APPENDIX 14B: CLINICAL EVIDENCE FOREST PLOTS: PSYCHOLOGICAL AND PSYCHOSOCIAL

INTERVENTIONS

| | OLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 AND YOUNGER2 |
|--------------|---|
| 1. week | Cognitive behavioural therapy (CBT) versus treatment as usual (TAU): 26 as post-treatment |
| 2. | CBT versus treatment as usual (TAU): 52 weeks' follow-up2 |
| 3. | CBT versus EPPIC treatment as usual (TAU): 14 weeks post-treatment3 |
| 4. | CBT versus EPPIC treatment as usual (TAU): 52 weeks' follow-up4 |
| 5. partic | CBT versus EPPIC treatment as usual (TAU) in acutely suicidal cipants: 10 weeks post-treatment5 |
| 6. partio | CBT versus EPPIC treatment as usual (TAU) in acutely suicidal cipants: 36 weeks' follow-up |
| 7. not a | CBT + clozapine versus clozapine in participants whose symptoms have dequately responded to treatment: 12 weeks post-treatment |
| 8. not a | CBT + clozapine versus clozapine in participants whose symptoms have dequately responded to treatment: 24 weeks' follow-up7 |
| 9. | Individual CBT versus family CBT: 52 weeks post-randomisation9 |
| 10. week | Individual and family CBT versus EPPICtreatment as usual (TAU): 30.33 as post-treatment9 |
| 11. (TAU | Any psychological intervention in addition to EPPIC treatment as usual J) versus EPPIC treatment as usual (TAU): post-treatment11 |
| | |

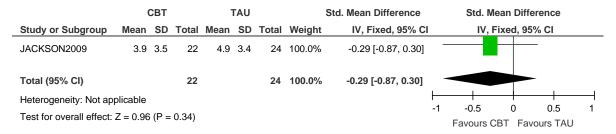
Abbreviations

| BDI | Beck Depression Inventory |
|-----------|---|
| BPRS (-P) | Brief Psychiatric Rating Scale (- Psychotic Subscale) |
| CBT | cognitive behavioural therapy |
| CDSS | Calgary Depression Scale for Schizophrenia |
| CGI | Clinical Global Impression scale |
| CI | confidence interval |
| EPPIC | Early Psychosis Prevention and Intervention Centre, Australia |
| QLS | Quality of Life Scale |
| SANS | Scale for Assessment of Negative Symptoms |
| SD | standard deviation |
| SOFAS | Social and Occupational Functioning Assessment Scale |
| TAU | treatment as usual |
| | |

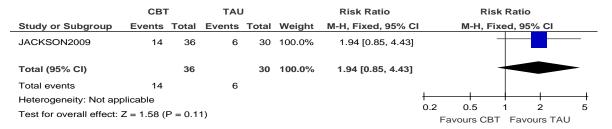
PSYCHOLOGICAL INTERVENTIONS IN CHILDREN AND YOUNG PEOPLE 25 YEARS AND YOUNGER

1. Cognitive behavioural therapy (CBT) versus treatment as usual (TAU): 26 weeks post-treatment

1.1 Mental state: depression (Calgary Depression Scale for Schizophrenia [CDSS])

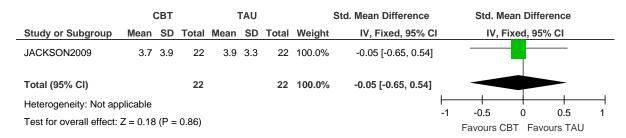


1.2 Leaving the study early for any reason



2. CBT versus treatment as usual (TAU): 52 weeks' follow-up

2.1 Mental state: depression (CDSS)

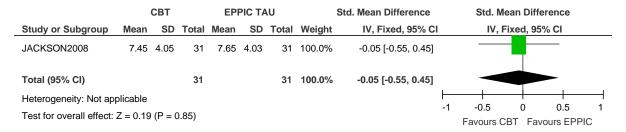


2.2 Leaving the study early for any reason

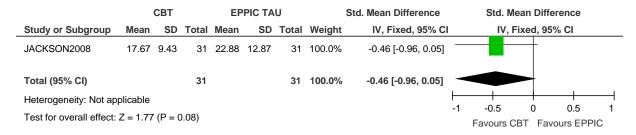


3. CBT versus EPPIC treatment as usual (TAU): 14 weeks posttreatment

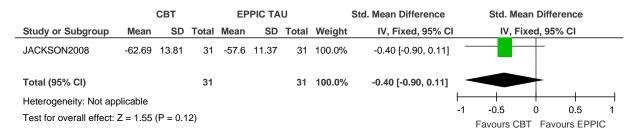
3.1 Mental state: positive symptoms (Brief Psychiatric Rating Scale Psychotic Subscale [BPRS-P])



