Weight Change From 3-Year Observational Data: Findings From the Worldwide Schizophrenia Outpatient Health Outcomes Database

Chris J. Bushe, MB, BS; Cees J. Slooff, MD, PhD; Peter M. Haddad, MD, FRCPsych; and Jamie L. Karagianis, MD

ABSTRACT

Background: Weight change data from randomized clinical trials are often of limited duration and trials do not always report a full range of clinically relevant categorical end points.

Method: We conducted a post hoc analysis of data from the observational Worldwide Schizophrenia Outpatient Health Outcomes database (2000–2005) on weight change in 4,626 patients completing 3 years of antipsychotic monotherapy with amisulpride, clozapine, olanzapine, quetiapine, risperidone, and oral and depot first-generation antipsychotics (FGAs). Reported outcomes included mean and categorical weight changes and the trajectories of different measures of weight change.

Results: Mean weight gain was lowest with amisulpride (1.8 kg; 95% CI, 0.2–3.3) and highest with olanzapine (4.2 kg; 95% CI, 3.9–4.5). Weight change for all antipsychotics was most rapid during the first 6 months; subsequent weight change was slower but did not plateau. All drugs showed considerable individual variation in weight change. The proportion losing ≥ 7% of their baseline bodyweight was highest with quetiapine (10%; 95% CI, 7%–16%) and lowest with depot FGAs (5%; 95% CI, 3%–10%). Between 7% and 15% of patients moved into an overweight or obese body mass index (kg/m^2) category (≥ 25).

Conclusions: The degree of weight gain varied between antipsychotics. All antipsychotics were associated with significant (≥ 7%) weight loss and gain from baseline. The mean rate of weight gain was maximal during the first 6 months but continued over 3 years without a plateau in this specific cohort. Patients should receive regular monitoring of weight throughout treatment.

J Clin Psychiatry 2012;73(6):e749–e755

Submitted: *July 5, 2011; accepted February 3, 2012 (doi:10.4088/JCP.11m07246).*
Corresponding author: *Chris J. Bushe, MB, BS, Lilly UK, Lilly House, Priestley Rd, Basingstoke, Hampshire, RG24 9NL, United Kingdom (bushe_chris@lilly.com and beesbeesbees@blueyonder.co.uk).*

Weight increase commonly occurs during treatment with many first-generation antipsychotics (FGAs) and second-generation antipsychotics (SGAs).[1,2] There is reasonable agreement about the differential risk of weight gain during antipsychotic treatment based on data from randomized controlled trials (RCTs).[2–5]

Interpreting weight change data is not always straightforward.[1,2,6] First, data from RCTs are limited in the duration of treatment and in the antipsychotics included. Second, the type of weight data reported is limited and not always relevant to clinical practice. Mean weight change occurring during a study is a frequently reported measure, for example, but obscures the fact that there may be marked individual variation in weight change with antipsychotics. One categorical measure of weight change that is relevant to clinical practice is the number of patients who migrate to potentially harmful body mass index (BMI [kg/m^2]) categories (eg, BMI ≥ 25),[4] but few studies report this measure. It is also important to appreciate that some patients lose rather than gain weight in clinical trials. In the 6-month, randomized study reported by Bushe and colleagues,[2] for example, 9.0% of the olanzapine and 9.6% of the quetiapine cohort lost ≥ 7% of their initial bodyweight. Given the limitations of the weight change data reported in many RCTs, it is important to consider other sources of data, including observational studies. The observational Schizophrenia Outpatient Health Outcomes (SOHO) studies are one source of such data. The main strengths of the SOHO studies are their large size, the representative nature of the patients included, and the opportunity afforded to assess outcomes (including weight change) over a long period of time (3 years). The SOHO data presented here include a range of continuous and categorical weight change variables. These outcomes are provided for adult patients completing 3 years of monotherapy with a range of antipsychotics, allowing us to address the clinical question, What weight change may take place over a 3-year period for patients who continue on the same medication? In the absence of a placebo cohort, it may be relevant to also consider the increasing obesity reported in the unmedicated general population over the last decade. There is little doubt that excessive weight gain is a worldwide issue in the general population at all ages.

METHOD

Study Design

The European SOHO and Intercontinental SOHO studies were 3-year, prospective, nonrandomized, observational studies started in 2000 and completed in 2005.[7,8] The 2 SOHO studies were conducted in different geographical regions, but the key elements of the design were identical, enabling the data to be pooled. The patient populations consisted of outpatients aged 18 years or older with schizophrenia. Patients were included in the studies when they started or changed antipsychotic medication and were evaluated until 36 months (3 years). The studies complied with regulations relating to informed patient consent and appropriate ethics review. Further methodological details are available elsewhere.[7] The European

Clinical Points

- Weight gain in schizophrenia, although maximal initially, continues for at least 3 years.
- All antipsychotics in this study are associated with weight loss and weight gain in a significant number of patients.
- During a 3-year period, between 7% and 15% of patients had an increase in body mass index (kg/m^2) to ≥ 25.
- Regular weight monitoring should continue long term. Change alone in mean weight value may hide the varying changes in individual patients.

SOHO was conducted in 10 European countries and enrolled 10,972 patients.[9] The Intercontinental SOHO enrolled 7,658 patients.[8] By combining the data from both studies, the largest dataset of its kind was produced—the Worldwide SOHO database.[10]

Cohort Definition

A total of 17,384 patients were available for analysis. Of these, 12,763 were prescribed antipsychotic monotherapy at baseline. In the present analysis, cohorts were defined by the antipsychotic initiated as monotherapy at baseline. A total of 11,088 patients completed the 3-year study (referred to as the monotherapy cohort). Of these, 4,626 remained on their initial antipsychotic for at least 3 years (referred to as the monotherapy-completer cohort).

Statistical Analysis

The primary analysis cohorts were monotherapy completers; sensitivity analyses were also conducted on the monotherapy cohort (data available on request). An initial exploratory plot of weight at study entry versus weight change after 3 years revealed a moderate negative relationship as expected, indicating the presence of regression to the mean. As a result, all adjusted analyses account for a patient's baseline weight (or BMI [kg/m^2]). Longitudinal 3-year profiles of adjusted mean weight change were evaluated by using generalized linear mixed models (GLIMMIX),[11] adjusting for weight at study entry, time (log transformed), age, Clinical Global Impressions score, monotherapy treatment group, sex, region, independent housing status (yes/no), involvement in social activities (yes/no), and antipsychotic use before study entry (yes/no) along with (log) time-by-treatment group and weight at study entry–by-treatment group interaction terms. The number needed to treat (NNT) and number needed to harm (NNH) were evaluated using a Cox proportional hazards model.[12]

RESULTS

Baseline Demographics

Comparison of the baseline demographics for the monotherapy and monotherapy-completer cohorts revealed the 2 groups to be similar in terms of mean values for age, gender, overall symptoms, baseline weight, BMI, and percentage of patients who were underweight, normal weight, overweight, and obese.

