Practical Exercise 1 - Unit of analysis issues and Data Extraction

Consider the following excerpt from a recent review, and the following Forest plots – Which studies would concern you? What would you do?

Cluster-randomised trials

There are 14 cluster-randomised trials in the analyses along with individually randomised trials. Their sample sizes have been adjusted using the methods described in the *Handbook* and by <u>Donner 2000</u> using an estimate of the intracluster correlation coefficient (ICC) derived from the trial (if possible), or from another source. If ICCs from other sources were used, we have noted this and carried out sensitivity analyses to investigate the effect of variation in ICC. We have synthesised the findings from individually- and cluster-randomised trials provided that there was little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit was considered to be unlikely.

Trials with multiple groups

In order to avoid 'double counting', the data provided by studies that involved one comparison group but two interventions groups had the number of events and number of participants halved.

Figure 1: outcome 1

	Suppo	ort	Usual	care		Risk Ratio	Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI			
Study 72	1	27	8	25	0.1%	0.12 [0.02, 0.86]	· · · · · · · · · · · · · · · · · · ·			
Study 90	3	50	35	50	0.2%	0.09.00.03.0.261	←			
Study 32	11	67	17	67	0.4%	0.65 (0.33, 1.28)				
Study 67	26	80	11	30	0.6%	0.89 [0.50, 1.56]				
Study 80	10	26	17	26	0.0.0	0.59 [0.34 1 03]				
Study 55 Study 74	12	20	12	20	0.07%	0.00[0.04, 1.00]				
Oludy 74 Otudu 0	24	21	20	100	0.770	0.00 [0.34, 1.44]				
oluuy o Otudu 7	31	221	29	108	0.0%					
Oludy 7 Chudu 22	40	400	32	100	0.8%	0.55 (0.01, 1.83)				
Study 22 Otradu 22	20	132	43	120	0.9%					
Study 73	15	30	22	30	0.9%	0.68 [0.45, 1.04]				
Study 4	25	94	41	94	1.0%	0.61 [0.41, 0.92]				
Study 88	34	179	42	178	1.0%	0.81 [0.54, 1.20]				
Study 63	26	69	33	81	1.0%	0.92 [0.62, 1.38]				
Study 29	36	154	41	176	1.0%	1.00 [0.68, 1.49]				
Study 34	45	292	51	294	1.1%	0.89 [0.62, 1.28]				
Study 97	30	79	46	107	1.2%	0.88 [0.62, 1.26]				
Study 54	73	315	45	157	1.3%	0.81 [0.59, 1.11]				
Study 12	49	163	100	234	1.6%	0.70 [0.53, 0.93]				
Study 94	21	26	21	27	1.6%	1.04 [0.79, 1.37]				
Study 18	45	90	51	75	1.7%	0.74 [0.57, 0.95]				
Study 83	43	78	51	78	1.7%	0.84 [0.65, 1.09]				
Study 11a	50	80	30	40	1.8%	0.83 [0.65, 1.07]				
Study 31	68	171	82	172	1.8%	0.83 [0.65, 1.06]				
Study 95	23	30	39	42	2.0%	0.83 [0.67, 1.02]				
Study 58	81	135	79	135	2.1%	1.03 [0.84, 1.25]	<u>+</u>			
Study 11a	173	253	30	40	2.1%	0.91 [0.75, 1.11]	-			
Study 13	39	58	52	57	2.1%	0.74 [0.61, 0.90]				
Study 59	147	425	130	424	2.1%	1 1 3 10 9 3 1 3 7				
Study 25	129	303	118	302	2.2%		<u>+</u>			
Study 20	84	175	110	175	2.2%	0.76 [0.63, 0.93]				
Study 21 Study 91	86	200	166	300	2.2.%	0.78 [0.64 0.94]	-			
Study 31 Study 76	49	65	55	71	2.2.%	0.07 [0.04, 0.04]				
Otudy 10 Otudy 27	40	40	20	40	2.2.0					
Otudy 57 Otudy 55	42	602	226	600 600	2.2.0	0.75 0.64 0.971	-			
Otudy 55 Otudy 97	101	140	200	151	2.570	0.75 [0.04, 0.07]	\perp			
Otudu 11 h	101	148	100	101	2.070					
Study I D Otwale 4.4	90	130	100	139	2.0%	0.80 [0.73, 0.99]				
Study 14 Study 02	110	101	113	180	2.5%	1.10[0.99, 1.33]				
Study 65	/0	100	80	100	2.5%	0.95 [0.82, 1.10]				
Study 51	153	291	171	269	2.6%	0.83 [0.72, 0.95]	-			
Study 75	119	168	115	160	2.6%	0.99 [0.86, 1.13]	Т			
Study 68	86	112	93	113	2.6%	0.93 [0.82, 1.07]	7			
Study 24	33	38	40	40	2.6%	0.87 [0.76, 0.99]				
Study 47	142	228	257	355	2.7%	0.86 [0.76, 0.97]	-			
Study 50	188	265	162	242	2.7%	1.06 [0.94, 1.19]	Ť			
Study 10	137	188	149	194	2.8%	0.95 [0.84, 1.07]	-			
Study 35	220	363	226	357	2.8%	0.96 [0.85, 1.07]	-			
Study 61	280	759	600	906	2.8%	0.56 [0.50, 0.62]	-			
Study 6	280	450	293	450	2.9%	0.96 [0.87, 1.05]	-			
Study 70	325	576	343	578	2.9%	0.95 [0.86, 1.05]	+			
Study 41	360	490	357	500	3.0%	1.03 [0.95, 1.11]	÷			
Study 61	552	887	608	918	3.1%	0.94 [0.88, 1.01]	-			
Study 66	259	311	264	312	3.1%	0.98 [0.92, 1.05]	+			
Study 64	216	237	217	223	3.2%	0.94 [0.90, 0.98]	•			
Total (95% CI)		10850		10858	100.0%	0.89 [0.85, 0.93]	•			
Total events	5482		6217							
Heterogeneity: Tour=	0.02° Chiž	= 217	65 df= 5	7 (P < ∩	00001\-	² = 76%				
Test for overall effect:	7 = 4 99 /	2 < 0.00	00, 01 – 0. 1001)	- (· - 0.	500017,1	. 0 70	0.05 0.2 1 5 20			
reactor overall cliebt.	∠ - 4.03 (F	- 0.00	,001)				Favours support Favours usual care			

