	48	42.79	25.24	48	5.0%	-45.36 [-53.43, -37.29]	5.0%	-2.23 [-2.74, -1.72]
[16] Small Trial	-3.97	15.81	22	3.21	34.54	22	4.9%	-7.18 [-23.05, 8.69]	4.9%	-0.26 [-0.86, 0.33]
[17] Small Trial	18.75	31.28	24	9.51	16.56	24	4.9%	9.24 [-4.92, 23.40]	4.9%	0.36 [-0.21, 0.93]
[18] Small Trial	-17.25	18.79	41	-42.65	25.45	41	5.0%	25.40 [15.72, 35.08]	5.0%	1.12 [0.66, 1.59]
[19] Small Trial	-16.49	19.89	30	-13.64	26.52	30	5.0%	-2.85 [-14.71, 9.01]	5.0%	-0.12 [-0.63, 0.39]
[20] Small Trial	0.97	9.09	10	30.33	23.76	10	4.8%	-29.36 [-45.13, -13.59]	4.6%	-1.56 [-2.59, -0.53]
Subtotal (95% CI)			472620			472620	100.0%	2.02 [-14.16, 18.20]	100.0%	0.08 [-0.61, 0.77]

Heterogeneity: Tau² = 1344.80; Chi² = 619642.38, df = 19 (P < 0.00001); I² = 100%
Test for overall effect: Z = 0.24 (P = 0.81)

Heterogeneity: Tau² = 2.40; Chi² = 389710.71, df = 19 (P < 0.00001); I² = 100%
Test for overall effect: Z = 0.23 (P = 0.82)

Mixture of methods

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Weight	Std. Mean Difference IV, Random, 95% CI
[01] Mega Trial	99.95	24.01	54708	76.97	8.98	54708	5.1%	22.98 [22.77, 23.19]	5.2%	1.27 [1.25, 1.28]
[02] Mega Trial	35.11	24.03	97951	-13.99	16.23	97951	5.1%	49.10 [48.92, 49.28]	5.2%	2.39 [2.38, 2.41]
[03] Mega Trial	55.91	18.01	85819	55.01	18.95	85819	5.1%	0.90 [0.73, 1.07]	5.2%	0.05 [0.04, 0.06]
[04] Mega Trial	1.05	18.87	41236	-48.06	26.92	41236	5.1%	49.11 [48.79, 49.43]	5.2%	2.11 [2.10, 2.13]
[05] Mega Trial	71.03	18.96	51149	61.99	10.06	51149	5.1%	9.04 [8.85, 9.23]	5.2%	0.60 [0.58, 0.61]
[06] Mega Trial	23.09	20.91	60296	-1.95	24.28	60296	5.1%	25.04 [24.78, 25.30]	5.2%	1.11 [1.09, 1.12]
[07] Mega Trial	71.21	17.03	12813	97.72	23.19	12813	5.1%	-26.51 [-27.01, -26.01]	5.2%	-1.30 [-1.33, -1.28]
[08] Mega Trial	-8.02	15.08	24212	12.06	15.61	24212	5.1%	-20.08 [-20.35, -19.81]	5.2%	-1.31 [-1.33, -1.29]
[09] Mega Trial	95.86	7.03	4448	95.11	8.03	4448	5.1%	0.75 [0.44, 1.06]	5.2%	0.10 [0.06, 0.14]
[10] Mega Trial	2.17	22.89	39716	4.02	13.47	39716	5.1%	-1.85 [-2.11, -1.59]	5.2%	-0.10 [-0.11, -0.08]
[11] Small Trial	68.97	7.03	29	52.58	8.67	29	5.1%	16.39 [12.33, 20.45]	4.8%	2.05 [1.41, 2.69]
[12] Small Trial	-27.11	22.13	14	8.09	17.47	14	4.6%	-35.20 [-49.97, -20.43]	4.5%	-1.71 [-2.60, -0.83]
[13] Small Trial	93.39	8.15	31	49.07	16.14	31	5.0%	44.32 [37.96, 50.68]	4.6%	3.42 [2.63, 4.22]
[14] Small Trial	17.39	14.43	23	-10.73	15.16	23	5.0%	28.12 [19.57, 36.67]	4.8%	1.87 [1.17, 2.57]
[15] Small Trial	59.07	4.13	48	88.39	13.12	48	5.0%	-29.32 [-33.21, -25.43]	4.9%	-2.99 [-3.58, -2.40]
[16] Small Trial	-3.97	15.81	22	3.21	34.54	22	4.6%	-7.18 [-23.05, 8.69]	4.9%	-0.26 [-0.86, 0.33]
[17] Small Trial	78.92	23.22	24	66.41	12.34	24	4.9%	12.51 [1.99, 23.03]	4.9%	0.66 [0.08, 1.24]
[18] Small Trial	-17.25	18.79	41	-42.65	25.45	41	4.9%	25.40 [15.72, 35.08]	5.0%	1.12 [0.66, 1.59]
[19] Small Trial	72.97	5.68	30	56.12	26.31	30	4.9%	16.85 [7.22, 26.48]	4.9%	0.87 [0.34, 1.41]
[20] Small Trial	0.97	9.09	10	30.33	23.76	10	4.6%	-29.36 [-45.13, -13.59]	4.3%	-1.56 [-2.59, -0.53]
Subtotal (95% CI)			472620			472620	100.0%	7.90 [-2.50, 18.31]	100.0%	0.43 [-0.07, 0.94]