Baseline demographic characteristics of the monotherapy-completer cohort, by drug, are shown in Supplementary eTable 1 (available at PSYCHIATRIST.COM). There were some statistically significant differences between the groups receiving the different antipsychotics; olanzapine, for example, was used less often in patients who were obese.

Mean and Categorical Weight Changes

Mean weight change. For all drugs, the mean weight change over 3 years represented a gain in weight. The rank order of mean weight change from baseline by antipsychotic among monotherapy completers at 3 years was, from lowest to highest, amisulpride (1.8 kg; 95% CI, 0.2–3.3), oral FGAs (2.3 kg; 95% CI, 1.5–3.2), depot FGAs (2.5 kg; 95% CI, 1.3–3.7)/quetiapine (2.5 kg; 95% CI, 1.4–3.6), risperidone (3.1 kg; 95% CI, 2.6–3.6), clozapine (3.3 kg; 95% CI, 2.3–4.3), and olanzapine (4.2 kg; 95% CI, 3.9–4.5) (data shown in Supplementary eFigure 1). Individual weight change varied considerably with all drugs (Figure 1). During 3 years of olanzapine monotherapy, for example, the interquartile range was 0 to 9 kg, indicating that half of the patients experienced weight change confined within these bounds, approximately 25% of patients actually lost weight, 25% gained more than 9 kg, and cases of extreme weight gain and loss were evident, with changes of –20 kg and +30 kg.

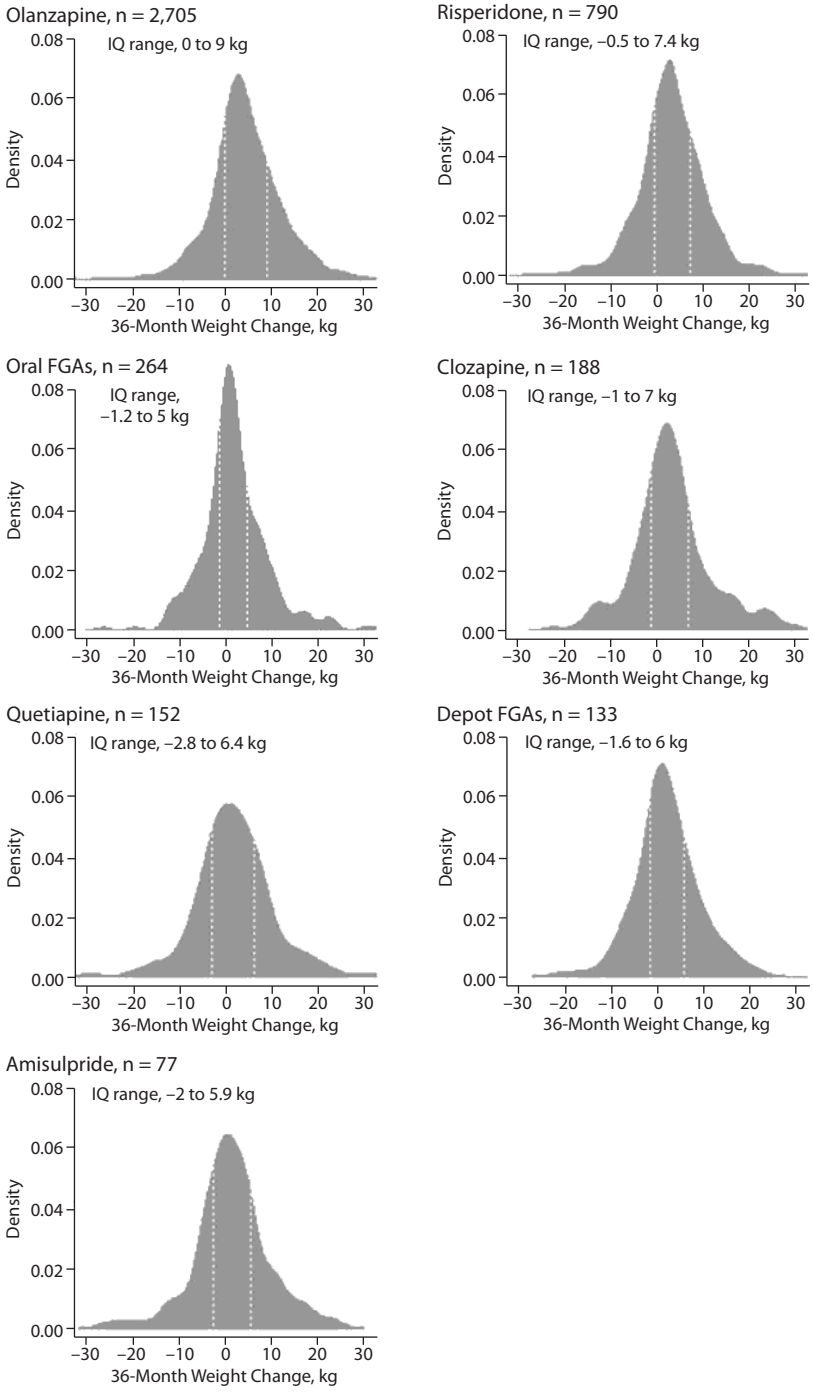
Gained ≥ 7% bodyweight. The proportion of patients who completed 3 years of monotherapy and who gained ≥ 7% of their baseline bodyweight with each antipsychotic was, in rank order from lowest to highest, oral FGAs (30%; 95% CI, 25%–36%), clozapine (33%; 95% CI, 26%–41%), quetiapine (35%; 95% CI, 28%–44%), amisulpride (36%; 95% CI, 25%–48%), depot FGAs (39%; 95% CI, 31%–49%), risperidone (40%; 95% CI, 37%–44%), and olanzapine (45%; 95% CI, 43%–48%) (Figure 2).

The number of patients that would need to be treated with olanzapine compared with the other agents to expect 1 additional instance of a ≥ 7% increase in bodyweight from baseline to end point (the NNH) was calculated. The NNH values were not significant for all comparisons with olanzapine, except for oral FGAs, where the NNH was 4 (95% CI, 2–12).