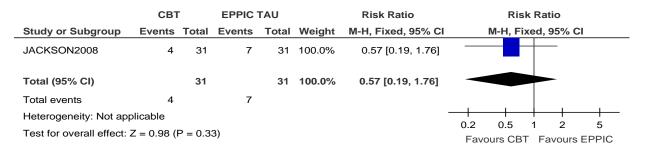
3.2 Mental state: negative symptoms (Scale for Assessment of Negative Symptoms [SANS])



3.3 Functioning: social (Social and Occupational Functioning Assessment Scale [SOFAS])



3.4 Leaving the study early for any reason



4. CBT versus EPPIC treatment as usual (TAU): 52 weeks' follow-up

4.1 Mental state: positive symptoms (BPRS-P)

| | | СВТ | | EPI | PIC TA | U | | Std. Mean Difference | | Std. Me | ean Diff | erence | |
|--------------------------|----------|--------|-------|------|--------|-------|--------|----------------------|----------|-------------------|--------------|-----------------|---------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | | IV, F | ixed, 95 | % CI | |
| JACKSON2008 | 7.2 | 4.08 | 31 | 7.55 | 4.76 | 31 | 100.0% | -0.08 [-0.58, 0.42] | | | | | |
| Total (95% CI) | | | 31 | | | 31 | 100.0% | -0.08 [-0.58, 0.42] | | | | - | |
| Heterogeneity: Not ap | plicable | | | | | | | | <u> </u> | | | | |
| Test for overall effect: | Z = 0.31 | (P = 0 | 0.76) | | | | | | -1 | -0.5 Favours C | 0 BT Fav | 0.5 ours EPP | 1 IC |

4.2 Mental state: negative symptoms (SANS)

| | | СВТ | | EP | PIC TA | U | | Std. Mean Difference | | Std. Me | an Diff | erence | |
|--------------------------|----------|--------|-------|-------|--------|-------|--------|----------------------|------------|-----------------|---------|-----------|----------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | | IV, F | ixed, 9 | 5% CI | |
| JACKSON2008 | 14.66 | 10.9 | 31 | 19.55 | 14.79 | 31 | 100.0% | -0.37 [-0.87, 0.13] | _ | | | | |
| Total (95% CI) | | | 31 | | | 31 | 100.0% | -0.37 [-0.87, 0.13] | - | | | | |
| Heterogeneity: Not ap | plicable | | | | | | | | <u></u> -1 | -0.5 | 0 | 0.5 | —— 1 |
| Test for overall effect: | Z = 1.45 | (P = 0 |).15) | | | | | | • | Favours Cl | - | vours EPP | IC . |

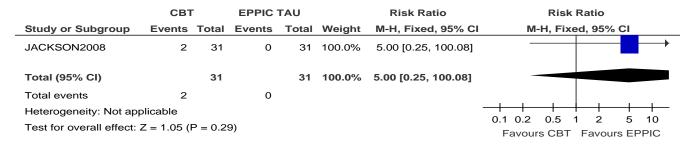
4.3 Functioning: social (SOFAS)

| | | CBT | | EP | PIC TA | U | | Std. Mean Difference | | Std. Me | ean Diff | erence | |
|--------------------------|----------|-----------|-------------|--------|--------|-------|--------|----------------------|----|-----------|----------|-------------|---------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | | IV, F | ixed, 95 | 5% CI | |
| JACKSON2008 | -64.21 | 15.18 | 31 | -62.91 | 15.18 | 31 | 100.0% | -0.08 [-0.58, 0.41] | | | | | |
| Total (95% CI) | | | 31 | | | 31 | 100.0% | -0.08 [-0.58, 0.41] | | | | > | |
| Heterogeneity: Not ap | plicable | | | | | | | ŀ | -1 | -0.5 | 0 | 0.5 | <u></u> |
| Test for overall effect: | Z = 0.33 | (P = 0.7) | 7 4) | | | | | | ٠, | Favours C | - | vours EPP | IC |

