

Weight change during long-term treatment with lurasidone: pooled analysis of studies in patients with schizophrenia

Jonathan M. Meyer^a, Yongcai Mao^b, Andrei Pikalov^b, Josephine Cucchiaro^b and Antony Loebel^b

The objective of this analysis was to evaluate the effect of 12 months of treatment with lurasidone on weight in patients with schizophrenia. Post-hoc, observed-case analysis included pooled data from six studies on 40–160 mg/day lurasidone; two studies included active comparators (2–6 mg/day risperidone or 200–800 mg/day quetiapine XR). Overall, 593 patients completed 12 months of treatment ($N = 471$ lurasidone, $N = 89$ risperidone, $N = 33$ quetiapine XR). The mean baseline weight was 72.8, 80.8, and 72.4 kg in the lurasidone, risperidone, and quetiapine XR groups, respectively. The mean weight change at month 12 was -0.4 kg with lurasidone, $+2.6$ kg with risperidone, and $+1.2$ kg with quetiapine XR. Weight gain of at least 7% from study baseline was observed in 16.0, 25.8, and 15.2% of patients, and weight loss of at least 7% was seen in 18.5, 6.7, and 9.1% of patients treated with lurasidone, risperidone, and quetiapine XR, respectively. A shift from normal/underweight baseline BMI status to overweight/obese at month 12 occurred in 10.2, 27.6, and 15.0% of

patients in the lurasidone, risperidone, and quetiapine XR groups, respectively. Conversely, 14.3, 1.7, and 7.7% of patients, respectively, shifted from overweight/obese to normal/underweight. In summary, a low potential for clinically significant weight gain was observed in patients with schizophrenia treated continuously with lurasidone for 12 months. *Int Clin Psychopharmacol* 30:342–350
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Introduction

According to recent estimates, more than one-third of adults in the USA are obese ($BMI \geq 30$ kg/m²; Flegal *et al.*, 2012; Ogden *et al.*, 2012). Obesity and other cardiovascular disease risk factors are more prevalent in individuals with schizophrenia than in the general population (McEvoy *et al.*, 2005; Goff *et al.*, 2005a, 2005b; McElroy, 2009; De Hert *et al.*, 2009b; Correll *et al.*, 2010; Casey *et al.*, 2011). Increased body weight is associated with elevated risk of developing hypertension, dyslipidemia, metabolic syndrome, type 2 diabetes mellitus, and coronary heart disease (Must *et al.*, 1999; Nguyen *et al.*, 2008, 2010). Two recent meta-analyses demonstrated

that longer duration of illness was associated with the development of metabolic syndrome and increased cardiovascular risk in patients with schizophrenia (Mitchell *et al.*, 2013a, 2013b).

Atypical antipsychotic medications vary in their propensity for causing weight gain and metabolic disturbances (American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity, 2004; Newcomer, 2005; Henderson, 2007; Newcomer, 2007). A recent meta-analysis of 212 short-term trials comprising more than 40 000 patients with schizophrenia or related disorders found that the mean weight gain was generally higher for olanzapine, clozapine, and iloperidone; intermediate for quetiapine, risperidone, and paliperidone; and lower for lurasidone, asenapine, amisulpride, aripiprazole, and ziprasidone (Leucht *et al.*, 2013). A similar pattern has been observed in controlled studies of longer-term treatment (12 months or more; Csernansky *et al.*, 2002; Kasper *et al.*, 2003; Meltzer *et al.*, 2010; Pappadopulos *et al.*, 2012) and large, ‘real-world’ effectiveness studies of long-term therapy (up to 36 months; Lieberman *et al.*, 2005; Bushe *et al.*, 2012).

Lurasidone is an atypical antipsychotic agent that acts as an antagonist with high affinity for dopamine D₂, 5-hydroxytryptamine (5-HT)_{2A}, and 5-HT₇ receptors, and as a partial

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agonist with moderate to high affinity for 5-HT_{1A} receptors (Ishibashi *et al.*, 2010). Notably, lurasidone demonstrates weak affinity for 5-HT_{2C} receptors and no appreciable affinity for muscarinic M₁ and histamine H₁ (Ishibashi *et al.*, 2010). The negligible activity at 5-HT_{2C} and H₁ receptors suggests that lurasidone may have a low propensity for causing weight gain (Kroeze *et al.*, 2003).

In five double-blind, placebo-controlled, 6-week studies, lurasidone has demonstrated efficacy at fixed daily doses of 40, 80, 120, and 160 mg in the treatment of schizophrenia (Nakamura *et al.*, 2009; Meltzer *et al.*, 2011; Nasrallah *et al.*, 2013; Ogasa *et al.*, 2013; Loebel *et al.*, 2013a). The mean change in weight from baseline to study endpoint in short-term studies was +0.43 kg for lurasidone-treated patients (20–160 mg/day, *N*=1486) and –0.02 kg for patients receiving placebo (*N*=696); the proportion of patients with at least 7% weight gain was 4.8% for lurasidone and 3.3% for placebo (Sunovion Pharmaceuticals Inc., 2013). The present analysis pooled data from six long-term clinical studies to evaluate change in weight and BMI in patients with schizophrenia who received 12 months of treatment with lurasidone at doses of 20–160 mg/day.