Lost ≥ 7% bodyweight. The proportion of patients who completed 3 years of monotherapy and who lost ≥ 7% of their baseline bodyweight with each antipsychotic was, in rank order from highest to lowest, quetiapine (10%; 95% CI, 7%–16%), risperidone (8%; 95% CI, 6%–11%)/clozapine (8%; 95% CI, 5%–13%)/oral FGAs (8%; 95% CI, 5%–11%), amisulpride (7%; 95% CI, 3%–14%)/olanzapine (7%; 95% CI, 6%–8%), and depot FGAs (5%; 95% CI, 3%–10%) (Figure 3).

The number of patients who would need to be treated with olanzapine compared with the other agents to expect 1 additional instance of ≥ 7% decrease in weight from baseline

Figure 1. Density Plots of Mean Weight Change (kg) From Baseline at 3 Years (unadjusted data)[a]



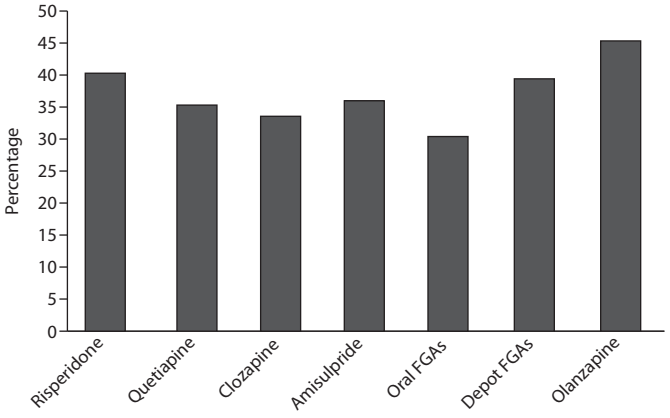
[a]Weight change in 50% of patients occurred in the interquartile range (indicated by the two dotted white lines).
Abbreviations: IQ = interquartile, FGA = first-generation antipsychotic.

to end point (the NNT) was calculated. The NNT values were not significant for all comparisons with olanzapine, except for quetiapine, where the NNT was –7 (95% CI, –3 to –86).

Mean change in BMI. For all drugs, the mean change in BMI over 3 years represented an increase in BMI. The mean change in BMI from baseline over 3 years was, in rank order from lowest to highest, amisulpride (0.7; 95% CI, 0.2–1.2), quetiapine (0.9; 95% CI, 0.5–1.3)/oral FGAs (0.9; 95% CI, 0.6–1.2), depot FGAs (1.2; 95% CI, 0.8–1.6)/clozapine (1.2; 95% CI, 0.9–1.6)/risperidone (1.2; 95% CI, 1.0–1.3), and olanzapine (1.6; 95% CI, 1.5–1.7) (Supplementary eFigure 2).

BMI moved into an overweight category. The percentage of patients who started with a BMI < 25 and moved to a BMI ≥ 25 over 3 years was, in rank order from lowest to highest,

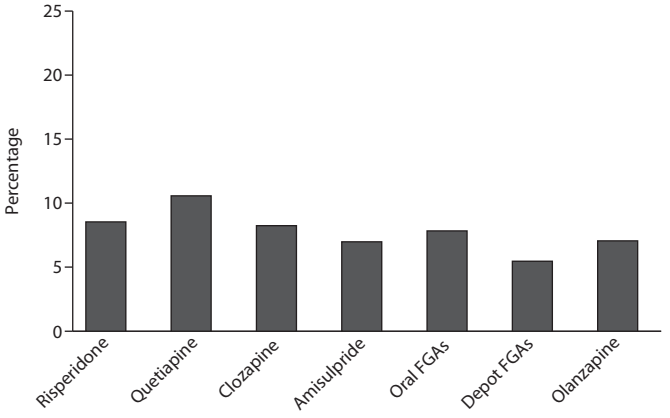
Figure 2. Patients Gaining ≥ 7% of Baseline Bodyweight at 3 Years



	Risperidone	Quetiapine	Clozapine	Amisulpride	Oral FGAs	Depot FGAs	Olanzapine
N	786	149	187	78	270	130	2,706
Patients gaining ≥ 7% of their baseline bodyweight (proportion)	0.40	0.35	0.33	0.36	0.30	0.39	0.45
95% CI	0.37–0.44	0.28–0.44	0.26–0.41	0.25–0.48	0.25–0.36	0.31–0.49	0.43–0.48

Abbreviation: FGA = first-generation antipsychotic.

Figure 3. Patients Losing ≥ 7% of Baseline Bodyweight at 3 Years



	Risperidone	Quetiapine	Clozapine	Amisulpride	Oral FGAs	Depot FGAs	Olanzapine
N	786	149	187	78	270	130	2,706
Patients gaining ≥ 7% of their baseline bodyweight (proportion)	0.08	0.10	0.08	0.07	0.08	0.05	0.07
95% CI	0.06–0.11	0.07–0.16	0.05–0.13	0.03–0.14	0.05–0.11	0.03–0.10	0.06–0.08

Abbreviation: FGA = first-generation antipsychotic.

depot FGAs (7%; 95% CI, 4%–11%), amisulpride (10%; 95% CI, 6%–18%)/oral FGAs (10%; 95% CI, 8%–14%), quetiapine (11%; 95% CI, 7%–17%), clozapine (13%; 95% CI, 9%–18%), risperidone (14%; 95% CI, 11%–16%), and olanzapine (15%; 95% CI, 13%–17%).

Trajectory of Weight Change

Mean weight change. Both raw and adjusted data for the trajectory of mean weight change with the different antipsychotics over 3 years are shown in Figure 4. These trajectories show that, in 6 of 7 cases, the model fit is good; only in the case of depot FGAs is the model fit poor. These trajectories also show that, for all drugs, the rate of weight change was most rapid during the first 6 to 12 months of treatment. Although subsequent weight change occurred at a slower rate, there was no plateauing. The trajectories of the response to all antipsychotics appeared to be similar.

Gained ≥ 7% bodyweight. The trajectory of patients gaining ≥ 7% of baseline bodyweight over 3 years is shown in Supplementary eFigure 3. The trajectories of the responses to all antipsychotics except depot FGAs and risperidone appear similar. As with mean weight gain, the rate of increase in the proportion of patients gaining ≥ 7% baseline bodyweight was most marked in the first 6 to 12 months, with less evidence of plateau than for mean weight change.