Figure 2: outcome 2

Study of Subgroup Events Total Events Total Weight M.H., Random, 95% C1 M.H., Random, 95% C1 Study 72 5 27 16 25 0.2% 0.29 (0.12, 0.67) Study 74 6 19 15 18 0.3% 0.31 (0.16, 0.63) Study 73 17 68 23 33 0.5% 0.36 (0.2, 0.67) Study 74 16 22 23 0.3% 0.36 (0.2, 0.67)		Support	Usual o	care		Risk Ratio	Risk Ratio			
Bitudy 90 3 60 33 60 0.1% 0.09 [0.3, 0.28] Bitudy 45 6 19 15 19 0.3% 0.40 [0.20, 0.81] Situdy 74 6 19 15 19 0.3% 0.40 [0.20, 0.81] Situdy 74 15 21 0.3% 0.46 [0.20, 0.57]	Study or Subgroup	Events Tota	I Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI			
Study 72 5 27 16 25 0.2% 0.29	Study 90	3 5) 33	50	0.1%	0.09 [0.03, 0.28]	←			
Shudy 45 6 19 15 19 0.3% 0.40 [0.20, 0.81] Shudy 78 17 68 23 33 0.5% 0.36 [0.22, 0.57] Shudy 74 15 21 17 20 0.9% 0.44 [0.61, 0.53] Shudy 63 38 69 26 30 1.1% 0.52 [0.30, 0.69] Shudy 63 38 69 48 81 1.1% 0.52 [0.30, 0.69] Shudy 63 38 69 48 81 1.1% 0.53 [0.42, 0.67] Shudy 63 38 69 221 110 189 1.4% 0.53 [0.42, 0.67] Shudy 81 69 221 110 189 1.4% 0.53 [0.42, 0.67]	Study 72	5 2	7 16	25	0.2%	0.29 [0.12, 0.67]	←			
Study 989a 6 22 20 23 0.3% 0.31 0.16 0.6.0 Study 3 20 33 26 157 0.6% 3.66 2.4.5 7.2 Study 67 36 80 26 30 1.1% 0.52 0.37 0.37 0.37 Study 67 36 80 26 30 1.1% 0.52 0.37	Study 45	6 1	3 15	19	0.3%	0.40 [0.20, 0.81]				
Study 76 17 66 23 33 0.5% 0.36 [0.22, 0.57] Study 74 15 21 17 20 0.9% 0.44 [0.51, 1.17] Study 67 36 80 2.6 30 1.1% 0.52 [0.30, 0.69] Study 63 38 68 48 81 1.1% 0.55 [0.34, 0.73] Study 81 68 2.21 110 110 1.4% 0.55 [0.44, 0.69] Study 81 59 1.2% 0.55 [0.44, 0.69]	Study 89a	6 23	2 20	23	0.3%	0.31 [0.16, 0.63]				
Study 3 20 33 26 157 0.6% 3.66 [2.34, 5.72] Study 67 36 80 26 30 11% 0.52 [0.39, 0.69] Study 80b 31 63 52 59 1.2% 0.56 [0.43, 0.73] Study 80b 31 63 67 1.4% 0.56 [0.44, 0.70]	Study 79	17 6	3 23	33	0.5%	0.36 [0.22, 0.57]				
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Study 3	20 33	3 26	157	0.6%	3.66 [2.34, 5.72]				
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Study 98b 31 63 52 59 1.2% 0.56 0.40 0.70 Study 8 68 221 110 189 1.4% 0.53 0.42 0.67 Study 8 68 221 110 189 1.4% 0.55 0.44 0.69 Study 97 50 78 70 107 1.5% 0.55 0.44 0.69 Study 34 109 222 123 294 1.6% 0.99 0.71 1.04 Study 54 164 315 71 94 1.7% 0.86 0.71 1.04 Study 54 164 315 73 77 2.1% 0.39 1087 1.11 Study 50 237 425 240 424 2.3% 0.99 1087 1.11 Study 35 260 363 271 357 2.6% 0.79 0.84 - Study 35 260 363 271 357 2.6% 0.99 0.91 - - Study 21 131<	Study 63	38 6	3 48	81	1.1%	0.93 [0.70, 1.23]				
Study 32 35 67 63 67 1.4% 0.56 0.44 0.70 Study 8 68 221 110 189 1.4% 0.55 0.44 0.69 Study 91 59 148 108 150 1.5% 0.55 0.44 0.69 Study 41 61 94 71 94 1.7% 0.96 0.97 1.09 Study 44 61 94 71 94 1.7% 0.86 0.71 1.04 Study 38 101 227 346 333 2.0% 0.47 0.04.1 - Study 50 201 266 175 242 2.4% 1.05 0.97 0.87 - Study 69 237 425 240 424 2.3% 0.99 0.87 1.11 - - Study 69 237 425 240 424 2.3% 0.99 0.87 1.11 - - - - - - - - - - - - - <td>Study 89b</td> <td>31 6:</td> <td>3 52</td> <td>59</td> <td>1.2%</td> <td>0.56 [0.43, 0.73]</td> <td></td>	Study 89b	31 6:	3 52	59	1.2%	0.56 [0.43, 0.73]				
Study 8 68 221 110 189 1.4% 0.53 0.42 0.67 Study 91 59 148 108 150 15% 0.55 0.40 0.69 Study 97 50 79 70 107 1.5% 0.65 0.66 0.71 1.04 Study 41 09 227 13 294 1.6% 0.99 0.73 1.04 Study 43 109 227 13 71 94 1.7% 0.86 0.71 1.04 Study 53 617 79 2.1% 0.97 0.88 0.71 1.04 Study 59 237 422 240 424 2.3% 0.99 0.87 1.11 Study 50 201 257 242 24% 105 0.56 10.95 116 Study 61 231 152 157 2.5% 0.66 0.79 0.94 Study 91 212 152 152 152 152 152 153 153 153 Stu	Study 32	35 6	7 63	67	1.4%	0.56 [0.44, 0.70]				
Study 81 59 148 108 160 1.5% 0.55 0.44, 0.69 Study 34 109 292 123 294 1.6% 0.89 0.73, 1.09 Study 44 61 94 71 94 1.7% 0.66 0.71, 1.04 Study 54 164 315 31 67 19% 0.88 0.74, 1.04 Study 59 237 425 240 424 2.3% 0.99 0.87, 1.11 Study 50 201 265 175 242 2.4% 0.99 0.87, 1.11 Study 50 201 265 175 242 2.4% 0.99 0.87, 1.11 Study 69 99 120 115 120 2.5% 0.79 0.94 - Study 29 132 154 152 2.6% 0.86 0.79, 0.93 - - Study 29 232 308 134 152 2.6% 0.83 0.76, 0.90 - - Study 87 127 149 140 152 2.6%	Study 8	68 22	110	189	1.4%	0.53 [0.42, 0.67]				
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Study 34 109 292 123 294 1.6% 0.88 [0.71, 1.04] Study 54 164 315 31 1.7% 0.86 [0.71, 1.04] Study 54 164 315 31 57 1.9% 0.88 [0.74, 1.04] Study 38 101 227 346 363 2.0% 0.47 [0.40, 0.54] Study 59 237 425 240 242 2.3% 0.99 [0.87, 1.11] Study 50 201 265 175 242 2.4% 1.05 [0.95, 1.16] Study 51 131 175 166 175 2.2% 0.86 [0.70, 0.94] Study 69 99 120 115 120 2.5% 0.99 [0.91, 1.08] Study 99 265 363 314 152 2.6% 0.89 [0.81, 0.96] Study 99 265 363 314 152 2.6% 0.89 [0.81, 0.96] Study 99 265 363 314 152 2.6% 0.89 [0.81, 0.96] Study 91 169 2.07 7.30 0.99 [0.84, 0.96] -	Study 97	50 79	9 70	107	1.5%	0.97 [0.78, 1.20]				
