

Table S1. Characteristics of Lithium studies

| Study | Type of study | | | Indication for treatment | Intervention group | Comparison group | Total Sample Size | Appraisal of Quality (Newcastle-Ottawa Scale) | | | |
|------------------|---------------|--------------|--------------|------------------------------|--------------------|---|-------------------|---|---------------------------|---------------------|-------------|
| | RCT | Case-control | Cohort study | | | | | Selection (range 0-4) | Comparability (range 0-2) | Outcome (range 0-3) | Total (0-9) |
| Greil, 1997 | X | | | Bipolar | Lithium | AED/MS (Carbamazepine) | 175 | 4 | 2 | 2 | 8 |
| Sondergard, 2008 | | | X | Bipolar | Lithium | AED/MS (Divalproex) | 464 | 4 | 0 | 3 | 7 |
| Ahearn, 2013 | | | X | Bipolar | Lithium | AED/MS (Divalproex) or Antipsychotic | 1,716 | 4 | 0 | 3 | 7 |
| Ahearn, 2013 | | | X | Bipolar | Lithium | No Lithium | 1,551 | 4 | 0 | 3 | 7 |
| Tsai, 2016 | | | X | Bipolar | Lithium | AED/MS (Divalproex/Carbamazepine) | 2,200 | 4 | 2 | 3 | 9 |
| Collins, 2008 | | | X | Bipolar | Lithium | AED/MS (Divalproex/Gabapentin/Carbamazepine) | 11,787 | 4 | 0 | 3 | 7 |
| Calabrese, 2003 | X | | | Bipolar | Lithium | AED/MS (Lamotrigine) | 342 | 4 | 2 | 2 | 8 |
| Licht, 2010 | X | | | Bipolar | Lithium | AED/MS (Lamotrigine) | 155 | 4 | 2 | 3 | 9 |
| Tohen, 2005 | X | | | Bipolar | Lithium | Antipsychotic (Olanzapine) | 431 | 4 | 2 | 3 | 9 |
| Prien, 1973a | X | | | Bipolar | Lithium | Placebo/No lithium treatment | 205 | 4 | 2 | 3 | 9 |
| Toffol, 2015 | | | X | Bipolar | Lithium | Placebo/No lithium treatment | 826 | 4 | 1 | 3 | 8 |
| Tsai, 2016 | | | X | Bipolar | Lithium | Placebo/No lithium treatment | 3,395 | 4 | 2 | 3 | 9 |
| Hayes, 2016 | | | X | Bipolar disorder and MDD | Lithium | AED/MS (Valproate) or Antipsychotic (Olanzapine/Quetiapine) | 6,671 | 4 | 2 | 3 | 9 |
| Ahlfors, 1981 | X | | | Bipolar disorder and MDD | Lithium | Antipsychotic (Flupenthixol decanoate) | 219 | 3 | 2 | 2 | 7 |
| Smith, 2009 | | | X | Mixed psychiatric disorders | Li+Antipsy | AED/MS (Carbamazepine/ Valproic acid/ Oxcarbazepine/ Lamotrigine) | 16,645 | 4 | 1 | 2 | 7 |
| Smith, 2014 | | | X | Mood and psychotic disorders | Lithium | AED/MS (Valproate) | 42,388 | 4 | 2 | 3 | 9 |