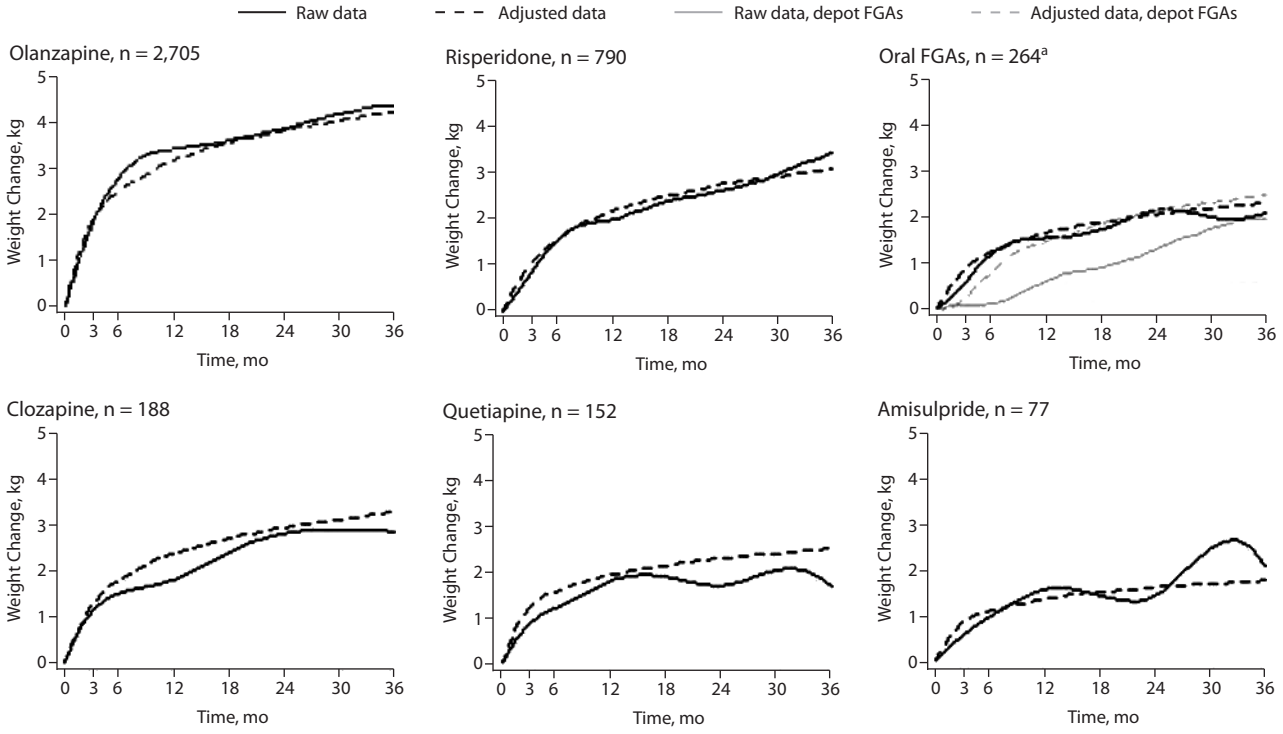
BMI moved into an overweight category. The trajectories of patients who moved into an overweight BMI category (ie, ≥ 25) during 3 years of monotherapy with the different antipsychotics are shown in Figure 5. The trajectories of the responses to all antipsychotics were less uniform, with a suggestion of less plateauing with olanzapine and risperidone than other drugs.

DISCUSSION

This post hoc analysis of data from the SOHO studies explored mean and categorical weight changes and the trajectories of different measures of weight change during 3 years of continual treatment with the same antipsychotic. Consistent with other work, our results show that mean weight gain varies among individual antipsychotics, with olanzapine and clozapine being associated with the highest mean weight gain over 3 years. A key finding is that weight gain (assessed as mean weight change, the percentage of patients gaining ≥ 7% of baseline bodyweight, and the percentage of patients moving to a BMI of ≥ 25) did not plateau; although the rate of increase was most marked during the first 6 to 12 months, weight gain continued throughout the 3 years, albeit more slowly. This finding is not in line with some other reports, and potential reasons for this are discussed below. Between 7% and 15% of patients moved into an overweight BMI category over 3 years. These data add to the body of evidence for the need for relevant weight management strategies in all patients receiving antipsychotics.[13–16]

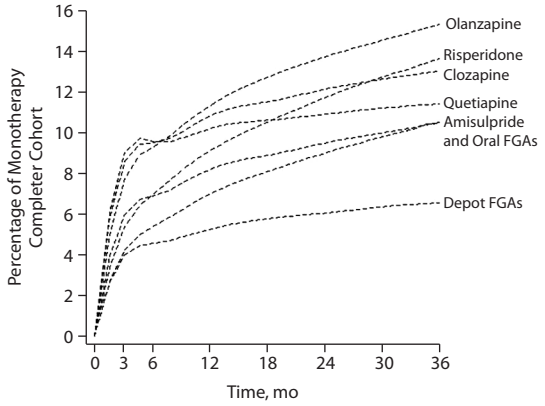
The SOHO studies began in 2000.[7,8] Since then, weight management in individuals with severe mental illness has become a greater priority, and weight management programs have become available as part of routine clinical practice.[15–17]

Figure 4. Trajectory of Mean Weight Change From Baseline (kg) Over 3 Years: Raw and Adjusted Data



[a]Depot FGAs, n = 133.
Abbreviation: FGA = first-generation antipsychotic.

Figure 5. Proportion of Patients Who Moved Into an Overweight BMI (> 25 kg/m^2) Category Over 3 Years (adjusted data)



Abbreviations: BMI = body mass index, FGA = first-generation antipsychotic.

It is possible that if the SOHO studies were conducted now, the amount of weight gained and the proportion of patients with weight gain might be lower.

Mean and Categorical Weight Changes

Data from short-term RCTs show that significant weight gain (≥ 7% from baseline) is more common with many antipsychotics than with placebo.[1] These results from the SOHO studies are consistent with this finding. Short-term (10-week) RCT data show that individual antipsychotics, both FGAs and SGAs, vary in terms of mean weight gain,[3] with clozapine and olanzapine being associated with the highest mean weight gain. In terms of mean weight gain, approximately the same rank order of antipsychotics was seen in the long-term SOHO studies. While quetiapine has not always been associated with weight gain to the extent of olanzapine, recent RCT data suggest that weight gain with this agent may be significant.[2,4,5] Data on longer term weight change with amisulpride over 1 year have previously been limited to that reported by Kahn and colleagues.[4] The SOHO studies are, therefore, the first to provide long-term data over 3 years for this agent, albeit in a small cohort of 77 patients. Amisulpride was associated with the lowest mean weight gain (1.8 kg) and had 1 of the smallest proportions of individuals moving into an adverse BMI category (10%). Cohort sizes, however, for some of the analyses with amisulpride in particular are small and therefore may be confounding.