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Study 54 164 315 93 157 19% 0.88 074 104 Study 38 101 227 346 363 2.0% 0.47 1040 0.54 Study 83 66 79 67 79 2.1% 0.09 0.87, 1.11	Study 4	61 9-	4 71	94	1.7%	0.86 [0.71, 1.04]				
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Study 83 65 79 67 79 2.1% 0.97 (0.84, 1.11) Study 59 237 425 240 424 2.3% 0.99 (0.87, 1.11) Study 50 201 266 175 242 2.4% 1.05 (0.95, 1.16) Study 69 99 120 115 120 2.5% 0.86 (0.79, 0.94) Study 50 201 135 120 2.5% 0.86 (0.79, 0.94)	Study 38	101 22	7 346	363	2.0%	0.47 [0.40, 0.54]	<u> </u>			
Study 59 237 425 240 424 2.3% 0.99 [0.87, 1.11] Study 50 201 225 175 242 2.4% 1.05 [0.95, 1.16] Study 21 131 175 166 175 2.25% 0.86 [0.79, 0.84] - Study 29 132 154 152 176 2.6% 0.94 [0.86, 1.03] - Study 99 232 308 134 152 2.6% 0.86 [0.78, 0.93] - Study 99 265 363 134 152 2.6% 0.86 [0.78, 0.93] - Study 87 127 149 140 151 2.6% 0.82 [0.81, 0.86] - Study 87 127 149 140 151 2.6% 0.92 [0.87, 1.01] - Study 88 159 179 159 178 2.7% 0.99 [0.92, 1.07] - Study 93 2.66 337 2.7% 0.99 [0.92, 1.07] - - Study 51 169 2.00 281 300 2.7% 0.93 [0.86, 1.01] - <tr< td=""><td>Study 83</td><td>65 7</td><td>9 67</td><td>79</td><td>2.1%</td><td>0.97 [0.84, 1.11]</td><td></td></tr<>	Study 83	65 7	9 67	79	2.1%	0.97 [0.84, 1.11]				
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Study 59	237 42	5 240	424	2.3%	0.99 [0.87, 1.11]	-			
Study 21 131 175 166 175 2.5% 0.79 [0.72, 0.87]	Study 50	201 26	5 175	242	2.4%	1.05 (0.95, 1.16)	+			
Study 69 99 120 115 120 2.5% 0.86 [0.79, 0.94] Study 35 260 363 271 367 2.6% 0.94 [0.86, 1.03] Study 99 232 308 134 152 2.6% 0.99 [0.91, 1.08]	Study 21	131 17	5 166	175	2.5%	0.79 [0.72, 0.87]	-			
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Study 29 132 154 152 176 2.6% 0.99 [0.91, 1.08] Study 99 232 308 134 152 2.6% 0.85 [0.78, 0.93]	Study 35	260 36:	3 271	357	2.6%	0.94 [0.86, 1.03]	-			
Study 99 232 308 134 152 2.6% 0.85 [0.78, 0.93] Study 99 265 363 134 152 2.6% 0.83 [0.76, 0.90] Study 12 132 163 215 234 2.6% 0.83 [0.76, 0.90] Study 87 127 149 140 151 2.6% 0.93 [0.85, 1.00] Study 80 159 179 159 178 2.7% 0.99 [0.92, 1.07] Study 80 169 179 159 178 2.7% 0.99 [0.94, 1.07] Study 91 266 337 2.77 300 2.7% 0.93 [0.84, 1.00] Study 91 169 200 281 300 2.7% 0.93 [0.84, 1.00] Study 91 162 171 161 172 2.8% 1.01 [0.96, 1.07] Study 66 278 311 284 312 2.8% 0.98 [0.95, 1.04] Study 12 182 188 183 194 2.9	Study 29	132 15	152	176	2.6%	0.99 [0.91, 1.08]	+			
Study 99 265 363 134 152 2.6% 0.03 0.76 0.90 Study 12 132 163 215 234 2.6% 0.88 0.81 0.96 Study 97 127 149 140 151 2.6% 0.92 0.85 1.00 Study 97 127 149 140 151 2.6% 0.92 0.85 1.00 Study 93 266 337 2.77 300 2.7% 0.99 0.92 1.07 Study 93 266 337 2.77 300 2.7% 0.99 0.92 1.07 Study 91 169 200 281 300 2.7% 0.90 0.84 0.96	Study 99	232 30	3 134	152	2.6%	0.85 (0.78, 0.93)	-			
Study 12 132 163 215 224 2.6% 0.56 [0.81, 0.96] Study 87 127 149 140 151 2.6% 0.92 [0.85, 1.00] Study 7 232 301 249 301 2.6% 0.92 [0.85, 1.00] Study 88 159 179 159 159 178 2.7% 0.99 [0.92, 1.07] Study 93 266 337 277 330 2.7% 0.94 [0.87, 1.01]	Study 99	265 36	3 134	152	2.6%					
Study 871271491401512.6%0.92 [0.85, 1.00]Study 72323012493012.6%0.93 [0.86, 1.01]Study 881591791591782.7%0.99 [0.92, 1.07]Study 932663372773302.7%0.94 [0.87, 1.01]Study 911692002813002.7%0.90 [0.84, 0.96]Study 553795034035002.7%0.90 [0.84, 0.96]Study 553795034035002.7%0.93 [0.86, 1.07]Study 553795034035002.7%0.99 [0.95, 1.04]Study 24383840402.8%1.00 [0.95, 1.05]Study 11a798040402.8%0.99 [0.93, 1.01]Study 522953203183342.9%0.97 [0.93, 1.01]Study 101821881831942.9%0.99 [0.95, 1.03]Study 522953203183342.9%0.97 [0.93, 1.01]Study 512442622402422.9%0.98 [0.95, 1.01]Study 512442624402.9%0.99 [0.95, 1.03]Study 512442624402.9%0.99 [0.95, 1.01]Study 512442624402.9%0.98 [0.97, 1.03]Study 512442644402.9%0.98 [0.97, 1.03]Study 51244264476 <t< td=""><td>Study 12</td><td>132 16</td><td>3 215</td><td>234</td><td>2.6%</td><td>0.88 [0.81 0.96]</td><td>-</td></t<>	Study 12	132 16	3 215	234	2.6%	0.88 [0.81 0.96]	-			