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|----------------------------|---|---|---|-------------------------------|----------------------|------------------------------|------------|---|---|---|---|
| Greil, 1997b | X | | | Psychotic disorders | Lithium | AED/MS (Carbamazapine) | 110 | 4 | 2 | 2 | 8 |
| Glen, 1984 | X | | | Unipolar | Lithium | Amitriptyline | 107 | 4 | 2 | 2 | 8 |
| Greil, 1996 | X | | | Unipolar | Lithium | Amitriptyline | 81 | 4 | 2 | 2 | 8 |
| Felber, 1994 | | | X | Bipolar disorder and MDD | Lithium | Placebo/No lithium treatment | 36 | 2 | 0 | 2 | 4 |
| Kallner, 2000 | | | X | Bipolar disorder and MDD | Lithium | Placebo/No lithium treatment | 405 | 2 | 0 | 1 | 3 |
| Prien, 1973b | X | | | Bipolar disorder and MDD | Lithium | Placebo/No lithium treatment | 84 | 4 | 2 | 3 | 9 |
| Bocchetta, 1998 | | | X | Mood and psychotic disorders | Lithium | Placebo/No lithium treatment | 100 | 2 | 0 | 2 | 4 |
| Coryell, 2001 | | X | | Mood and psychotic disorders | Lithium | Placebo/No lithium treatment | 30 | 2 | 0 | 3 | 5 |
| Müller-Oerlinghausen, 1992 | | | X | Mood and psychotic disorders | Lithium | Placebo/No lithium treatment | 68 | 2 | 0 | 2 | 4 |
| Nilsson, 1995 | | | X | Mood and psychotic disorders | Lithium | Placebo/No lithium treatment | 230 | 2 | 0 | 2 | 4 |
| Modestin, 1992 | | X | | Mood and psychotic disorders* | Lithium | Placebo/No lithium treatment | 128 | 1 | 0 | 3 | 4 |
| Reutfors, 2013 | | X | | Psychotic disorders | Lithium | No lithium | 168 | 3 | 0 | 2 | 5 |
| Bauer, 2000 | X | | | Unipolar | Lithium augmentation | Placebo/No lithium treatment | 29 | 3 | 2 | 2 | 7 |
| Lauterbach, 2008 | X | | | Unipolar | Lithium | Placebo/No lithium treatment | 167 | 4 | 2 | 3 | 9 |
| Song 2017 | | | X | Bipolar | Lithium | No lithium | 25,780 | 4 | 2 | 3 | 9 |
| Song 2017 | | | X | Bipolar | Lithium | AED/MS (Valproate) | 29,540 | 4 | 2 | 3 | 9 |
| Goodwin 2003 | | | X | Bipolar disorder | Lithium | AED (CBZ, VPA) | *23,930 PY | 4 | 1 | 2 | 8 |
| Goodwin 2003 | | | X | Bipolar disorder | Lithium | No lithium treatment | *35,159 PY | 4 | 1 | 2 | 8 |
| Storosum 2005 | X | | | Bipolar disorder | Lithium | AED/MS or Antipsychotics | 1,201 | 4 | 2 | 3 | 9 |

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|---------------|---|--|---|------------------|----------------------|-------------------------|-----|---|---|---|---|
| Coppen 1998 | | | X | Bipolar disorder | Lithium | No lithium treatment | 102 | 2 | 0 | 3 | 5 |
| Tondo 1998 | | | X | Bipolar disorder | Lithium | No lithium treatment | 310 | 2 | 0 | 3 | 5 |
| Bech 1976 | | | X | Mood disorders | Lithium | No lithium treatment | 74 | 2 | 0 | 3 | 5 |
| Angst 2005 | | | X | Mood disorders | Lithium | No lithium treatment | 220 | 2 | 0 | 2 | 4 |
| Girlanda 2014 | X | | | MDD | Lithium + usual care | No lithium + usual care | 58 | 3 | 2 | 3 | 8 |

**Person counts could not be obtained from published literature. In this case, person-years (PY) is given. RCT – randomized controlled trial. MDD – major depressive disorder; AED/MS – antiepileptic drug/mood stabilizer*

Table S2. Characteristics of Clozapine studies

| Study | Type of study | | | Indication for treatment | Intervention group | Comparison group | Total Sample Size | Appraisal of Quality (Newcastle-Ottawa Scale) | | | |
|----------------|---------------|--------------|--------------|--------------------------|--------------------|-------------------------|-------------------|---|---------------------------|---------------------|-------------|
| | RCT | Case-control | Cohort study | | | | | Selection (range 0-4) | Comparability (range 0-2) | Outcome (range 0-3) | Total (0-9) |
| Weitoft, 2014 | | X | | Psychotic disorder | Clozapine | Haloperidol | 26,046 | 4 | 0 | 3 | 7 |
| Reutfors, 2013 | | X | | Psychotic disorder | Clozapine | No Clozapine | 168 | 3 | 0 | 2 | 5 |
| Tiihonen, 2009 | | | X | Psychotic disorder | Clozapine | Perphenazine | *49,930 PY | 4 | 2 | 2 | 8 |
| Sernyak, 2001 | | | X | Psychotic disorder | Clozapine | No Clozapine | 3,795 | 4 | 1 | 2 | 7 |
| Reid, 1998 | | | X | Psychotic disorder | Clozapine | No Clozapine | 30,983 | 3 | 0 | 2 | 5 |
| Walker, 1997 | | | X | Psychotic disorder | Clozapine | Past Clozapine Exposure | *86,747 PY | 3 | 0 | 1 | 4 |
| Meltzer, 2003 | X | | | Psychotic disorder | Clozapine | Olanzapine | 980 | 4 | 2 | 3 | 9 |

*Person counts could not be obtained from published literature. In this case, person-years (PY) is given. RCT – randomized controlled trial.