Mean Data Hide Categorical Information of Interest

In the current analysis, individual weight change was shown to vary considerably; simply reporting the mean weight change from baseline would have hidden the observed variation. Recording a wider range of data and presenting it in different ways, as has been done here (eg, density plots in Figure 1), provides information that is potentially useful to clinicians for tailoring therapy for individual patients.

Trajectory of Weight Change and the Importance of the Patient Cohort

For all the antipsychotics studied in this analysis, the rate of weight gain was maximal during the first 6 to 12 months of treatment, which is consistent with other studies[18–20] and previous findings from the European SOHO study.[21,22] Patients should receive regular monitoring of weight throughout treatment. This finding has implications for the timing of the initiation of weight management programs and indicates that, prior to starting treatment with any antipsychotic, patients should be warned about the risk of weight gain. It also implies that active weight management should commence from the start of treatment in an attempt to minimize or prevent weight gain.[14,23] However, given the lack of a plateau in our 3-year data, it is important that weight management should continue for the duration of antipsychotic treatment and not be time limited. It has already been shown that long-term weight management strategies to accompany antipsychotic therapy can be successful even in patients with current psychotic symptoms.[13,15–17]

Previous RCT findings suggest that weight gain with antipsychotics plateaus over time, as evidenced by the plateauing of weight gain at 38 weeks with olanzapine.[24] In the 6-month and 36-month analyses of naturalistic data from the European SOHO study, plateauing of weight was also observed.[21,22] However, this analysis of Worldwide SOHO data found that weight gain did not plateau with olanzapine or with any other antipsychotics in the naturalistic setting. Instead, weight gain continued throughout the 3 years. Other researchers have also noted the absence of a plateau with antipsychotic therapy in some patient cohorts: Millen and colleagues[20] reported that weight gain with olanzapine reached a plateau with some cohorts but did not plateau with others in their analysis of pooled data from 86 clinical trials, and Addington and coworkers[25] also reported that weight gain did not plateau but continued to increase over 3 years in a consecutive series of patients receiving a variety of FGAs and SGAs for first-episode schizophrenia. These findings suggest that longer term observational studies may complement RCTs for following safety parameters over time.

The discrepancy in this analysis of Worldwide SOHO data and previous European SOHO findings[21,22] may be due to the different patient cohorts that were studied. In the 6-month and 36-month analyses of European SOHO data, cohorts were defined by the antipsychotic that was initiated as monotherapy at baseline; patients were followed for 6 months and 3 years but may have changed antipsychotics during this time.[21,22] In the present analysis (Worldwide SOHO), cohorts were defined by the antipsychotic initiated at baseline and maintained for 3 years; while this is a specific subgroup (given that many patients were likely to switch, augment, or discontinue therapy), it provides important data on weight gain with long-term monotherapy. The potentially important influence of the cohort studied on weight gain with antipsychotics is demonstrated by different findings in studies using different cohorts.

When comparing categorical and mean change weight parameters, there may be clinical utility in the finding that there is far less evidence of any plateauing when measuring the numbers of patients either gaining or losing ≥ 7% of baseline bodyweight than when assessing the trajectory or mean weight change.

Limitations

The main limitation of the observational SOHO studies is that the groups were not randomized and so the possibility that variables other than the prescribed antipsychotic may have impacted differences in weight change cannot be excluded.

A number of other general limitations should also be taken into account when considering these findings. This was a post hoc analysis, which means that it was an exploratory investigation, and the results may be complex to interpret. A variety of models can be used to analyze data, and it is not always easy to select a model that provides the most appropriate and accurate presentation of the data. In the specific drug cohort analyses, some of the cohorts are small, which may provide another potential cause for confounding.

Specific limitations of this analysis include the fact that this was a completer analysis; the reasons for dropout are unknown, and it must be acknowledged that some patients may have discontinued due to weight gain. However, a sensitivity analysis was conducted on the starter monotherapy cohorts, and the results were similar to the monotherapy completers, indicating that dropouts did not bias these results. Another limitation is that both of the SOHO studies were largely composed of patients with established schizophrenia; the results cannot therefore be applied directly to recent-onset patients. It is generally accepted that such patients are more prone to weight gain with a range of antipsychotics.[1]

Due to the absence of a placebo arm the proportion of weight change seen due to the treatment rather than time is unknown.

CONCLUSIONS

From a clinical viewpoint, these findings may help clinicians and patients understand the long-term weight changes that are likely to occur in individual patients receiving the different antipsychotics and the implications for health. Weight change data are important when selecting antipsychotic drugs, though many other considerations come into selection, including the risk of other adverse events, efficacy, and formulation. Concentrating on a single outcome measure of weight change, such as mean weight gain, is not ideal, as it hides the marked individual variation in weight change that occurs with all antipsychotics. It is better to consider a range of outcomes, including mean and categorical weight changes and the trajectories of different measures of weight change. Patients should receive regular monitoring of weight throughout treatment.

Drug names: clozapine (FazaClo, Clozaril, and others), olanzapine (Zyprexa and others), quetiapine (Seroquel and others), risperidone (Risperdal and others).

Author affiliations: Eli Lilly and Company Ltd, Basingstoke (Dr Bushe); Greater Manchester West Mental Health NHS Foundation Trust, and University of Manchester, Manchester (Dr Haddad), United Kingdom; Psychiatric University Clinic Groningen, Mental Health Services Drenthe, Assen, The Netherlands (Dr Slooff); and Lilly USA, Indianapolis, Indiana, and Memorial University of Newfoundland, St. John's, Newfoundland and Labrador, Canada (Dr Karagianis).

Potential conflicts of interest: **Drs Bushe** and **Karagianis** are employees of and stock shareholders in Eli Lilly. **Dr Haddad** has received fees for lecturing and consultancy, plus conference expenses, from the manufacturers of various antipsychotics, including Astra Zeneca, Bristol-Myers Squibb, Eli Lilly, Janssen-Cilag, and Lundbeck. **Dr Slooff** has no conflicts of interest.

Funding/support: The Schizophrenia Outpatient Health Outcomes studies were funded by Eli Lilly and Company, manufacturer of olanzapine.

