Brain Injury Psychiatry Workshop

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Psychosis

Psychosis in TBI

“James”: brain injury and psychosis

- James sustained a severe traumatic brain injury in a four metre cliff fall with a GCS at the scene of 3-6/15 and a duration of PTA of three weeks. CT brain findings showed bilateral punctate intra axial haemorrhage and a small right posterior parietal haemorrhage consistent with a possible subdural. He required urgent insertion of an extraventricular drain and spent eight days in ICU at a major Sydney hospital with a further week in a high dependency unit before being transferred to the Brain Injury Unit and being discharged on after five weeks. His admission was complicated by right basilic vein and large right ilio-femoral DVTs which required heparinisation and warfarinisation.
- While recovering well cognitively, James developed psychotic symptoms about three weeks after his injury including persecutory delusions and the development of delusions of misidentification (Capgras delusions) regarding his parents, believing that they had been substituted by others. This sense of unreality subsequently extended to his home to a belief that perhaps he was not alive and had been transferred to some other plane of existence. He described this as “a glitch in the matrix”.

“James”: initial assessment continued

- A trial of olanzapine up to 7.5mg daily was associated with sedation and sleeping for more than 12 hours daily but did not appear to significantly ameliorate the symptoms. James cross tapered over to risperidone and when I first saw him post-discharge was taking 2.5mg of olanzapine and 2mg twice daily of risperidone. He had noticed the emergence of sexual side effects on the risperidone but was not unduly distressed by this at that stage.
- Apart from these very unsettling symptoms which at times have been so distressing for James that he has had suicidal thoughts and has asked his parents to kill him the rest of his rehabilitation has progressed well. He has not had aggressive or violent thoughts about his parents. Other psychosis symptoms that have been present have included thought broadcasting and what sounds like some grandiose delusions at one point in his recovery where he thought he might be some kind of god, but these have both resolved.
- James was referred to a psychologist for some depressive symptoms and low self-esteem in 2015 but his mood improved after he got a job working in a restaurant and he did not end up seeing the psychologist. He has significant history of substance abuse including binge alcohol use, regular daily cannabis, and periodic use of LSD. His parents also noted that he had an interest in fairly abstract philosophy and science fiction prior to his injury.
- His medical history is significant for a depressed parietal skull fracture at the age of four. He also had low grade asthma as a child and was quite allergic to pollen. There is no other significant medical history. He was a smoker until the time of his injury but he is not currently smoking.
- There is a family history of psychosis with a paternal great aunt who developed schizophrenia.

“James”: initial assessment continued

- On mental state examination James was a slim well looking young man who was polite and attentive throughout the interview. He answered questions freely and was receptive to discussion about the pathological nature of these experiences as a result of his traumatic brain injury. He showed no signs of motor restlessness or any other extrapyramidal signs.
- In summary James described the emergence of an organic psychotic disorder following a traumatic brain injury with the development of Capgras syndrome features of delusional misidentification. At times this feeling had been extended into a general sense of delusional mood or unreality but there was a sense that these symptoms had improved a little particularly with the recent change from olanzapine to risperidone.
- I asked James to stop the olanzapine and continue on risperidone 2mg twice daily. We discussed potential motor and hormonal adverse effects.
- I recommended regular cognitive challenge with a clinical psychologist familiar with psychosis.

“James”: subsequent progress

- Motor restlessness on risperidone so dose reduced to 2mg.
- Generally ok but some odd preoccupations and mood variability. Parents thought “close to normal”.
- Elevated prolactin, sexual side effects, risperidone reduced to 1mg.
- More prominent irritability. *We discussed three possible explanations for his increasing irritability: 1. That this is just a natural reaction to the limitations that have been placed on him and the frustrations of being in the care of his parents at present. 2. That he has some ongoing irritability and affective liability from his head injury which had previously been masked by the higher dose of risperidone. 3. That this could represent an “at risk state” for a recurrence of his psychosis.*
- SSRI added (escitalopram)

James: subsequent progress

- Referred to early psychosis (EP)service for co-management
- Risperidone increased to 2mg again because of lability, “strange” thoughts.
- Persistent symptoms even after risperidone increased to 2.5mg, EP team changed him to aripiprazole. Sexual function improved, but more preoccupied with whether experiences are real, whether parents are lying to him.
- EP team changed him to quetiapine, persistent symptoms.
- I began to lobby for a trial of clozapine, resisted by family and EP team less enthusiastic.
- Remained on clozapine. Collapse on skiing trip, ?? seizure, ? functional.
- Aripiprazole added