Study 571211011260.030.080.040.07Study 932663372773302.7%0.990.92, 1.07]Study 932663372773302.7%0.940.08Study 704285764295782.7%1.000.94, 1.07]Study 911692002813002.7%0.900.94, 1.07]Study 911692002813002.7%0.930.981.00]Study 553795034035002.7%0.930.981.00]Study 662783112843122.8%0.980.931.03]Study 24383840402.8%0.990.95, 1.04]Study 101821881831942.9%1.030.98, 1.07]Study 442512702592702.9%0.97(0.93, 1.01]Study 522953203183342.9%0.99(0.95, 1.03]Study 512442622402422.9%0.94(0.97, 1.03]Study 681101121131132.9%0.98(0.97, 1.03]Study 911631371392.9%1.00(0.97, 1.03]Study 141611611803.0%1.00(0.97, 1.03]Study 925165264764773.0%0.98(0.97, 1.03]St	Study 87	127 14	A 140	151	2.6%					
Study 88 159 179 159 178 120% 0.001 0.00	Study 7	232 30	249	301	2.6%		-			
Study 03 266 337 277 330 2.7% 0.94 [0.87, 1.01] Study 70 428 576 429 578 2.7% 0.90 [0.84, 0.96] - Study 91 169 200 281 300 2.7% 0.90 [0.84, 0.96] - Study 55 379 503 403 500 2.7% 0.90 [0.84, 0.96] - Study 55 379 503 403 500 2.7% 0.90 [0.84, 0.96] - Study 55 379 503 403 500 2.7% 0.90 [0.84, 0.96] - Study 55 379 503 403 500 2.7% 0.90 [0.88, 1.00] - Study 41 162 171 161 172 2.8% 1.00 [0.95, 1.05] - Study 14 188 38 40 40 2.8% 0.99 [0.95, 1.04] - Study 10 182 188 183 194 2.9% 0.97 [0.93, 1.01] - Study 41 241 251 270 259 270 2.9% 0.94	Study 88	159 17	, 150	178	2.0%	0.00 [0.00, 1.07]	4			
Study 00 428 576 429 578 2.7% 1.00 [0.94, 1.07] Study 91 169 200 281 300 2.7% 0.90 [0.84, 0.96]	Study 93	266 33	7 777	330	2.7%	0.00 [0.02, 1.01]	-			
Study 911692002813002.7%0.900.984, 0.96]Study 553795034035002.7%0.930.88, 1.00]Study 562783112843122.8%0.980.931.03]Study 24383840402.8%0.990.95, 1.04]Study 101821881831942.9%0.97[0.93, 1.01]Study 442512702592702.9%0.97[0.93, 1.01]Study 522953203183342.9%0.99[0.95, 1.03]Study 512442622402422.9%0.94[0.91, 0.97]Study 512442622402.9%0.98[0.97, 1.03]Study 11b1341361371392.9%1.00[0.97, 1.03]Study 141611611801803.0%1.00[0.99, 1.01]Total (95% CI)93838920100.0%0.89[0.86, 0.93]Total events70357338Heterogeneity: Tau"= 0.01; Chi"= 975.97, df = 47 (P < 0.00001); I"= 95%	Study 70	428 57	3 429	578	2.7%		4			
Study 553795034035002.7%0.930.880.001Study 311621711611722.8%1.010.961.07Study 662783112843122.8%0.980.931.03Study 24383840402.8%1.00[0.95, 1.05]Study 11a798040402.8%0.99[0.95, 1.04]Study 101821881831942.9%0.97[0.93, 1.01]Study 442512702592702.9%0.97[0.93, 1.01]Study 522953203183342.9%0.97[0.93, 1.01]Study 512442622402422.9%0.94[0.91, 0.97]Study 681101121131132.9%0.98[0.95, 1.01]Study 80c5165264764773.0%0.98[0.97, 1.00]Study 141611611803.0%1.00[0.99, 1.01]Total events70357338Heterogeneity: Tau ² = 0.01; Chi ² = 975.97, df = 47 (P < 0.00001); I ² = 95%1.020.51.2Total events70357338Heterogeneity: Tau ² = 0.01; Chi ² = 975.97, df = 47 (P < 0.00001); I ² = 95%1.020.51.2Favours supportFavours usual care	Study 91	169 20	281	300	2.7%	0.90 [0.84, 0.96]	-			
Study 31 162 171 161 172 2.8% 1.01 [0.96, 1.07] Study 66 278 311 284 312 2.8% 0.98 [0.93, 1.03] Study 24 38 38 40 40 2.8% 1.00 [0.95, 1.04] Study 11a 79 80 40 40 2.8% 0.99 [0.95, 1.04] Study 10 182 188 183 194 2.9% 1.03 [0.98, 1.07] Study 52 295 320 318 334 2.9% 0.97 [0.93, 1.01] - Study 52 295 320 318 334 2.9% 0.97 [0.93, 1.01] - Study 51 244 262 240 242 2.9% 0.94 [0.91, 0.97] - Study 68 110 112 113 113 2.9% 0.98 [0.95, 1.01] - Study 89c 516 526 476 477 3.0% 0.98 [0.97, 1.00] - Study 14 161 161 180	Study 55	379 50	403	500	2.7%		-			
Study 66 278 311 284 312 2.8% 0.98 [0.93, 1.03] Study 24 38 38 40 40 2.8% 1.00 [0.95, 1.04] Study 11a 79 80 40 40 2.8% 0.99 [0.95, 1.04] Study 10 182 188 183 194 2.9% 1.03 [0.98, 1.07] Study 44 251 270 259 270 2.9% 0.97 [0.93, 1.01] Study 52 295 320 318 334 2.9% 0.97 [0.93, 1.01] Study 51 244 262 240 242 2.9% 0.99 [0.95, 1.03] Study 68 110 112 113 113 2.9% 0.98 [0.97, 1.03] Study 80c 516 526 476 477 3.0% 0.98 [0.97, 1.00] Study 14 161 161 180 3.0% 1.00 [0.99, 1.01] 1.01 Study 80c 516 526 476 477 3.0% 0.89 [0.86, 0.93] 1.01 Study 14 161 161 180 3.0% 1.00 [Study 33	162 17	, 400 161	172	2.1%		+			
Study 024 38 38 40 2.0% $1.00[0.95, 1.05]$ Study 11a 79 80 40 2.8% $0.99[0.95, 1.04]$ Study 10 182 188 183 194 2.9% $0.97[0.93, 1.01]$ Study 44 251 270 259 270 2.9% $0.97[0.93, 1.01]$ Study 52 295 320 318 334 2.9% $0.97[0.93, 1.01]$ Study 51 244 262 240 242 2.9% $0.94[0.91, 0.97]$ Study 68 110 112 113 113 2.9% $0.98[0.95, 1.03]$ Study 68 110 112 113 1.39 2.9% $0.94[0.91, 0.97]$ Study 68 110 112 113 1.39 2.9% $0.98[0.95, 1.01]$ Study 11b 134 136 137 139 2.9% $1.00[0.97, 1.03]$ Study 124 161 161 180 3.0% $1.00[0.99, 1.01]$ $0.29, 0.5$ 1.02 Total events 7035 7338 7338 $0.$	Study 66	278 31	284	312	2.0%	0.98 [0.93, 1.03]	4			