Acknowledgments: The authors would like to thank Pritibha Singh, BSc, for statistical analysis and Richard Walton, MSc, for statistical review of the manuscript. The authors were assisted in writing this article by Sarah Smith, BSc, medical writer. Mss Singh and Smith and Mr Walton are employees of Eli Lilly.

Supplementary material: See accompanying pages.

REFERENCES

1. Haddad P. Weight change with atypical antipsychotics in the treatment of schizophrenia. *J Psychopharmacol*. 2005;19(suppl):16–27.
2. Bushe C, Sniadecki J, Bradley AJ, et al. Comparison of metabolic and prolactin variables from a six-month randomised trial of olanzapine and quetiapine in schizophrenia. *J Psychopharmacol*. 2010;24(7):1001–1009.
3. Allison DB, Mentore JL, Heo M, et al. Antipsychotic-induced weight gain: a comprehensive research synthesis. *Am J Psychiatry*. 1999;156(11): 1686–1696.
4. Kahn RS, Fleischhacker WW, Boter H, et al; EUFEST study group. Effectiveness of antipsychotic drugs in first-episode schizophrenia and schizophreniform disorder: an open randomised clinical trial. *Lancet*. 2008;371(9618):1085–1097.
5. Lieberman JA, Stroup TS, McEvoy JP, et al; Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med*. 2005;353(12):1209–1223.
6. Hamer S, Haddad PM. Adverse effects of antipsychotics as outcome measures. *Br J Psychiatry suppl*. 2007;191(suppl 50):s64–s70.
7. Haro JM, Edgell ET, Jones PB, et al; SOHO Study Group. The European Schizophrenia Outpatient Health Outcomes (SOHO) study: rationale, methods and recruitment. *Acta Psychiatr Scand*. 2003;107(3):222–232.
8. Dossenbach M, Erol A, el Mahfoud Kessaci M, et al; IC-SOHO Study Group. Effectiveness of antipsychotic treatments for schizophrenia: interim 6-month analysis from a prospective observational study (IC-SOHO) comparing olanzapine, quetiapine, risperidone, and haloperidol. *J Clin Psychiatry*. 2004;65(3):312–321.
9. Haro JM, Suarez D, Novick D, et al; SOHO Study Group. Three-year antipsychotic effectiveness in the outpatient care of schizophrenia: observational versus randomized studies results. *Eur Neuropsychopharmacol*. 2007;17(4):235–244.
10. Karagianis J, Novick D, Pecenak J, et al. Worldwide-Schizophrenia Outpatient Health Outcomes (W-SOHO): baseline characteristics of pan-regional observational data from more than 17,000 patients. *Int J Clin Pract*. 2009;63(11):1578–1588.
11. Fitzmaurice G, Davidian M, Verbeke G, et al, eds. *Handbooks of Modern Statistical Methods: Longitudinal Data Analysis*. Boca Raton, LA: Chapman & Hall/CRC Press; 2008.
12. Laubender RP, Bender R. Estimating adjusted risk difference (RD) and number needed to treat (NNT) measures in the Cox regression model. *Stat Med*. 2010;29(7–8):851–859.
13. Smith S, Yeomans D, Bushe CJP, et al. A well-being programme in severe mental illness: reducing risk for physical ill-health: a post-programme service evaluation at 2 years. *Eur Psychiatry*. 2007;22(7):413–418.
14. Bushe CJ, Bradley AJ, Doshi S, et al. Changes in weight and metabolic parameters during treatment with antipsychotics and metformin: do the data inform as to potential guideline development? a systematic review of clinical studies. *Int J Clin Pract*. 2009;63(12):1743–1761.
15. Holt RIG, Pendlebury J, Wildgust HJ, et al. Intentional weight loss in overweight and obese patients with severe mental illness: 8-year experience of a behavioral treatment program. *J Clin Psychiatry*. 2010;71(6):800–805.
16. Bushe CJ, McNamara D, Haley C, et al. Weight management in a cohort of Irish inpatients with serious mental illness (SMI) using a modular behavioural programme; a preliminary service evaluation. *BMC Psychiatry*. 2008;8(1):76.
17. Pendlebury J, Bushe CJ, Wildgust HJ, et al. Long-term maintenance of weight loss in patients with severe mental illness through a behavioural treatment programme in the UK. *Acta Psychiatr Scand*. 2007;115(4): 286–294.
18. Brecher M, Leong RW, Stening G, et al. Quetiapine and long-term weight change: a comprehensive data review of patients with schizophrenia. *J Clin Psychiatry*. 2007;68(4):597–603.
19. Perez-Iglesias R, Crespo-Facorro B, Martinez-Garcia O, et al. Weight gain induced by haloperidol, risperidone and olanzapine after 1 year: findings of a randomized clinical trial in a drug-naïve population. *Schizophr Res*. 2008;99(1–3):13–22.
20. Millen BA, Campbell GM, Beasley CM. Weight changes over time in adults treated with the oral or depot formulations of olanzapine: a pooled analysis of 86 clinical trials. *J Psychopharmacol*. 2011;25(5):639–645.
21. Lambert M, Haro JM, Novick D, et al. Olanzapine vs other antipsychotics in actual out-patient settings: six months tolerability results from the European Schizophrenia Out-patient Health Outcomes study. *Acta Psychiatr Scand*. 2005;111(3):232–243.
22. Novick D, Haro JM, Perrin E, et al. Tolerability of outpatient antipsychotic treatment: 36-month results from the European Schizophrenia Outpatient Health Outcomes (SOHO) study. *Eur Neuropsychopharmacol*. 2009;19(8):542–550.
23. Bushe C, Haddad P, Peveler R, et al. The role of lifestyle interventions and weight management in schizophrenia. *J Psychopharmacol*. 2005;19 (suppl):28–35.
24. Kinon BJ, Kaiser CJ, Ahmed S, et al. Association between early and rapid weight gain and change in weight over one year of olanzapine therapy in patients with schizophrenia and related disorders. *J Clin Psychopharmacol*. 2005;25(3):255–258.
25. Addington J, Saeedi H, Addington D. Weight gain in first-episode psychosis over three years. *Schizophr Res*. 2006;86(1–3):335–336.

Supplementary material follows this article.

 © Copyright 2012 Physicians Postgraduate Press, Inc.