Methods

Study design

The lurasidone clinical trial database includes six studies of at least 12 months in duration in patients with schizophrenia or schizoaffective disorder (Table 1). In this post-hoc analysis, individual patient data from all six of these long-term studies were pooled for lurasidone; data for risperidone and extended-release quetiapine (quetiapine XR) were from one study each. The dose range of lurasidone in these studies was 20–160 mg/day, whereas risperidone was flexibly dosed between 2 and 6 mg/day, and quetiapine XR was flexibly dosed between 200 and 800 mg/day. Study medication was taken once daily with a meal or within 30 min of eating. Patients were instructed to take the study medication in the morning in three of the studies and in the evening in one study; timing of administration was not specified in the other two studies (Table 1).

All study protocols were approved by an independent ethics committee or institutional review board, and written informed consent was provided by all patients before initiation of study procedures. All studies were conducted in accordance with the International Conference on Harmonization Good Clinical Practice guidelines and with the ethical principles of the Declaration of Helsinki.

Patients

Eligible patients were adults aged between 18 and 75 years with a diagnosis of schizophrenia (all studies) or schizoaffective disorder (Citrome *et al.*, 2012). Other, more specific inclusion criteria, such as duration of illness and baseline disease severity, varied among studies.

Patients were excluded if they presented with an acute or unstable medical condition, a recent history of substance abuse, evidence of tardive dyskinesia or another severe, chronic movement disorder, or were judged to be at imminent risk of injury to self or others. Patients with BMI less than 18.5 kg/m² or greater than 40 kg/m² were excluded from three of the studies (Table 1).

Statistical analysis

The analysis population included all patients who completed 12 months of study treatment in any of the included studies. Duration of exposure was calculated from the first dose of active study medication. Intermediate visits were assigned to the closest assessment time point (3, 6, 9, or 12 months). Month 3 was operationally defined as study days 61–151, month 6 as days 152–242, month 9 as days 243–333, and month 12 as days 334–424. These assessment windows were selected to accommodate differences in the timing of assessments across studies.

Standard criteria for BMI categories were applied: underweight was defined as BMI less than 18.5 kg/m², normal weight was defined as BMI of at least 18.5 kg/m² and less than 25 kg/m², overweight defined as BMI of at least 25 kg/m² and less than 30 kg/m², and obese was defined as BMI of at least 30 kg/m² (Centers for Disease Control and Prevention, 2015).

Changes from baseline in weight, BMI, and waist circumference were summarized by treatment group at each time point, and comparisons of lurasidone (pooled) with risperidone, as well as with quetiapine XR, were conducted using *t*-tests with *P*-values unadjusted for multiple comparisons. The proportion of patients with an increase or decrease in weight of at least 7% from baseline was compared for lurasidone (pooled) versus risperidone and for lurasidone (pooled) versus quetiapine XR using Fisher's exact tests. Comparisons of risperidone versus quetiapine XR were not performed. The proportion of patients with a shift in BMI category (normal/underweight, overweight/obese) was calculated from baseline (start of active study medication) to month 12 for each treatment group.

Classification and regression tree (CART) analysis and stepwise multiple regression analysis were used to investigate patient age, sex, race, and duration of illness as potential predictors of change in body weight during treatment with lurasidone. CART analysis assessed the impact of the input variables (age, sex, race, and duration of illness) on the dichotomous outcome of at least 7% weight gain (yes vs. no). In the stepwise regression analysis, these variables were examined as predictors of weight change measured as a continuous variable.

Results

This analysis included 593 patients who completed 12 months of treatment (*N*=471 lurasidone, *N*=89 risperidone, *N*=33 quetiapine XR; Fig. 1). Study completion rates