Study 11a 79 80 40 2.8% 0.99 [0.95, 1.04] Study 10 182 188 183 194 2.9% 0.97 [0.93, 1.07] Study 44 251 270 259 270 2.9% 0.97 [0.93, 1.01] Study 52 295 320 318 334 2.9% 0.97 [0.93, 1.01] - Study 51 244 262 240 242 2.9% 0.99 [0.95, 1.03] - Study 51 244 262 240 242 2.9% 0.94 [0.91, 0.97] - Study 10 132 113 113 2.9% 0.98 [0.95, 1.01] - Study 51 244 262 240 242 2.9% 0.98 [0.97, 1.03] - Study 88 110 112 113 113 2.9% 1.00 [0.97, 1.03] - Study 14 161 161 180 3.0% 1.00 [0.99, 1.01] - Total (95% CI) 9383 8920 100.0% 0.89 [0.86, 0.93] - - Total events 7035 7338 <td>Study 28</td> <td>38 3</td> <td>204</td> <td>40</td> <td>2.0%</td> <td></td> <td>+</td>	Study 28	38 3	204	40	2.0%		+			
Study 10 182 188 184 194 2.9% 1.03 [0.88, 1.07] Study 44 251 270 259 270 2.9% 0.97 [0.93, 1.01] Study 52 295 320 318 334 2.9% 0.97 [0.93, 1.01] Study 52 295 320 318 334 2.9% 0.97 [0.93, 1.01] Study 51 244 262 240 242 2.9% 0.94 [0.91, 0.97] Study 68 110 112 113 113 2.9% 0.98 [0.95, 1.01] Study 11b 134 136 137 139 2.9% 0.98 [0.97, 1.00] Study 14 161 161 180 3.0% 1.00 [0.99, 1.01] Total (95% Cl) 9383 8920 100.0% 0.89 [0.86, 0.93] Total events 7035 7338 1.00 [0.99, 1.01] 1.02 0.5 2.5 5 Test for overall effect: Z = 5.84 (P < 0.00001) V 0.89 0.80 0.5 2.5 5	Study 11a	79 8) 40 1 40	40	2.8%	0.99 [0.95, 1.04]	4			
Study 10 102 103 103 2.5 % 1.05 (0.05, 1.01) Study 44 251 270 2.9 % 0.97 [0.93, 1.01] Study 52 295 320 318 334 2.9 % 0.97 [0.93, 1.01] Study 11a 247 253 40 40 2.9 % 0.97 [0.93, 1.01] - Study 11a 247 253 40 40 2.9 % 0.99 [0.95, 1.03] - Study 51 244 262 240 242 2.9 % 0.94 [0.91, 0.97] - Study 68 110 112 113 113 2.9 % 0.98 [0.95, 1.01] - Study 11b 134 136 137 139 2.9 % 1.00 [0.97, 1.03] - Study 14 161 161 180 3.0 % 1.00 [0.99, 1.01] - Total events 7035 7338 -	Study 10	182 18	2 183	194	2.0%		-			
Study 47 201 210	Study 18 Study 44	251 271	, 100 1 259	270	2.0%	0.97 [0.93, 1.01]	-			
Study 51 253 253 40 40 2.9% 0.99 [0.95, 1.03] Study 51 244 262 240 242 2.9% 0.94 [0.91, 0.97] Study 68 110 112 113 113 2.9% 0.98 [0.95, 1.01] Study 68 110 112 113 113 2.9% 0.98 [0.97, 1.03] Study 89c 516 526 476 477 3.0% 0.98 [0.97, 1.00] Study 14 161 161 180 3.0% 1.00 [0.99, 1.01]	Study 52	295 321	, 200 I 318	334	2.0%	0.37 [0.33, 1.01]	-			
Study 110 241 250 100 100 100, 100, 100, 100, 100, 100, 100, 100,	Study 52 Study 11a	200 02	2 40	40	2.0%	0.01 [0.00, 1.01]	4			
Study 51 244 254 255 0.54 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1 0.55 1	Study 114 Study 51	241 20	, 40 , 240	242	2.0%	0.00 [0.00, 1.00]	-			
Study 00 110 112 110 123.4 0.00	Study 51 Study 68	110 11	240	113	2.3%	0.34 [0.31, 0.37]	_			
Study 110 134 136 137 135 2.3 % 1.00 [0.37, 1.00] Study 89c 516 526 476 477 3.0% 0.98 [0.97, 1.00] Study 14 161 161 180 3.0% 1.00 [0.99, 1.01] Total (95% CI) 9383 8920 100.0% 0.89 [0.86, 0.93] Total events 7035 7338 Heterogeneity: Tau ² = 0.01; Chi ² = 975.97, df = 47 (P < 0.00001); l ² = 95% 0.2 0.5 1 2 5 Test for overall effect: Z = 5.84 (P < 0.00001)	Study 55 Study 11h	134 13	5 137	120	2.370		Ļ			
Study 53c 510 520 410 411 50.00 0.50 [0.57, 1.55] Study 14 161 161 180 3.0% 1.00 [0.99, 1.01] Total (95% CI) 9383 8920 100.0% 0.89 [0.86, 0.93] Total events 7035 7338 Heterogeneity: Tau ² = 0.01; Chi ² = 975.97, df = 47 (P < 0.00001); l ² = 95% 0.2 0.5 1 2 5 Test for overall effect: Z = 5.84 (P < 0.00001)	Study 115 Study 89c	516 52	5 137 S 176	477	2.370					
Total (95% CI) 9383 8920 100.0% 0.89 [0.86, 0.93] Total events 7035 7338 Heterogeneity: Tau ² = 0.01; Chi ² = 975.97, df = 47 (P < 0.00001); I ² = 95% 0.2 0.5 1 2 5 Test for overall effect: Z = 5.84 (P < 0.00001)	Study 050 Study 14	161 16) 470 I 190	477	2.0%					
Total (95% CI) 9383 8920 100.0% 0.89 [0.86, 0.93] Total events 7035 7338 Heterogeneity: Tau ² = 0.01; Chi ² = 975.97, df = 47 (P < 0.00001); I ² = 95% 0.2 0.5 1 2 5 Test for overall effect: Z = 5.84 (P < 0.00001)	Study 14	101 10	100	100	5.070	1.00 [0.88, 1.01]				
Total events 7035 7338 Heterogeneity: Tau ² = 0.01; Chi ² = 975.97, df = 47 (P < 0.00001); l ² = 95% 0.2 0.5 1 2 5 Test for overall effect: Z = 5.84 (P < 0.00001)	Total (95% CI)	938	3	8920	100.0%	0.89 [0.86, 0.93]	•			
Heterogeneity: Tau ² = 0.01; Chi ² = 975.97, df = 47 (P < 0.00001); I ² = 95% I	Total events	7035	7338							
Test for overall effect: Z = 5.84 (P < 0.00001) 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	Heterogeneity: Tau² =	0.01; Chi² = 9;	'5.97, df =	47 (P <	0.00001)	; I² = 95%				
	Test for overall effect:	Z = 5.84 (P < 0	.00001)				Favours support Favours usual care			