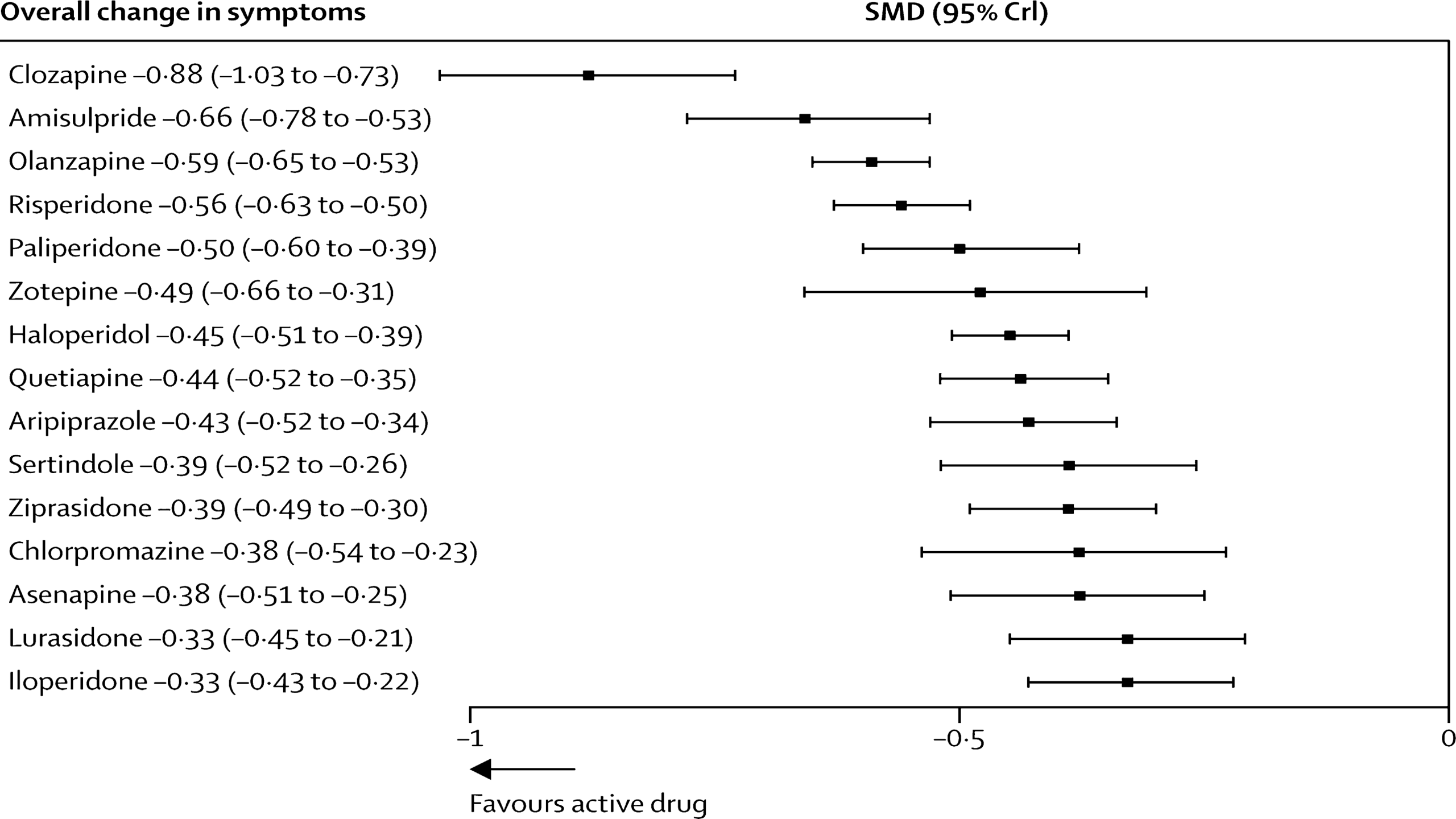
“James”: subsequent progress

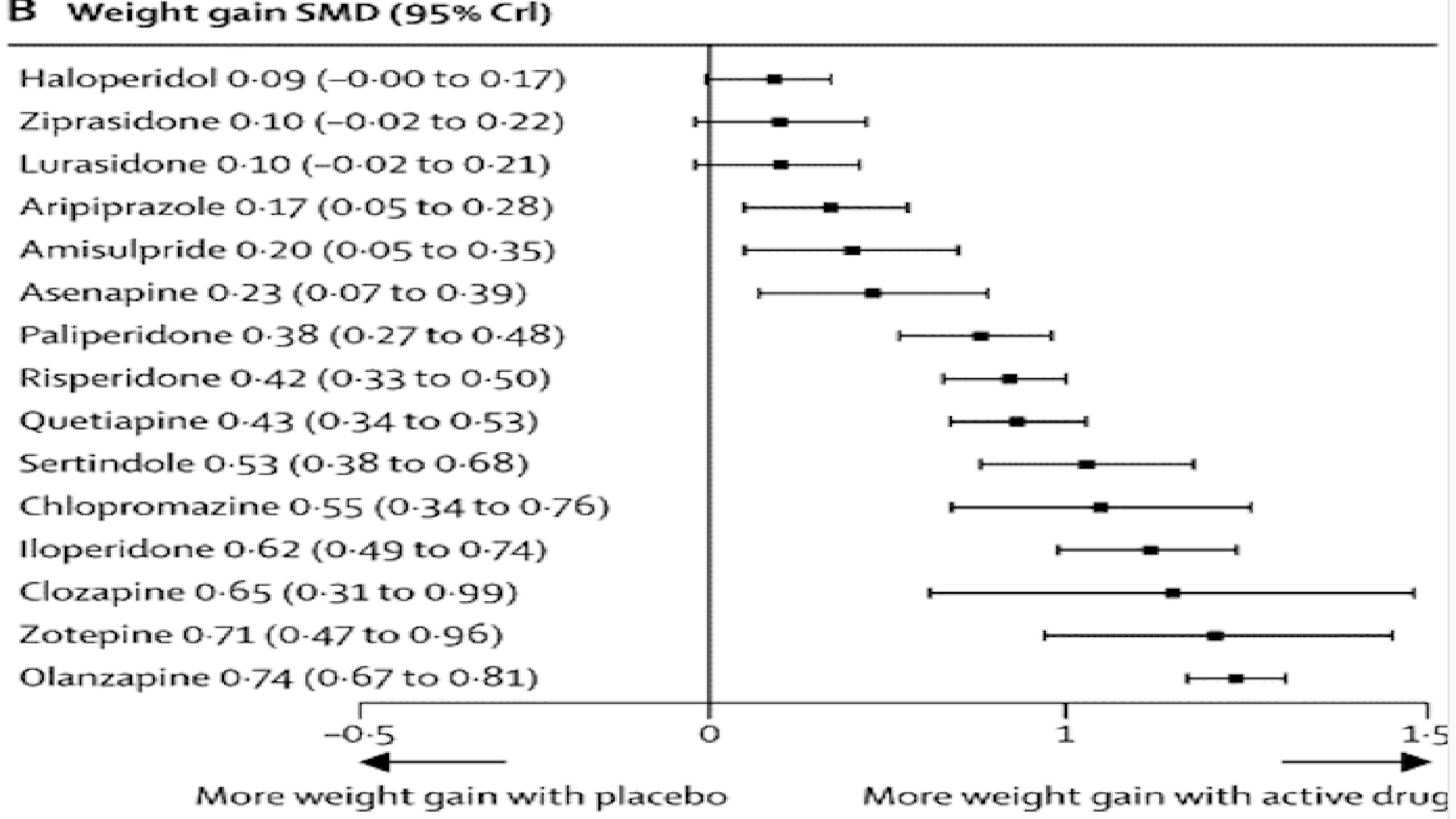
- Persistent disability, doing some bar work. DSP application made.
- After two years, moved with family to regional area, care transferred.
- My last entry: *James remains on quetiapine 300 mg at night and aripiprazole 5 mg in the morning. He is generally doing okay, but his mood remains quite up and down. He starts the day with feelings of motivation and positivity which rapidly dissipate and by the early afternoon he says "I feel like giving up, everything is too difficult". He is also bothered by apparent blepharospasm of the left eye which seems to worsen at times of stress. At a recent family wedding in southwestern Sydney James became very tired and had some quite pronounced dissociative symptoms with concerns about the nature of reality and whether he existed which were very troubling for him. He was able to be reassured by his father and the symptoms had settled by the next morning but he was keen to discuss their significance with his parents the next evening.*
- *In summary, James seems to be doing well but he does have some residual psychosis symptoms I think, including some positive symptoms and significant negative and cognitive symptoms. I have always favoured James having a trial of clozapine but he and his family have been cautious about this. It may be something that can be revisited by Dr Xxxxx as it would be good to see whether something can be done to make his recovery more complete.*