4.4 Relapse: number of participants hospitalised

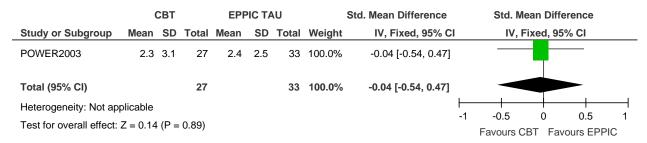
| | СВТ | Γ | EPPIC | TAU | | Risk Ratio | | Ri | sk Ratio | | |
|--------------------------|------------|---------|--------|-------|--------|--------------------|------------|-----------------|--------------|-------------|-----------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Fixed, 95% CI | | M-H, F | ixed, 95 | % CI | |
| JACKSON2008 | 12 | 30 | 8 | 27 | 100.0% | 1.35 [0.65, 2.80] | | _ | | | |
| Total (95% CI) | | 30 | | 27 | 100.0% | 1.35 [0.65, 2.80] | | - | | - | |
| Total events | 12 | | 8 | | | | | | | | |
| Heterogeneity: Not ap | plicable | | | | | | + | | + | + | + |
| Test for overall effect: | Z = 0.81 (| P = 0.4 | 2) | | | | 0.2 Fav | 0.5 vours CE | 1 BT Favo | 2 ours E | 5 PPIC |

4.5 Mortality: number of deaths by suicide

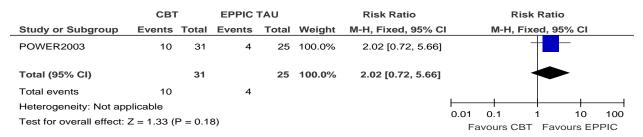


5. CBT versus EPPIC treatment as usual (TAU) in acutely suicidal participants: 10 weeks post-treatment

5.1 Quality of life (Quality of Life Scale [QLS])



5.2 Leaving the study early for any reason

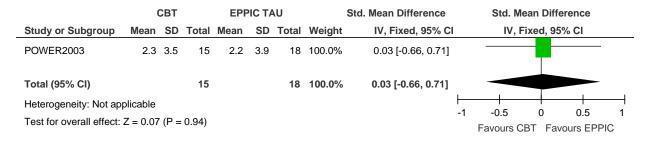


5.3 Mortality: number of deaths by suicide (assuming dropout did not die by suicide)

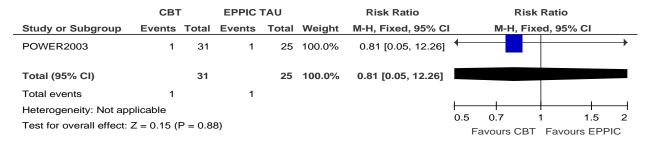
| | СВТ | Γ | EPPIC 1 | TAU | | Risk Ratio | | F | Risk | Ratio | | |
|--------------------------|------------|-------|---------|-------|--------|--------------------|----------|-----------------|------|-------------|--------------|----------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Fixed, 95% CI | | M-H, | Fixe | ed, 95% | CI | |
| POWER2003 | 0 | 31 | 0 | 25 | | Not estimable | | | | | | |
| Total (95% CI) | | 31 | | 25 | | Not estimable | | | | | | |
| Total events | 0 | | 0 | | | | | | | | | |
| Heterogeneity: Not app | olicable | | | | | | <u> </u> | | | | | |
| Test for overall effect: | Not applic | able | | | | | 0.5 F | 0.7 avours C | ВТ | i Favour | 1.5 s EPF | 2 PIC |