ANSWERS

In figure 1, study 61 is a multiarm trial and also a cluster trial and although it has been adjusted for clustering, the usual care arm has not been split in half and so participants are double counted. Also the number of events in the support arm in the first entry is incorrect but this difficult to see without access to the trial report.

Figure 3: outcome 1

Supp	Support Usual		care		Risk Ratio	Risk Ratio		
Study or Subgroup Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl		
Study 72 1	27	8	25	0.1%	0.12 [0.02, 0.86]			
Study 90 3	50	35	50	0.2%	0.09 [0.03, 0.26]	•		
Study 32 11	67	17	67	0.4%	0.65 [0.33, 1.28]			
Study 67 26	80	11	30	0.6%	0.89 [0.50, 1.56]			
Study 80 10	26	17	26	0.6%	0.59 [0.34, 1.03]			
Study 74 12	21	13	20	0.7%	0.88 [0.54, 1.44]			
Study 8 31	221	29	189	0.8%	0.91 [0.57, 1.46]			
Study 7 40	301	32	301	0.9%	1.25 [0.81, 1.93]			
Study 22 25	132	43	126	0.9%	0.55 [0.36, 0.85]			
Study 73 15	30	22	30	0.9%	0.68 [0.45, 1.04]			
Study 4 25	94	41	94	1.0%	0.61 [0.41, 0.92]			
Study 88 34	179	42	178	1.0%	0.81 [0.54, 1.20]			
Study 63 26	69	33	81	1.0%	0.92 [0.62, 1.38]			
Study 29 36	154	41	176	1.0%	1.00 [0.68, 1.49]			
Study 34 45	292	51	294	1.1%	0.89 [0.62, 1.28]			
Study 97 30	79	46	107	1.2%	0.88 [0.62, 1.26]			
Study 54 73	315	45	157	1.3%	0.81 [0.59, 1.11]			
Study 12 49	163	100	234	1.6%	0.70 [0.53, 0.93]			
Study 94 21	26	21	27	1.6%	1.04 [0.79, 1.37]			
Study 18 45	90	51	75	1.7%	0.74 [0.57, 0.95]			
Study 83 43	78	51	78	1.7%	0.84 [0.65, 1.09]			
Study 11a 50	80	30	40	1.8%	0.83 [0.65, 1.07]			
Study 31 68	171	82	172	1.8%	0.83 [0.65, 1.06]			
Study 95 23	30	39	42	2.0%	0.83 [0.67, 1.02]			
Study 58 81	135	79	135	2.1%	1.03 [0.84, 1.25]			
Study 11a 173	253	30	40	2.1%	0.91 [0.75, 1.11]	-		
Study 13 39	58	52	57	2.1%	0.74 [0.61, 0.90]			
Study 59 147	425	130	424	2.1%	1.13 [0.93, 1.37]			
Study 25 129	303	118	302	2.2%	1.09 [0.90, 1.32]			
Study 21 84	175	110	175	2.2%	0.76 [0.63, 0.93]			
Study 91 86	200	166	300	2.2%	0.78 [0.64, 0.94]	-		
Study 76 49	65	55	(1	2.2%	0.97 [0.81, 1.17]	Ť		
Study 37 42	49	38	48	2.2%	1.08 [0.90, 1.30]			
Study 55 177	503	235	500	2.5%	0.75 [0.64, 0.87]			
Study 87 101	149	108	151	2.5%	0.95 [0.82, 1.10]			
Study 11b 90	136	108	139	2.5%	0.85 [0.73, 0.99]			
Study 14 116	101	113	180	2.5%	1.15 [0.99, 1.33]			
Study 65 /6	100	80	100	2.5%	0.95 [0.82, 1.10]			
Study 51 153	291	171	269	2.6%	0.83 [0.72, 0.95]			
Study 75 119	168	115	160	2.6%	0.99 [0.86, 1.13]	I		
Study 08 80	112	93	113	2.0%	0.93 [0.82, 1.07]			
Study 24 33	38	40	40	2.0%	0.87 [0.76, 0.99]			
Study 47 142	228	207	300	2.1%	0.86 [0.76, 0.97]			
Study 50 188	200	102	242	2.1%	1.06 [0.94, 1.19]	Ţ		
Study 10 137	188	149	194	2.8%				
220 Study 61 200	303 750	220	35/ 006	∠.Ծ%0 ጋ.০০∕	0.90[0.85, 1.07]	(-)		
Siduy 01 200	709	202	900	2.070	0.00 [0.00, 0.02]			
Study 0 200	400	280	400	2.8%				
Otudy70 325 Otude 41 300	010	343 967	510	2.970	0.90 [0.80, 1.05]	Ļ		
Study 61 550	490	307 200	010	3.U70 3.10/	1.03 [0.83, 1.11]	1		
Oluuy 01 552 Oluuy 66 550	00/	008 264	310 242	3.170 3.407	0.34 [0.88, 1.01]	Ļ		
	317	204	312	ა. 1% ე ე ი /	0.98 [0.92, 1.05]			
oluuy 04 210	231	217	223	3.270	0.94 [0.90, 0.98]			
Total (95% CI)	10850	0015	10858	100.0%	0.89 [0.85, 0.93]	•		
Hotorogonoity Tours 5482	8 - 047	6217 65 df - 71	2/0 - 0	000043-12	- 76W			
Test for overall effect: Z = 4.89	r = 217. (P ≤ 0.00	oo, ut = 5: 0001)	∠(⊢ < U.	00001); I*	- 10%	0.05 0.2 1 5 20		

In figure 2, study 3 is an outlier. The trial report was accessed and the data checked. The total in the usual care arm was incorrect, it should have been 33 not 157