Table S3. Characteristics of ECT studies

| Study | Type of study | | | Indication for treatment | Intervention group | Comparison group | Total Sample Size | Appraisal of Quality (Newcastle-Ottawa Scale) | | | |
|--------------------------|---------------|--------------|--------------|------------------------------|--------------------|------------------|-------------------|---|---------------------------|---------------------|-------------|
| | RCT | Case-control | Cohort study | | | | | Selection (range 0-4) | Comparability (range 0-2) | Outcome (range 0-3) | Total (0-9) |
| Ahmadi, 2016 | | | X | MDD + PTSD | ECT | No ECT | 3,485 | 4 | 0 | 3 | 7 |
| Avery, 1978 | | | X | MDD | ECT | No ECT | 519 | 4 | 0 | 2 | 6 |
| Bradvik, 2000 | | X | | Mood disorder | ECT | No ECT | 178 | 2 | 0 | 2 | 4 |
| Liang, 2018 | | | X | Mood disorder | ECT | No ECT | 2,435 | 3 | 1 | 2 | 6 |
| Milstein, 1986 | | X | | Psychotic disorder, Others | ECT | No ECT | 32 | 3 | 0 | 2 | 5 |
| Sharma, 1999 | | X | | Mood and psychotic disorders | ECT | No ECT | 90 | 1 | 0 | 1 | 2 |
| Tsuang, 1979 | | | X | Psychotic Disorder | ECT | No ECT | 74 | 4 | 0 | 2 | 6 |
| Nordenskjold, 2013 | X | | | Mood disorders | ECT | No ECT | 56 | 4 | 2 | 3 | 9 |
| Huston and Locher, 1948a | | | X | Psychotic Disorder | ECT | No ECT | 154 | 3 | 0 | 2 | 5 |
| Huston and Locher, 1948b | | | X | Psychotic Disorder | ECT | No ECT | 154 | 3 | 0 | 2 | 5 |

| | | | | | | | | | | | |
|------------------------------|--|--|---|-----|-----|--------|---------------|---|---|---|---|
| Babigian and Guttmacher 1984 | | | X | MDD | ECT | No ECT | *37,729 PY | 4 | 0 | 2 | 6 |
|------------------------------|--|--|---|-----|-----|--------|---------------|---|---|---|---|

**Person counts could not be obtained from published literature. In this case, person-years (PY) is given. RCT – randomized controlled trial. PTSD – posttraumatic stress disorder; MDD – major depressive disorder*

Table S4. Characteristics Antipsychotics studies

| Study | Type of study | | | Indication for treatment | Intervention group | Comparison group | Total Sample Size | Appraisal of Quality (Newcastle-Ottawa Scale) | | | |
|----------------|---------------|--------------|--------------|--------------------------|----------------------------|-----------------------|-------------------|---|---------------------------|---------------------|-------------|
| | RCT | Case-control | Cohort study | | | | | Selection (range 0-4) | Comparability (range 0-2) | Outcome (range 0-3) | Total (0-9) |
| Storosum, 2003 | X | | | Psychotic disorder | Antipsychotic | Placebo | 7,152 | | 0 | | |
| Tiihonen, 2006 | | | X | Psychotic disorder | Antipsychotic | No Antipsychotic | 8,026 PY | 4 | 2 | 2 | 8 |
| Toffol, 2015 | | | X | Bipolar | Antipsychotic | No Antipsychotic | 826 | 4 | 1 | 3 | 8 |
| Reutfors, 2013 | | X | | Psychotic disorder | Antipsychotic | No Antipsychotic | 168 | 3 | 0 | 2 | 5 |
| Modestin, 1992 | | X | | RDC diagnosis | Antipsychotic | No Antipsychotic | 128 | 1 | 0 | 3 | 4 |
| Hayes 2016 | | | X | Bipolar | Olanzapine/ Quetiapine | Lithium | 5,001 | 4 | 2 | 3 | 9 |
| Hayes 2016 | | | X | Bipolar | Olanzapine/ Quetiapine | Valproate | 4,523 | 4 | 2 | 3 | 9 |
| Tohen 2005 | X | | | Bipolar | Olanzapine | Lithium | 431 | 4 | 2 | 3 | 9 |
| Ahlfors 1981 | X | | | Mood disorders | Flupenthixol decanoate | Lithium | 219 | 3 | 2 | 2 | 7 |
| Ahearn 2013 | | | X | Bipolar | Atypical antipsychotics | No Antipsychotic | 1,910 | 4 | 0 | 3 | 7 |
| Angst 2005 | | | X | Mood disorders | Antipsychotic | No Antipsychotic | 406 | 2 | 0 | 2 | 4 |
| Nasrallah 2010 | X | | | Psychotic disorder | Paliperidone | Placebo | 515 | 4 | 2 | 3 | 9 |
| Khan 2013 | X | | | Psychotic disorder | Atypical antipsychotics | Placebo | 30,067 | 4 | 2 | 2 | 8 |
| Khan 2013 | X | | | Bipolar | Atypical antipsychotics | Placebo and/or AED | 12,026 | 4 | 2 | 2 | 8 |

*Person counts could not be obtained from published literature. In this case, person-years (PY) is given. RCT – randomized controlled trial.