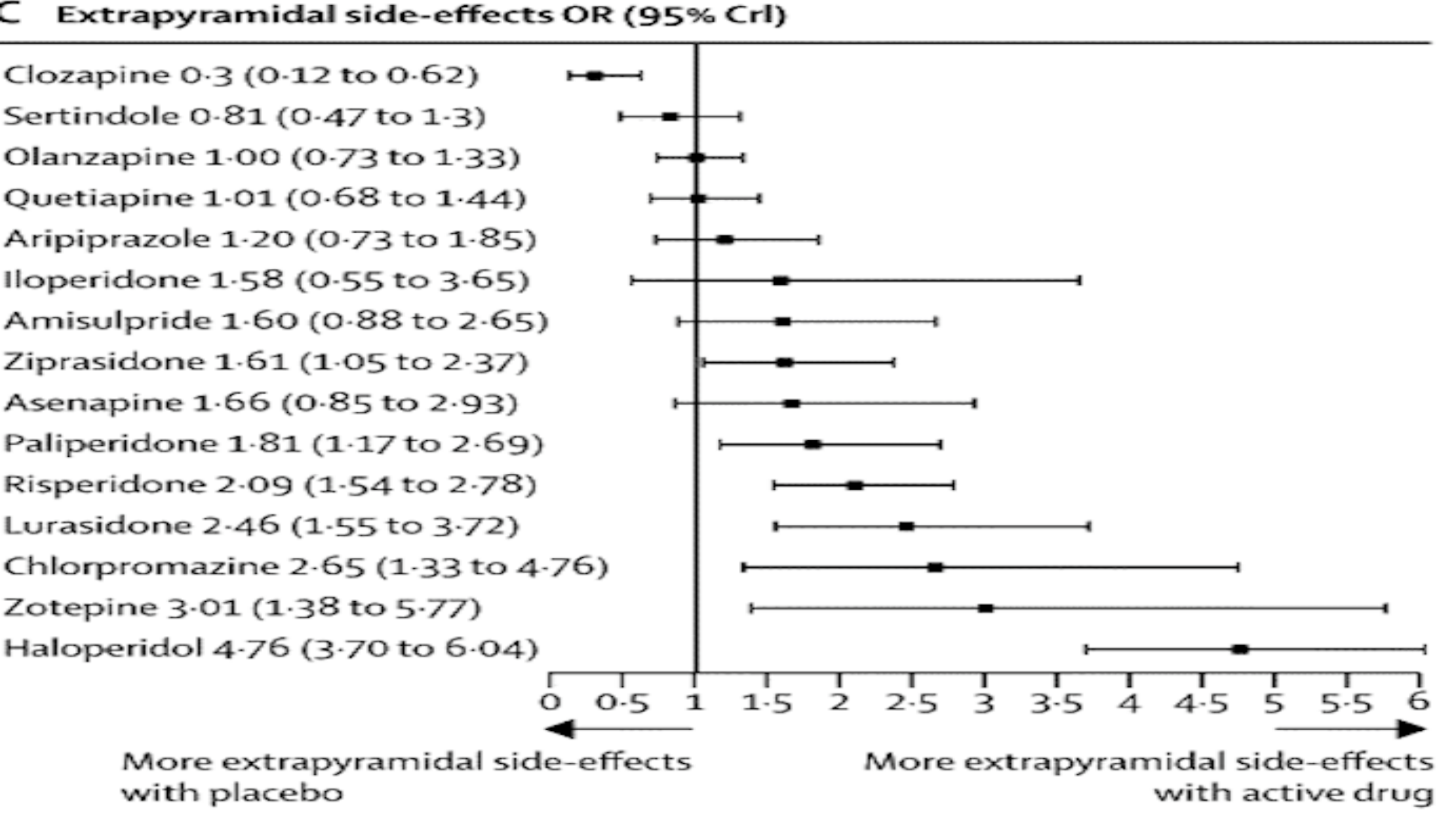
Psychosis and brain injury

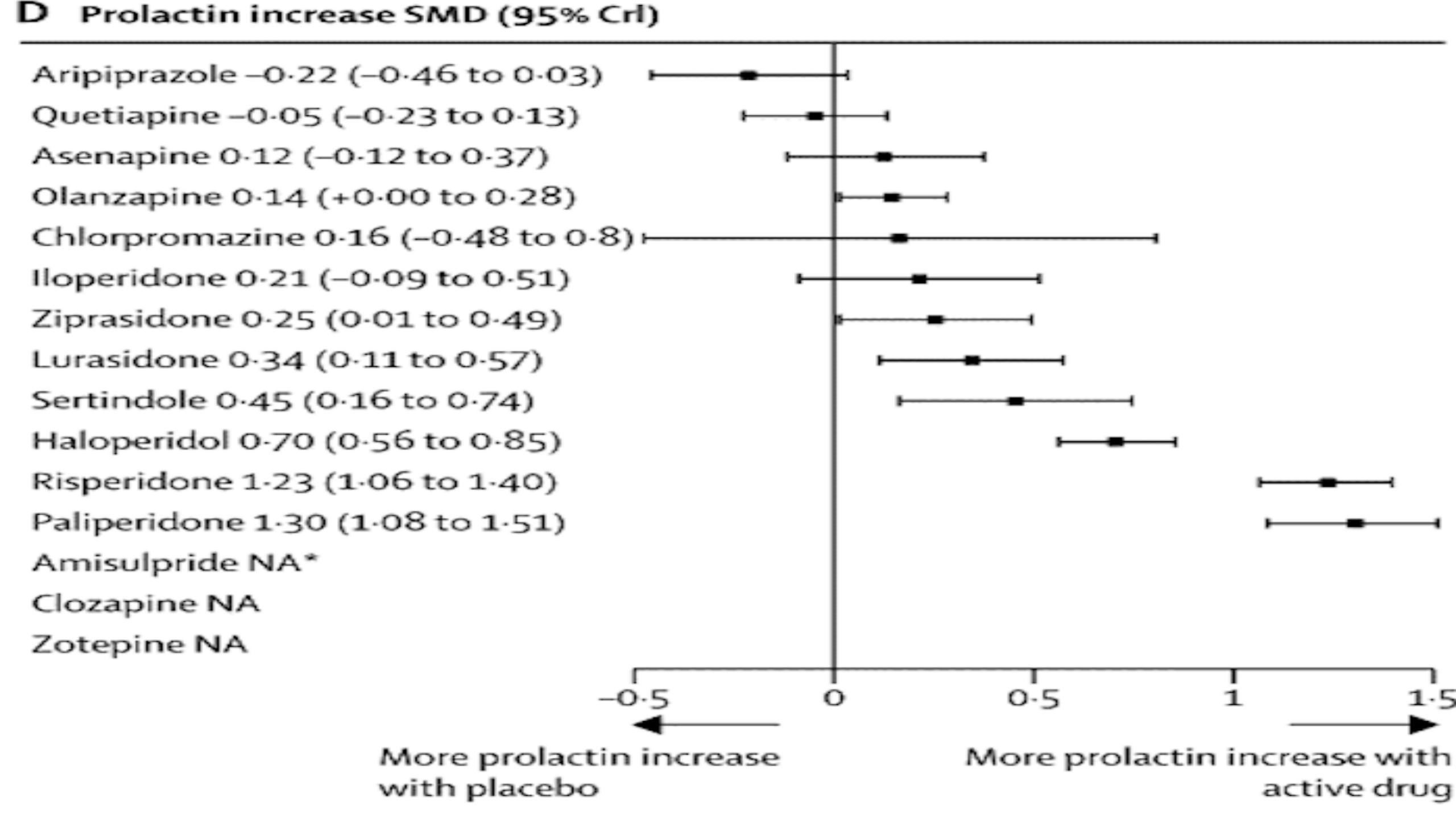
- Psychosis in TBI is rare, but there is a 2 to 3 fold increase in the risk of psychosis in head injured individuals compared to the general population (8% cf 2%)
- More sensitive to antipsychosis side effects, especially sexual and motor effects (restlessness, parkinsonism, dystonia).
- So, which to choose?