Figure 4: outcome 2

	Suppo	ort	Usual care			Risk Ratio	Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl			
Study 90	3	50	33	50	0.1%	0.09 [0.03, 0.28]	<u>←</u>			
Study 72	5	27	16	25	0.2%	0.29 [0.12, 0.67]	<			
Study 45	6	19	15	19	0.3%	0.40 [0.20, 0.81]				
Study 89a	6	22	20	23	0.3%	0.31 [0.16, 0.63]				
Study 79	17	68	23	33	0.5%	0.36 [0.22, 0.57]				
Study 3	20	33	26	157	0.6%	3.66 [2.34, 5.72]				
Study 74	15	21	17	20	0.9%	0.84 [0.61, 1.17]				
Study 67	36	80	26	30	1.1%	0.52 [0.39, 0.69]				
Study 63	38	69	48	81	1.1%	0.93 [0.70, 1.23]				
Study 89b	31	63	52	59	1.2%	0.56 [0.43, 0.73]				
Study 32	35	67	63	67	1.4%	0.56 [0.44, 0.70]				
Study 8	68	221	110	189	1.4%	0.53 [0.42, 0.67]				
Study 81	59	148	108	150	1.5%	0.55 [0.44, 0.69]				
Study 97	50	79	70	107	1.5%	0.97 [0.78, 1.20]				
Study 34	109	292	123	294	1.6%	0.89 [0.73, 1.09]				
Study 4	61	94	71	94	1.7%	0.86 [0.71, 1.04]				
Study 54	164	315	93	157	1.9%	0.88 [0.74, 1.04]				
Study 38	101	227	346	363	2.0%	0.47 [0.40, 0.54]	<u> </u>			
Study 83	65	79	67	79	2.1%	0.97 [0.84, 1.11]	_			
Study 59	237	425	240	424	2.3%	0.99 [0.87, 1.11]	-			
Study 50	201	265	175	242	2.4%	1.05 (0.95, 1.16)				
Study 21	131	175	166	175	2.5%	0.79 [0.72, 0.87]				
Study 69	99	120	115	120	2.5%	0.86 [0.79, 0.94]	-			
Study 35	260	363	271	357	2.6%	0.94 [0.86, 1.03]	-			
Study 29	132	154	152	176	2.6%	0.99 [0.91, 1.08]	+			
Study 99	232	308	134	152	2.6%	0.85 (0.78, 0.93)	-			
Study 99	265	363	134	152	2.6%	0.83 [0.76, 0.90]	-			
Study 12	132	163	215	234	2.6%	0.88 [0.81, 0.96]	-			
Study 87	127	149	140	151	2.6%	0.92 [0.85, 1.00]				
Study 7	232	301	249	301	2.6%	0.93 [0.86, 1.01]	~			
Study 88	159	179	159	178	2.7%	0.99 [0.92, 1.07]	+			
Study 93	266	337	277	330	2.7%	0.94 [0.87, 1.01]	-			
Study 70	428	576	429	578	2.7%	1.00 [0.94, 1.07]	+			
Study 91	169	200	281	300	2.7%	0.90 [0.84, 0.96]	-			
Study 55	379	503	403	500	2.7%	0.93 [0.88, 1.00]	-			
Study 31	162	171	161	172	2.8%	1.01 [0.96, 1.07]	+			
Study 66	278	311	284	312	2.8%	0.98 [0.93, 1.03]	-			
Study 24	38	38	40	40	2.8%	1.00 [0.95, 1.05]	+			
Study 11a	79	80	40	40	2.8%	0.99 [0.95, 1.04]	+			
Study 10	182	188	183	194	2.9%	1.03 [0.98, 1.07]	+			
Study 44	251	270	259	270	2.9%	0.97 [0.93, 1.01]	-			
Study 52	295	320	318	334	2.9%	0.97 [0.93, 1.01]	-			
Study 11a	247	253	40	40	2.9%	0.99 [0.95, 1.03]	+			
Study 51	244	262	240	242	2.9%	0.94 [0.91, 0.97]	-			
Study 68	110	112	113	113	2.9%	0.98 [0.95, 1.01]	-			
Study 11b	134	136	137	139	2.9%	1.00 [0.97, 1.03]	+			
Study 89c	516	526	476	477	3.0%	0.98 [0.97, 1.00]	-			
Study 14	161	161	180	180	3.0%	1.00 [0.99, 1.01]				
Total (95% CI)		9383		8920	100.0%	0.89 [0.86, 0.93]	•			
Total events	7035		7338							
Heterogeneity: Tau² =	0.01; Chi	² = 975	5.97, df=	47 (P <	0.00001)	; I² = 95%				
Test for overall effect:	Z= 5.84 (P < 0.0	0001)	,			U.Z U.S I Z 5 Eavours support Eavours usual care			
							Favours support Favours usual care			

Practical Exercise 2 – Subgroup Analyses

Intervention X is a device which is available in two variations – X (a) and X (b).

- What concerns might you have about the interpretation of the following analyses of intervention X?
- What changes might you suggest to the analyses and the interpretation?

1 – Intervention X vs no intervention

1.1 Outcome A

	Intervent	tion X	No interve	ntion		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	
Study 1	20	77	34	81	39.9%	0.62 [0.39, 0.98]		
Study 2	4	60	12	60	7.2%	0.33 [0.11, 0.98]		
Study 3	31	115	26	119	40.3%	1.23 [0.78, 1.94]		
Study 4	7	47	14	46	12.6%	0.49 [0.22, 1.10]		
Total (95% CI)		299		306	100.0%	0.76 [0.57, 1.01]	•	
Total events	62		86					
Heterogeneity: Chi ² =	8.55, df = 3	3 (P = 0.						
Test for overall effect: Z = 1.88 (P = 0.06) 0.01 0.1 1 10 100 Favours intervention X Favours no intervention								

2 – Intervention X (a) vs no intervention

2.1 Outcome A

	Intervention X (a) No intervention				Risk Ratio		Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Fixed, 95% CI		IV, Fixed,	95% CI		
Study 3	31	115	26	119	100.0%	1.23 [0.78, 1.94]		-	-		
Total (95% CI)		115		119	100.0%	1.23 [0.78, 1.94]					
Total events	31		26								
Heterogeneity: Not ap Test for overall effect:	plicable Z=0.91 (P=	0.36)					0.01	0.1 1 Favours X (a)	Favours no	10 interve	100 ention

3 – Intervention X (b) vs no intervention

3.1 Outcome A

	Intervention	X (b)	No interve	ention		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Study 1	20	77	34	81	66.8%	0.62 [0.39, 0.98]	
Study 2	4	60	12	60	12.0%	0.33 [0.11, 0.98]	
Study 4	7	47	14	46	21.1%	0.49 [0.22, 1.10]	
Total (95% CI)		184		187	100.0%	0.55 [0.38, 0.79]	•
Total events	31		60				
Heterogeneity: Tau ² =	= 0.00; Chi ² = 1	.17, df=	2 (P = 0.58				
l est for overall effect:	Z = 3.18 (P =	0.001)				Favours X (b) Favours no intervention	

Main results

Overall, intervention X was not associated with a statistically significant change in outcome A. In a subgroup analysis it was found that intervention X (b) may be associated with a significant reduction in outcome A.