THE JOURNAL OF CLINICAL PSYCHIATRY

Supplementary Material

Article Title: Weight Change From 3-Year Observational Data: Findings From the Worldwide Schizophrenia Outpatient Health Outcomes Database

Author(s): Chris J. Bushe, MB, BS; Cees J. Slooff, MD, PhD; Peter M. Haddad, MD, FRCPsych; and Jamie L. Karagianis, MD

Citation: J Clin Psychiatry 2012;73

DOI Number: 10.4088/JCP.11m07246

List of Supplementary Material for the article

1. Supplementary eTable 1 — Monotherapy Completers: Baseline Characteristics by Drug (unadjusted data)
2. Supplementary eFigure 1 — Mean Weight Change from Baseline at 3 Years (monotherapy and monotherapy completers, adjusted data)
3. Supplementary eFigure 2 — Mean Change in BMI from Baseline at 3 Years
4. Supplementary eFigure 3 — Proportion of Patients Gaining ≥ 7% of Baseline Bodyweight over 3 Years (adjusted data)

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

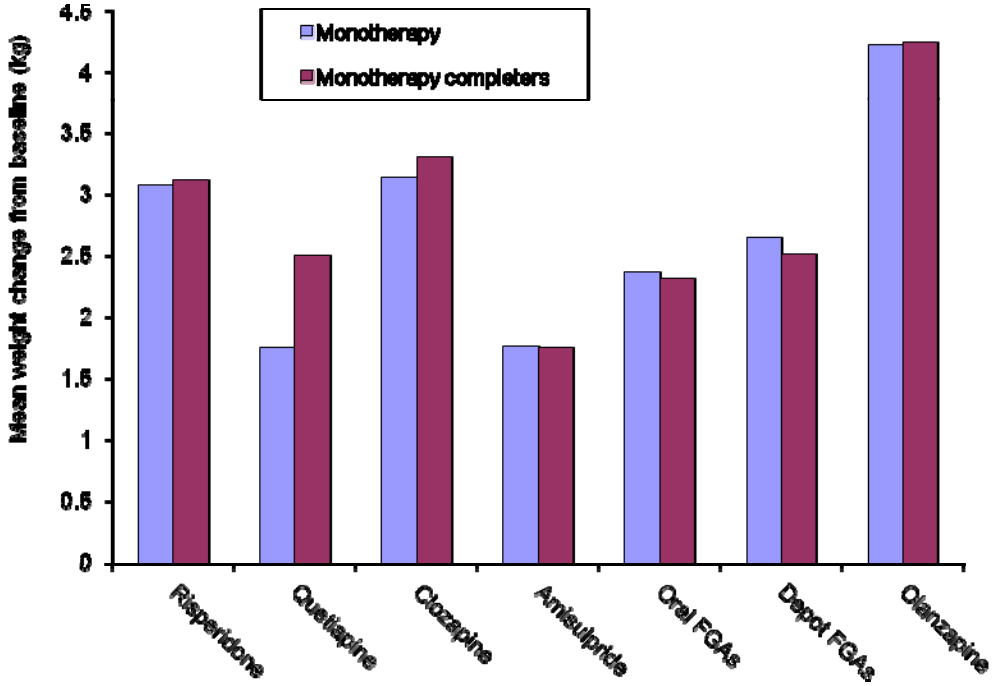
Supplementary eTable 1. Monotherapy Completers: Baseline Characteristics by Drug[a] (Unadjusted data)

Baseline Characteristic	Risperidone (N = 857)	Quetiapine (N = 161)	Clozapine (N = 198)	Amisulpride (N = 86)	Oral FGAs (N = 279)	Depot FGAs (N = 137)	Olanzapine (N = 2,908)	Total (N = 4,626)	p value
Age	37.88	38.40	35.42	39.62	41.31	41.39	37.51	37.91	< .0001*
(mean ± SD, years)	(12.85)	(12.84)	(10.76)	(13.85)	(11.97)	(11.61)	(13.11)	(12.91)	
Male (N, %)	499 (58.2)	78 (48.4)	125 (63.1)	43 (50.0)	131 (47.0)	77 (56.2)	1,573 (54.1)	2,527 (54.6)	.0019
Overall symptoms	4.2	4.3	4.6	4.4	4.0	4.3	4.3	4.3	< .0001*
(mean ± SD)	(0.97)	(0.95)	(0.99)	(0.99)	(1.11)	(1.01)	(1.01)	(1.01)	
Baseline weight	73.48	75.66	76.23	74.28	73.89	76.38	72.38	73.11	< .0001*
(mean ± SD, kg)	(14.35)	(13.34)	(14.39)	(16.45)	(14.22)	(15.93)	(14.01)	(14.23)	
BMI	25.75	26.55	26.39	25.48	26.14	26.13	25.30	25.55	< .0001*
(mean ± SD, kg/m^2)	(4.63)	(4.55)	(4.37)	(4.93)	(4.30)	(4.32)	(4.21)	(4.35)	
BMI category, (N, %)									0.0140
Underweight	21 (2.5)	1 (0.6)	2 (1.0)	2 (2.3)	1 (0.4)	2 (1.5)	78 (2.7)	107 (2.3)	
Normal	384 (44.8)	64 (39.8)	76 (38.4)	42 (48.8)	118 (42.3)	52 (38.0)	1,365 (46.9)	2,101 (45.4)	
Overweight	306 (35.7)	63 (39.1)	84 (42.4)	27 (31.4)	112 (40.1)	56 (40.9)	1,053 (36.2)	1,701 (36.8)	
Obese	132 (15.4)	30 (18.6)	34 (17.2)	14 (16.3)	45 (16.1)	26 (19.0)	373 (12.8)	654 (14.1)	

[a]GLIMMIX model adjusted for the following variables; age, gender, region, height, weight, and BMI (except where outcome was weight). *Overall F-test (ANOVA)

ANOVA, analysis of variance; BMI, body mass index; FGA, first-generation antipsychotics; SD, standard deviation