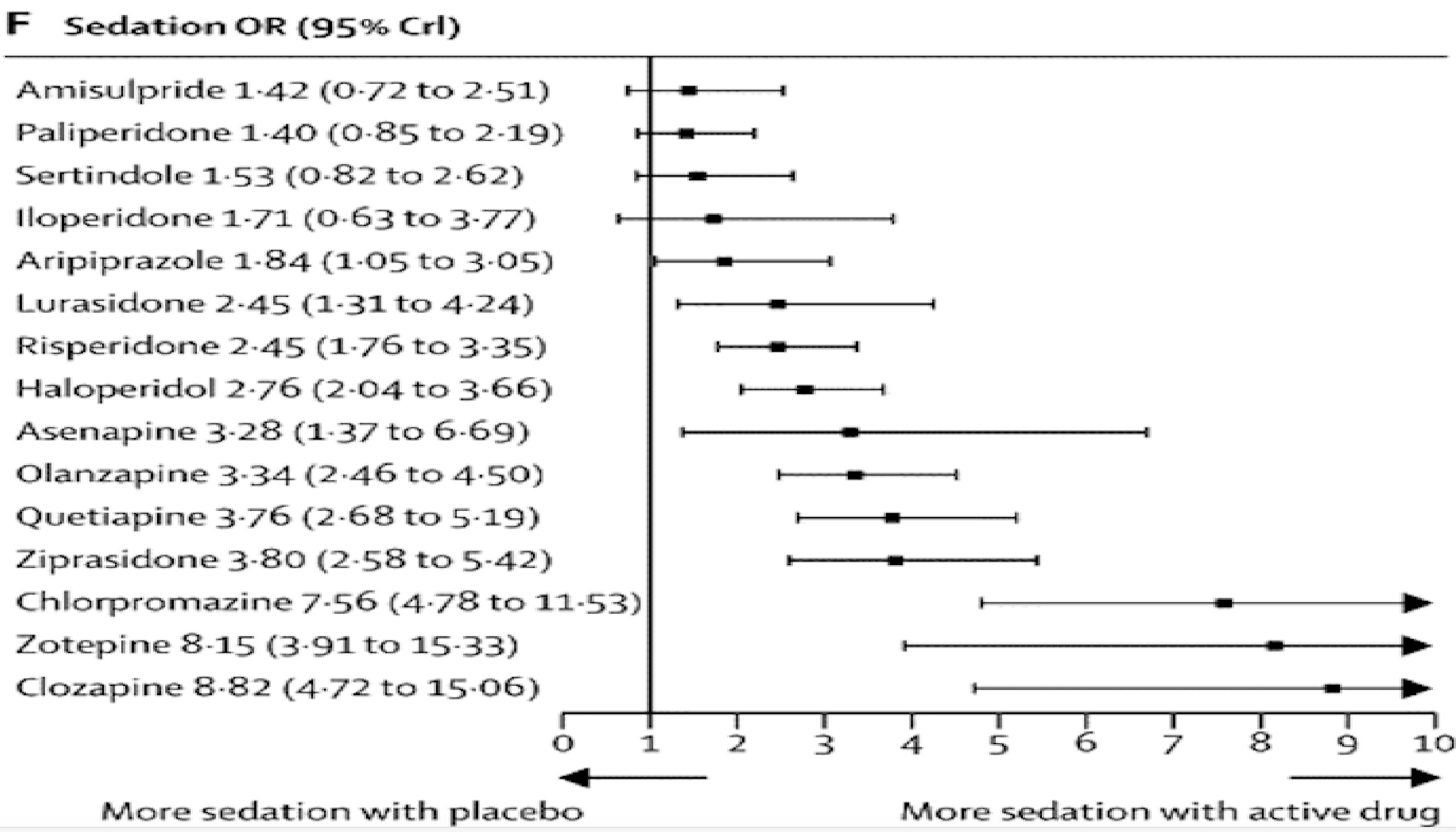
Leucht, Stefan, et al. "Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis." *The Lancet* 382.9896 (2013): 951-962.