Authors' conclusions

This systematic review suggests that the use of intervention X (b) may be beneficial. However only a limited number of RCTs with rather small sample sizes were available. Further RCTs on intervention X are needed.

ANSWERS

The data analyses are inappropriately structured. Fixed and random effects models have been inconsistently applied. The analyses should be restructured so that X (a) vs no intervention and intervention X (b) vs no intervention are presented as subgroups of the intervention X vs no intervention comparison, rather than as individual comparisons. This will allow for tests for subgroup differences to be applied and appropriate conclusions to be drawn about subgroup differences. The appropriate model should be used, following the methods specified for data synthesis in the protocol.

Appropriately structured forest plot and improved interpretation:

1 - Intervention X vs no intervention

1.1 Outcome A



Main results

The effect of intervention X on reducing outcome A was uncertain due to the low quality of the evidence (RR 0.67, 95% CI 0.39 to 1.14; 605 participants; 4 studies). Subgroup analysis by type of intervention X provided limited evidence that X (b) may lower the risk of outcome A.

Authors' conclusions

This systematic review has identified limited evidence on the effect of intervention X. We have not been able to identify convincing direct evidence of superiority of X (b) over X (a). We found a limited number of RCTs with small sample sizes. Further RCTs on intervention X are needed.

Practical Exercise 3 – Data Entry Errors

A review author wishes to assess the effect of an 'Exercise' intervention on the outcome 'Pain'.

Consider the following Forest Plot and the table from the published paper Gilbert 1995 from which data was extracted. Can you spot any data extraction errors?

<u> Original Study Data – Gilbert 1995</u>

	Group 1 Bed rest and	Group 2	Group 3	Group 4
	exercise and education (n = 50)	Exercise and education (n = 41)	Bed rest (n = 47)	Control (n = 48)
Improvement	22.27 (5.14)	23.30 (6.92)	21.66 (6.54)	21.54 (6.31)
Activities	24.35 (8.75)	21.34 (9.22)	24.34 (10.04)	20.90 (8.46)
Pain	23.77 (5.22)	25.94 (7.47)	24.15 (7.12)	22.88 (5.88)

Note: Lower total scores indicate a better clinical result

Forest Plot

	Experimental Control						Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% Cl	
Brown 2003	19.1	21	145	16	22	146	12.2%	3.10 [-1.84, 8.04]		
Gilbert 1995	23.77	5.88	65	22.88	5.22	65	81.3%	0.89 [-1.02, 2.80]		
Smith 2015	31	17.21	42	24	17.21	62	6.5%	7.00 [0.26, 13.74]		
Total (95% CI)			252			273	100.0%	1.56 [-0.17, 3.28]	•	
Heterogeneity: Chi ² = 3.35, df = 2 (P = 0.19); I ² = 40% -20 -10 0 10 20 Test for overall effect: Z = 1.77 (P = 0.08) Favours [experimental] Favours [control]										

ANSWERS

- Sample sizes in the forest plot are incorrect they should read 50 and 48 (not 65 and 65)
- The standard deviations are mixed up (experimental SD is 5.22, control is 5.88)
- The wrong intervention group data has been extracted from the paper. Authors should have extracted Group 2 data (Exercise + Education) and not Group 1 data (Exercise + Education and Bed Rest). If we compare Group 1 data with control, we cannot know if the effect is due to exercise + education, or to bed rest.

Practical Exercise 4 – Outliers

Analysis - Anxiety

	Expe	Experimental Control					:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl	ABCDEFGH
Study 1	0.07	0.3	69	-0.04	0.3	5	13.6%	0.36 [-0.55, 1.27]		
Study 2	-1.02	4.77	50	-5.93	4.57	52	14.8%	1.04 [0.63, 1.46]	-	•?•••
Study 3	3.02	0.08	62	2.59	0.08	40	13.8%	5.33 [4.49, 6.18]		•?•••
Study 4	-0.45	1.29	11	-1.11	1.45	9	13.6%	0.46 [-0.43, 1.36]		•••••
Study 5	-7.07	5.05	28	-7.85	3.59	26	14.6%	0.17 [-0.36, 0.71]	+	
Study 6	-0.5	4.3	37	-0.9	4.2	69	14.9%	0.09 [-0.31, 0.49]	+	•?•••
Study 7	0.31	3.08	31	0.06	2.85	41	14.7%	0.08 [-0.38, 0.55]	+	•?•••
Total (95% CI)			288			242	100.0%	1.05 [0.04, 2.07]	◆	
Heterogeneity: Tau ^z = 1.77; Chi ^z = 137.94, df = 6 (P < 0.00001); I ^z = 96%										
Test for overall effect: Z = 2.03 (P = 0.04)									Favours (control) Favours (experiment	1

Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Sample Size

(H) Other bias

Results > Effects of Intervention

Overall, a large effect was observed for intervention participants (n = 288) compared to usual care (n = 242) in the pooled analysis of Anxiety for all seven studies (SMD, 1.05, 95% CI, 0.04 to 2.07) (Figure 7). Study 3 contributed the largest effect difference and this may be due to potential bias in the timing of the assessment prior to initiation of the intervention. Anxiety is usually high in anticipation of treatment and this change in effect may be due to the reduction in this anticipatory anxiety rather than as a result of the intervention. However, our confidence in this effect is low as high heterogeneity based on the l² test that was statistically significant (l² = 96%, Chi2 = 137.94, df = 6, p < 0.001). We downgraded the quality of evidence for anxiety by two levels (very serious (-2)) for risk of bias in study design given that 4 of the 7 studies had selective outcome reporting and 5 of the 7 studies had unclear allocation concealment, and we downgraded one more level (-1) due to important inconsistency (Summary of findings table 1).

Practical Exercise Questions

- 1. Which study would you consider an 'Outlier' in this Forest Plot?
- 2. Have the authors addressed this outlier in their description/interpretation of the result?
- 3. Is the authors interpretation of this Forest Plot sufficient and appropriate? If so, why? If not, why not?

Practice Exercise Answers

- 1. Study 3
- 2. Yes They attribute it to the timing of the assessment prior to initiation of the intervention, leading to a 'reduction in this anticipatory anxiety'. They also downgrade the quality/certainty of the result for inconsistency.
- 3. No even with this explanation, it is a very notable outlier, and 96% is a very difficult level of heterogeneity to accept. Authors first instinct was to assume that the data was correct and that the outlier can be explained. Editors should still question this high level of heterogeneity and conduct our investigation?

In this case, we did question it. As it turned out, authors have entered the Standard Deviations incorrectly (They should read 0.8, not 0.08). When the correct SDs are entered, the graph would appear as follows;



Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Sample Size

(H) Other bias

Note that the I^2 has dropped from 96% to 58%.

Learning Point: Don't automatically accept outliers/high heterogeneity just because the authors think they can explain it