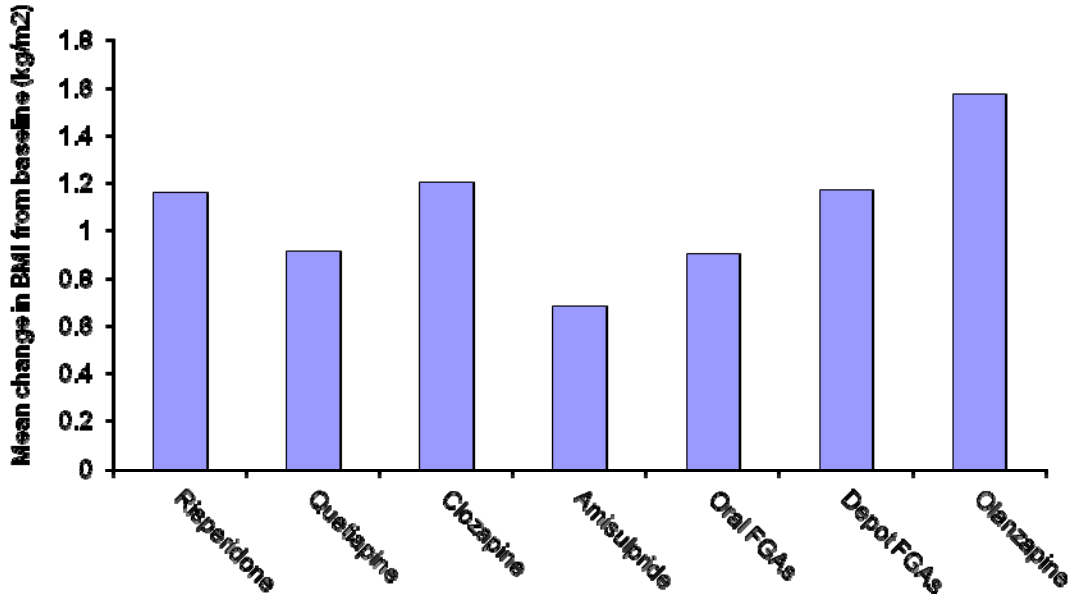
Supplementary eFigure 1. Mean Weight Change from Baseline at 3 Years (Monotherapy and Monotherapy Completers, Adjusted Data)



Patient Cohort	Drug						
	Risperidone	**Quetiapine**	**Clozapine**	**Amisulpride**	**Oral FGAs**	**Depot FGAs**	**Olanzapine**
N	786	149	187	78	270	130	2706
Monotherapy							
Mean adjusted weight change from baseline (kg)	3.07	1.75	3.14	1.76	2.37	2.64	4.22
(95% CI)	(2.68; 3.46)	(0.97; 2.52)	(2.32; 3.96)	(0.54; 2.98)	(1.77; 2.96)	1.77; 3.52)	(3.99; 4.45)
Monotherapy completers							
Mean adjusted weight change from baseline (kg)	3.12	2.5	3.30	1.75	2.31	2.51	4.24
(95% CI)	(2.61;3.62)	(1.39; 3.61)	(2.29; 4.31)	(0.22; 3.28)	(1.47; 3.15)	(1.31; 3.71)	(3.94; 4.54)

FGAs, first-generation antipsychotics

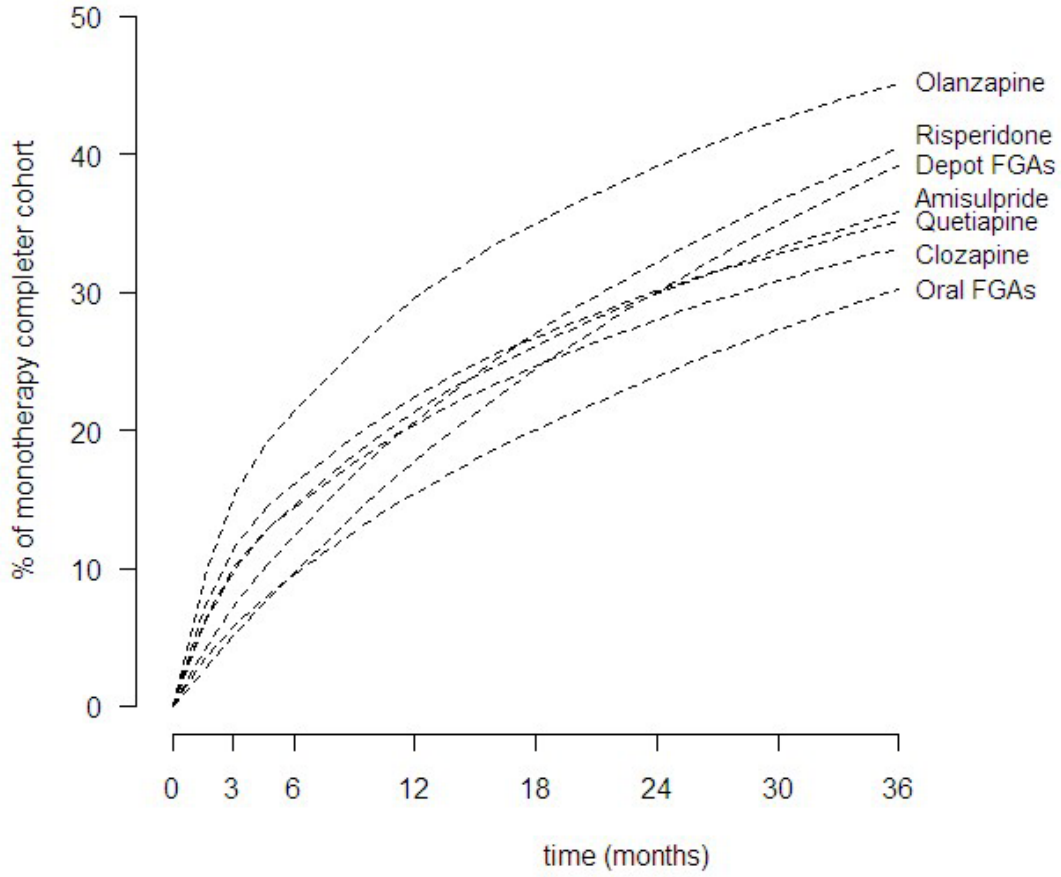
Supplementary eFigure 2. Mean Change in BMI from Baseline at 3 Years



	Drug						
	Risperidone	**Quetiapine**	**Clozapine**	**Amisulpride**	**Oral FGAs**	**Depot FGAs**	**Olanzapine**
N	780	148	186	78	269	129	2686
Mean change in BMI from baseline (kg/m^2)	1.16	0.91	1.20	0.68	0.90	1.17	1.57
(95% CI)	(0.99; 1.34)	(0.52; 1.30)	(0.85; 1.56)	(0.15; 1.22)	(0.61; 1.20)	(0.75; 1.59)	(1.47; 1.68)

FGAs, first-generation antipsychotics

Supplementary eFigure 3. Proportion of Patients Gaining ≥ 7% of Baseline Bodyweight over 3 Years (Adjusted Data)



FGAs, first-generation antipsychotics