Overall change in symptoms
SMD (95% CrI)
Clozapine –0·88 (–1·03 to –0·73)
Amisulpride –0·66 (–0·78 to –0·53)
Olanzapine –0·59 (–0·65 to –0·53)
Risperidone –0·56 (–0·63 to –0·50)
Paliperidone –0·50 (–0·60 to –0·39)
Zotepine –0·49 (–0·66 to –0·31)
Haloperidol –0·45 (–0·51 to –0·39)
Quetiapine –0·44 (–0·52 to –0·35)
Aripiprazole –0·43 (–0·52 to –0·34)
Sertindole –0·39 (–0·52 to –0·26)
Ziprasidone –0·39 (–0·49 to –0·30)
Chlorpromazine –0·38 (–0·54 to –0·23)
Asenapine –0·38 (–0·51 to –0·25)
Lurasidone –0·33 (–0·45 to –0·21)
Iloperidone –0·33 (–0·43 to –0·22)
–1
–0·5
0
Favours active drug


B Weight gain SMD (95% CrI)
Haloperidol 0·09 (–0·00 to 0·17)
Ziprasidone 0·10 (–0·02 to 0·22)
Lurasidone 0·10 (–0·02 to 0·21)
Aripiprazole 0·17 (0·05 to 0·28)
Amisulpride 0·20 (0·05 to 0·35)
Asenapine 0·23 (0·07 to 0·39)
Paliperidone 0·38 (0·27 to 0·48)
Risperidone 0·42 (0·33 to 0·50)
Quetiapine 0·43 (0·34 to 0·53)
Sertindole 0·53 (0·38 to 0·68)
Chlopromazine 0·55 (0·34 to 0·76)
Iloperidone 0·62 (0·49 to 0·74)
Clozapine 0·65 (0·31 to 0·99)
Zotepine 0·71 (0·47 to 0·96)
Olanzapine 0·74 (0·67 to 0·81)
–0·5
0
1
1·5
More weight gain with placebo
More weight gain with active drug


C Extrapyramidal side-effects OR (95% CrI)
Clozapine 0·3 (0·12 to 0·62)
Sertindole 0·81 (0·47 to 1·3)
Olanzapine 1·00 (0·73 to 1·33)
Quetiapine 1·01 (0·68 to 1·44)
Aripiprazole 1·20 (0·73 to 1·85)
Iloperidone 1·58 (0·55 to 3·65)
Amisulpride 1·60 (0·88 to 2·65)
Ziprasidone 1·61 (1·05 to 2·37)
Asenapine 1·66 (0·85 to 2·93)
Paliperidone 1·81 (1·17 to 2·69)
Risperidone 2·09 (1·54 to 2·78)
Lurasidone 2·46 (1·55 to 3·72)
Chlorpromazine 2·65 (1·33 to 4·76)
Zotepine 3·01 (1·38 to 5·77)
Haloperidol 4·76 (3·70 to 6·04)
0 0·5 1 1·5 2 2·5 3 3·5 4 4·5 5 5·5 6
More extrapyramidal side-effects with placebo
More extrapyramidal side-effects with active drug


D Prolactin increase SMD (95% CrI)
Aripiprazole –0·22 (–0·46 to 0·03)
Quetiapine –0·05 (–0·23 to 0·13)
Asenapine 0·12 (–0·12 to 0·37)
Olanzapine 0·14 (+0·00 to 0·28)
Chlorpromazine 0·16 (–0·48 to 0·8)
Iloperidone 0·21 (–0·09 to 0·51)
Ziprasidone 0·25 (0·01 to 0·49)
Lurasidone 0·34 (0·11 to 0·57)
Sertindole 0·45 (0·16 to 0·74)
Haloperidol 0·70 (0·56 to 0·85)
Risperidone 1·23 (1·06 to 1·40)
Paliperidone 1·30 (1·08 to 1·51)
Amisulpride NA*
Clozapine NA
Zotepine NA
–0·5
0
0·5
1
1·5
More prolactin increase with placebo
More prolactin increase with active drug


F Sedation OR (95% CrI)
Amisulpride 1·42 (0·72 to 2·51)
Paliperidone 1·40 (0·85 to 2·19)
Sertindole 1·53 (0·82 to 2·62)
Iloperidone 1·71 (0·63 to 3·77)
Aripiprazole 1·84 (1·05 to 3·05)
Lurasidone 2·45 (1·31 to 4·24)
Risperidone 2·45 (1·76 to 3·35)
Haloperidol 2·76 (2·04 to 3·66)
Asenapine 3·28 (1·37 to 6·69)
Olanzapine 3·34 (2·46 to 4·50)
Quetiapine 3·76 (2·68 to 5·19)
Ziprasidone 3·80 (2·58 to 5·42)
Chlorpromazine 7·56 (4·78 to 11·53)
Zotepine 8·15 (3·91 to 15·33)
Clozapine 8·82 (4·72 to 15·06)
0
1
2
3
4
5
6
7
8
9
10
More sedation with placebo
More sedation with active drug