6. CBT versus EPPIC treatment as usual (TAU) in acutely suicidal participants: 36 weeks' follow-up

6.1 Quality of life (QLS)

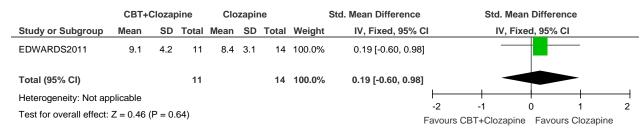


6.2 Mortality: number of deaths by suicide (assuming dropouts did not die by suicide)

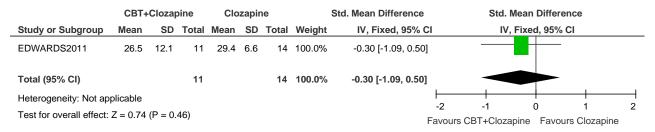


7. CBT + clozapine versus clozapine in participants whose symptoms have not adequately responded to treatment: 12 weeks post-treatment

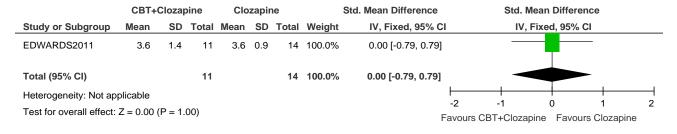
7.1 Mental state: positive symptoms (BPRS-P)



7.2 Mental state: negative symptoms (SANS)



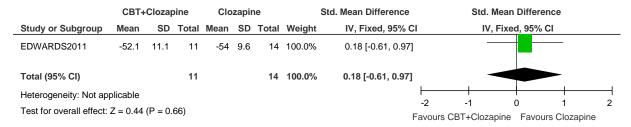
7.3 Global state (Clinical Global Impression [CGI] scale)



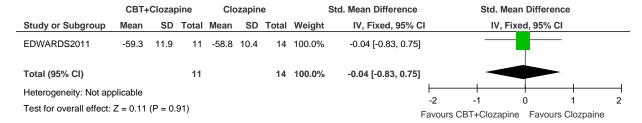
7.4 Mental state: depression symptoms (Beck Depression Inventory [BDI])

| | CBT+ | Clozap | oine | Clo | zapir | ne | | Std. Mean Difference | | Std. I | Mean Differ | ence | |
|--------------------------|----------|---------|-------|------|-------|-------|--------|----------------------|--------------|-----------------|-------------|------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | | IV, | Fixed, 95% | CI | |
| EDWARDS2011 | 22.5 | 9.6 | 11 | 18.1 | 5.5 | 14 | 100.0% | 0.56 [-0.25, 1.37] | | | | | |
| Total (95% CI) | | | 11 | | | 14 | 100.0% | 0.56 [-0.25, 1.37] | | | | | |
| Heterogeneity: Not ap | plicable | | | | | | | | <u> </u> | | + | + | |
| Test for overall effect: | Z = 1.37 | (P = 0. | 17) | | | | | F | -2 avours | -1 CBT+Cloza | pine Favo | ı urs Clozapi | 2 |

7.5 Functioning: social (SOFAS)

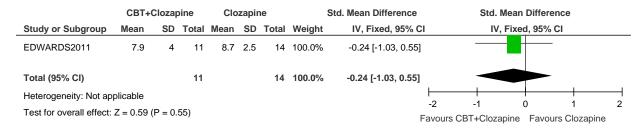


7.6 Quality of life (QLS)

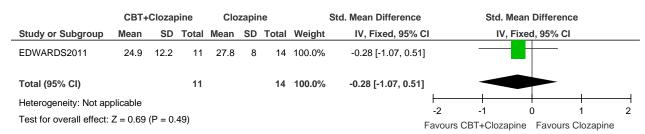


8. CBT + clozapine versus clozapine in participants whose symptoms have not adequately responded to treatment: 24 weeks' follow-up