Table S5. Characteristics of AED/Mood stabilizers studies

| Study | Type of study | | | Indication for treatment | Intervention group | Comparison group | Total Sample Size | Appraisal of Quality (Newcastle-Ottawa Scale) | | | |
|-------------------|---------------|--------------|--------------|------------------------------|--|-------------------------|-------------------|---|---------------------------|---------------------|-------------|
| | RCT | Case-Control | Cohort Study | | | | | Selection (range 0-4) | Comparability (range 0-2) | Outcome (range 0-2) | Total (0-9) |
| *Sondergard, 2008 | | | X | Bipolar | Divalproex, lamotrigine or oxcarbazepine | Lithium | 5,926 | 4 | 0 | 3 | 7 |
| Smith, 2014 | | | X | Mood and psychotic disorders | Valproate | Lithium | 42,388 | 4 | 2 | 3 | 9 |
| Collins, 2008 | | | X | Bipolar | Mood stabilizers | Lithium | 11,787 | 4 | 0 | 3 | 7 |
| Smith, 2009 | | | X | Bipolar | Carbamazepine, valproate, lamotrigine or oxcarbazepine | Lithium | 16,645 | 4 | 1 | 2 | 7 |
| Toffol, 2015 | | | X | Bipolar | AED/Mood stabilizers | No AED/Mood stabilizers | 826 | 4 | 1 | 3 | 8 |
| Hayes, 2016 | | | X | Bipolar | Valproate | Lithium | 3,818 | 4 | 2 | 3 | 9 |
| Hayes, 2016 | | | X | Bipolar | Valproate | No AED/Mood stabilizers | 2,853 | 4 | 2 | 3 | 9 |
| Modestin 1992 | | X | | Mood and psychotic disorders | AED/Mood stabilizers | No AED/Mood stabilizers | 128 | 3 | 0 | 3 | 6 |
| Goodwin 2003 | | | X | Bipolar | Carbamazepine, Valproate | Lithium | **19,326 PY | 4 | 1 | 2 | 8 |
| Goodwin 2003 | | | X | Bipolar | Carbamazepine, Valproate | No AED/Mood stabilizers | **26,033 PY | 4 | 1 | 2 | 8 |
| Tsai 2016 | | | X | Bipolar | Carbamazepine, Valproate | Lithium | 3,395 | 4 | 2 | 3 | 9 |
| Tsai 2016 | | | X | Bipolar | Carbamazepine, Valproate | No AED/Mood stabilizers | 1,373 | 4 | 2 | 3 | 9 |
| Calabrese 2003 | X | | | Bipolar | Lamotrigine | Lithium | 342 | 4 | 2 | 2 | 8 |

| | | | | | | | | | | | |
|----------------|---|--|---|--------------------------|---------------------------------------|-------------------------|--------|---|---|---|---|
| Calabrese 2003 | X | | | Bipolar | Lamotrigine | Placebo | 121 | 4 | 2 | 2 | 8 |
| Licht 2010 | X | | | Bipolar | Lamotrigine | Lithium | 155 | 4 | 2 | 3 | 9 |
| Greil 1997a | X | | | Bipolar | Carbamazepine | Lithium | 175 | 4 | 2 | 2 | 8 |
| Greil 1997b | X | | | Schizoaffective disorder | Carbamazepine | Lithium | 110 | 4 | 2 | 2 | 8 |
| Song 2017 | | | X | Bipolar | Valproate | Lithium | 29,540 | 4 | 2 | 3 | 9 |
| Leon 2012 | | | X | Bipolar | Carbamazepine, Lamotrigine, Valproate | No AED/Mood stabilizers | 199 | 4 | 1 | 2 | 7 |
| Ahearn 2013 | | | X | Bipolar | Valproate | No AED/Mood stabilizers | 2,165 | 4 | 0 | 3 | 7 |
| Ahearn 2013 | | | X | Bipolar | Valproate | Lithium | 1,551 | 4 | 0 | 3 | 7 |

**For Sondergard et al 2008, we used the conservative definition of 1 prescription of medication.*

***Person counts could not be obtained from published literature. In this case, person-years (PY) is given.*

RCT – randomized controlled trial.