Heterogeneity: Tau² = 549.60; Chi² = 334462.41, df = 19 (P < 0.00001); I² = 100%
Test for overall effect: Z = 1.49 (P = 0.14)

Heterogeneity: Tau² = 1.26; Chi² = 212817.57, df = 19 (P < 0.00001); I² = 100%
Test for overall effect: Z = 1.68 (P = 0.09)

Test for subgroup differences: Chi² = 0.39, df = 2 (P = 0.82), I² = 0%
Favours [experimental] Favours [control]

Test for subgroup differences: Chi² = 0.67, df = 2 (P = 0.71), I² = 0%
Favours [experimental] Favours [control]

Figure 2. Meta-analysis performed by post-intervention, change from baseline and mixture of methods.

Table 1. Differences of meta-analysis performed by post-intervention versus change from baseline.

Statistical Method or Sensibility Analyses	Effect Estimate	Test for overall effect
Mean Difference (IV, Random, 95% CI)		
All trials		
Post-intervention	5.01 [-4.82, 14.83]	Z = 1.00 (P = 0.32)
Change from baseline	2.02 [-14.16, 18.20]	Z = 0.24 (P = 0.81)
Mixture of methods	7.90 [-2.50, 18.31]	Z = 1.49 (P = 0.14)
Maga-trials		
Post-intervention	7.64 [-6.15, 21.43]	Z = 1.09 (P = 0.28)
Change from baseline	1.84 [-20.89, 24.58]	Z = 0.16 (P = 0.87)
Mixture of methods	10.85 [-3.68, 25.37]	Z = 1.46 (P = 0.14)
Small-trials		
Post-intervention	2.29 [-12.29, 16.86]	Z = 0.31 (P = 0.76)
Change from baseline	2.19 [-21.41, 25.78]	Z = 0.18 (P = 0.86)
Mixture of methods	4.60 [-14.31, 23.51]	Z = 0.48 (P = 0.63)
Std. Mean Difference (IV, Random, 95% CI)		
All trials		
Post-intervention	0.26 [-0.30, 0.83]	Z = 0.91 (P = 0.36)
Change from baseline	0.08 [-0.61, 0.77]	Z = 0.23 (P = 0.82)
Mixture of methods	0.43 [-0.07, 0.94]	Z = 1.68 (P = 0.09)
Maga-trials		
Post-intervention	0.46 [-0.32, 1.25]	Z = 1.15 (P = 0.25)
Change from baseline	-0.04 [-1.00, 0.92]	Z = 0.08 (P = 0.94)
Mixture of methods	0.49 [-0.20, 1.19]	Z = 1.39 (P = 0.17)
Small-trials		
Post-intervention	0.01 [-1.14, 1.16]	Z = 0.02 (P = 0.99)
Change from baseline	0.20 [-0.78, 1.18]	Z = 0.41 (P = 0.68)
Mixture of methods	0.36 [-0.77, 1.48]	Z = 0.62 (P = 0.54)