8.1 Mental state: positive symptoms (BPRS-P)



8.2 Mental state: negative symptoms (SANS)



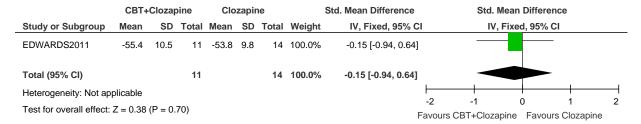
8.3 Global state (CGI)

| | CBT+ | Clozap | oine | Clo | zapir | ne | | Std. Mean Difference | | Std. N | lean Differ | ence | |
|--------------------------|----------|---------|-------|------|-------|-------|--------|----------------------|-----------|---------------------|-------------|------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | | IV, | Fixed, 95% | CI | |
| EDWARDS2011 | 3.5 | 0.8 | 11 | 3.4 | 8.0 | 14 | 100.0% | 0.12 [-0.67, 0.91] | | _ | | | |
| Total (95% CI) | | | 11 | | | 14 | 100.0% | 0.12 [-0.67, 0.91] | | • | | - | |
| Heterogeneity: Not ap | plicable | | | | | | | | ├── -2 | -1 | | 1 | |
| Test for overall effect: | Z = 0.30 | (P = 0. | 76) | | | | | Fa | _ | - ı s CBT+Clozar | oine Favo | urs Clozap | ine |

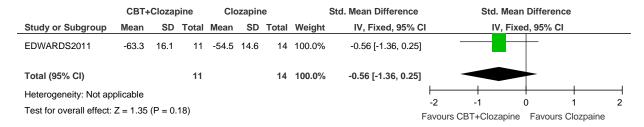
8.4 Mental state: depression symptoms (BDI)

| | CBT+ | Clozap | oine | Clo | zapir | ne | | Std. Mean Difference | | Std. Me | ean Differ | ence | |
|--------------------------|----------|---------|-------|------|-------|-------|--------|----------------------|-------------|---------------------|------------|------------------|---------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | | IV, F | ixed, 95% | CI | |
| EDWARDS2011 | 22.6 | 7.6 | 11 | 18.6 | 4.9 | 14 | 100.0% | 0.62 [-0.19, 1.43] | | | | | |
| Total (95% CI) | | | 11 | | | 14 | 100.0% | 0.62 [-0.19, 1.43] | | | | | |
| Heterogeneity: Not ap | plicable | | | | | | | | _ | + | | + | |
| Test for overall effect: | Z = 1.50 | (P = 0. | 13) | | | | | F | -2 avour | -1 s CBT+Clozapi | ne Favo | 1 urs Clozapi | ne 2 |

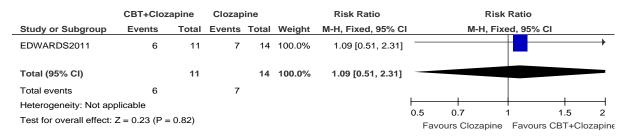
8.5 Functioning: social (SOFAS)



8.6 Quality of life (QLS)



8.7 Remission (score of 'mild' or less on each of the three items of the BPRS-P and a CGI severity item rating of 'mild' or less; assuming dropouts did not achieve remission)



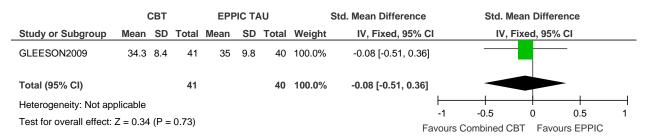
9. Individual CBT versus family CBT: 52 weeks post-treatment

9.1 Relapse: number of participants (BPRS; assuming dropouts relapsed)

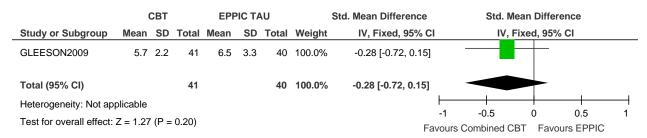


10. Individual and family CBT versus EPPIC treatment as usual (TAU): 30.33 weeks post-treatment

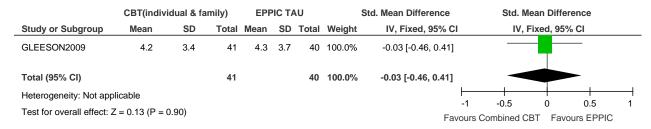
10.1 Mental state: total symptoms (BPRS)



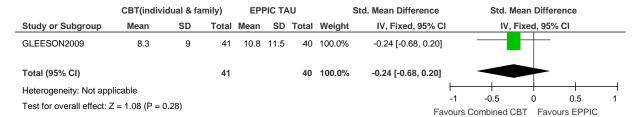
10.2 Mental state: positive symptoms (BPRS-P)



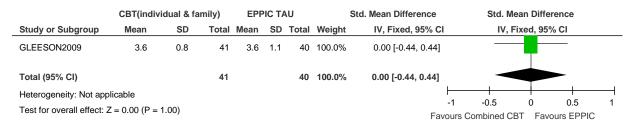
10.3 Mental state: negative symptoms (SANS)



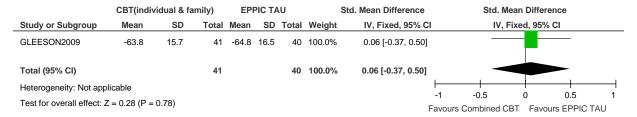
10.4 Mental state: depression symptoms (Montgomery-Åsberg Depression Rating Scale [MADRS])



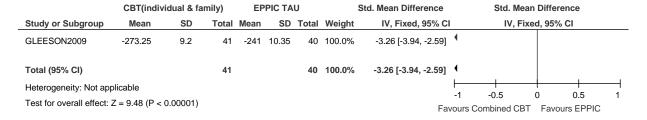
10.5 Quality of life (World Health Organization Quality of Life - abbreviated version)



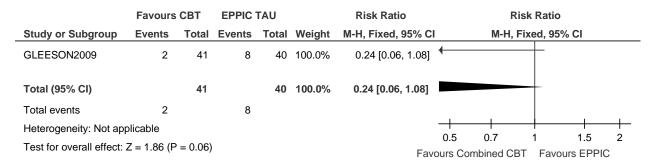
10.6 Functioning: social (SOFAS)



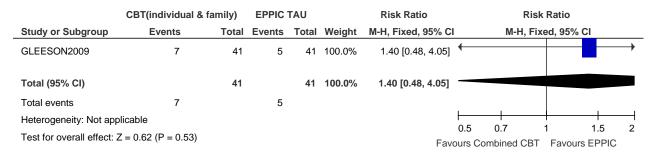
10.7 Relapse: time in days (BPRS)



10.8 Relapse: number of participants (BPRS; assuming dropouts relapsed)

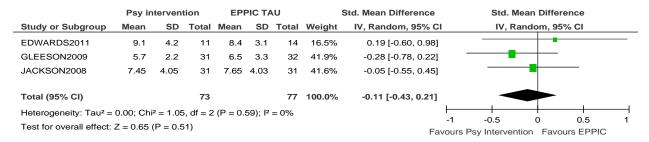


10.9 Leaving the study early for any reason

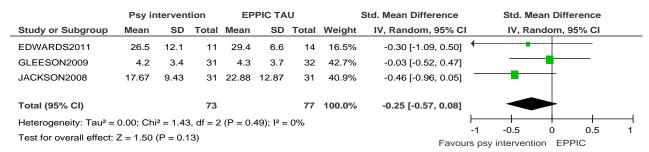


11. Any psychological intervention in addition to EPPIC treatment as usual (TAU) versus EPPIC treatment as usual (TAU): post-treatment

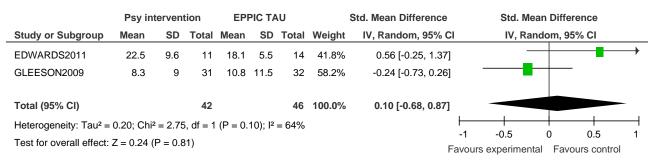
11.1 Mental state: positive symptoms



11.2 Mental state: negative symptoms



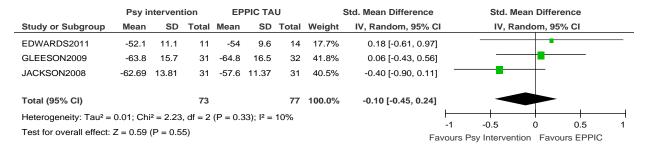
11.3 Mental state: depression symptoms



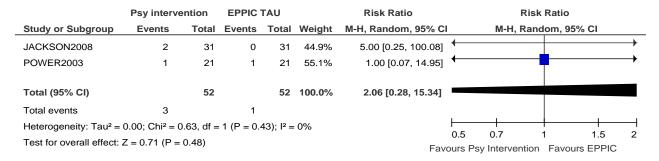
11.4 Quality of life

| lean | SD | Psy intervention | | | | | | Std. Mean Difference | | | | |
|---------------------------|-----------------------|--------------------------------------|--|--|---|--|--|--|---|---|---|---|
| | 00 | Total | Mean | SD | Total | Weight | IV, Random, 95% C | l | IV, R | andom, 9 | 5% CI | |
| 59.3 | 11.9 | 11 | -58.8 | 10.4 | 14 | 16.8% | -0.04 [-0.83, 0.75] | _ | | - | | |
| 3.6 | 0.8 | 31 | 3.6 | 1.1 | 32 | 42.8% | 0.00 [-0.49, 0.49] | | | + | | |
| 2.3 | 3.1 | 27 | 2.4 | 2.5 | 33 | 40.4% | -0.04 [-0.54, 0.47] | | | | | |
| | | 69 | | | 79 | 100.0% | -0.02 [-0.34, 0.30] | | - | | - | |
| | | | | 2 (P = 0.99); I ² = 0% | | | | <u> </u> | | | | |
| fect: Z = 0.13 (P = 0.90) | | | | | | | Fa | - | | | | 1 |
| • | 3.6 2.3 0; Chi² | 3.6 0.8 2.3 3.1 0; Chi² = 0.01 | 3.6 0.8 31 2.3 3.1 27 69 0; Chi² = 0.01, df = 2 | 3.6 0.8 31 3.6 2.3 3.1 27 2.4 69 0; Chi² = 0.01, df = 2 (P = 0.01) | 3.6 0.8 31 3.6 1.1 2.3 3.1 27 2.4 2.5 69 0; Chi² = 0.01, df = 2 (P = 0.99); l² | 3.6 0.8 31 3.6 1.1 32 2.3 3.1 27 2.4 2.5 33 69 79 0; Chi² = 0.01, df = 2 (P = 0.99); l² = 0% | 3.6 0.8 31 3.6 1.1 32 42.8% 2.3 3.1 27 2.4 2.5 33 40.4% 69 79 100.0% 0; Chi² = 0.01, df = 2 (P = 0.99); l² = 0% | 3.6 0.8 31 3.6 1.1 32 42.8% 0.00 [-0.49, 0.49] 2.3 3.1 27 2.4 2.5 33 40.4% -0.04 [-0.54, 0.47] 69 79 100.0% -0.02 [-0.34, 0.30] 0; Chi² = 0.01, df = 2 (P = 0.99); l² = 0% 0.13 (P = 0.90) | 3.6 0.8 31 3.6 1.1 32 42.8% 0.00 [-0.49, 0.49] 2.3 3.1 27 2.4 2.5 33 40.4% -0.04 [-0.54, 0.47] 69 79 100.0% -0.02 [-0.34, 0.30] 0; Chi² = 0.01, df = 2 (P = 0.99); l² = 0% 0.13 (P = 0.90) | 3.6 0.8 31 3.6 1.1 32 42.8% 0.00 [-0.49, 0.49] 2.3 3.1 27 2.4 2.5 33 40.4% -0.04 [-0.54, 0.47] 69 79 100.0% -0.02 [-0.34, 0.30] 0; Chi² = 0.01, df = 2 (P = 0.99); l² = 0% 0.13 (P = 0.90) | 3.6 0.8 31 3.6 1.1 32 42.8% 0.00 [-0.49, 0.49] 2.3 3.1 27 2.4 2.5 33 40.4% -0.04 [-0.54, 0.47] 69 79 100.0% -0.02 [-0.34, 0.30] 0; Chi² = 0.01, df = 2 (P = 0.99); l² = 0% 0.13 (P = 0.90) | 3.6 0.8 31 3.6 1.1 32 42.8% 0.00 [-0.49, 0.49] 2.3 3.1 27 2.4 2.5 33 40.4% -0.04 [-0.54, 0.47] 69 79 100.0% -0.02 [-0.34, 0.30] 0; Chi² = 0.01, df = 2 (P = 0.99); ² = 0% |

11.5 Functioning: social



11.6 Mortality: number of deaths by suicide (assuming dropouts did not die by suicide)



11.7 Leaving the study early for any reason