Table 1 Summary of studies included in this pooled analysis

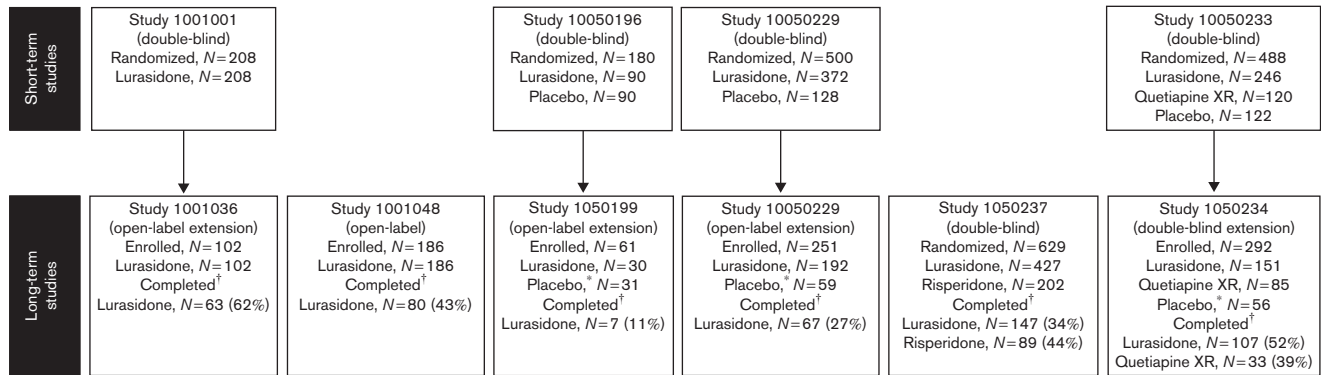
Study number/phase	Dates and locations	Study design/duration	Study medication	Patients in analysis (N)	Patient characteristics	Entry criteria
Study 1 (D1050199) NCT0088621	May 2004–October 2005 22 sites in the USA	12-month open-label extension of 6-week double-blind study (D1050196)	Lurasidone 80 mg/day Fixed dose Taken in the morning	7	18–65 years Schizophrenia (DSM-IV)	Completed double-blind study (D1050196) or discontinued because of lack of efficacy after ≥ 2 weeks of double-blind treatment
Study 2 (D1001036) ^a	August 2005–June 2007 50 sites in Japan	44-week open-label extension of 8-week double-blind study (D1001001)	Lurasidone 20–120 mg/day Flexibly dosed Timing of administration not specified	63	18–65 years Schizophrenia (ICD-10)	Completed 8-week double-blind study (D1001001)
Study 3 (D1001048) ^a	January 2007–April 2009 38 sites in Japan	Open-label study 12 months	Lurasidone 40–120 mg/day Flexibly dosed Timing of administration not specified	80	18–65 years Schizophrenia (ICD-10)	Initial episode or relapse (acute exacerbation)
Study 4 (D1050229 Ext) NCT00549718	October 2007–October 2010 Multinational 48 sites (21 in the USA)	22-month open-label extension of 6-week double-blind study	Lurasidone 40–120 mg/day Flexibly dosed Taken in the morning	67	18–75 years Schizophrenia (DSM-IV) ^b	Completed 6-week double-blind study (D1050229)
Study 5 (D1050237) (Citrome et al., 2012) NCT00641745	March 2008–July 2010 Multinational 68 sites (40 in the USA)	12-month randomized, double-blind parallel-group, active-controlled study	Lurasidone 40–120 mg/day, risperidone 2–6 mg/day Flexibly dosed Taken in the morning	147 89	18–75 years Schizophrenia or schizoaffective disorder (DSM-IV) ^b	Clinically stable for ≥ 8 weeks
Study 6 (D1050234)(Loebel et al., 2013b) NCT00789698	October 2008–June 2011 Multinational 59 sites (21 in the USA)	12-month randomized, double-blind, parallel-group, active-controlled continuation study	Lurasidone 40–160 mg/day, quetiapine XR 200–800 mg/day Flexibly dosed Taken in the evening	107 33	18–75 years Schizophrenia (DSM-IV) ^b	Completed 6-week, placebo-controlled study (D1050233)

DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition; ICD, International Statistical Classification of Diseases and Related Health Problems, 10th revision.

^aThe FDAAA 801 requirements for registering clinical trials did not apply to these studies, which were conducted entirely at sites in Japan before lurasidone was approved for any indication in the USA.

^bPatients with BMI < 18.5 kg/m² or > 40 kg/m² were excluded.

Fig. 1



Patient disposition. *Patients who received placebo during Studies 196, 229, and 233 were switched to lurasidone during Studies 199, 229ext, and 234, respectively. †Patients who completed 12 months of study treatment.

were 38.2% for the lurasidone group, 44.1% for the risperidone group, and 38.8% for the quetiapine XR group. The average age and sex were similar across the lurasidone, risperidone, and quetiapine XR groups; however, differences were observed in patients' racial backgrounds (Table 2). The mean weight and BMI at baseline were higher in the risperidone group (80.8 kg and 27.8 kg/m², respectively) compared with the lurasidone group (72.8 kg and 25.6 kg/m², respectively) and the quetiapine XR group (72.4 kg and 25.4 kg/m², respectively).

High rates of prior antipsychotic use (within 30 days of starting study medication) were observed: 90.7% for

patients in the lurasidone group (pooled), 91.0% for patients in the risperidone group, and 81.8% for patients in the quetiapine XR group (Table 3). No patients had taken clozapine for at least 30 days before study entry. The distribution of patients who had taken other antipsychotic agents associated with increased risk of weight gain (e.g. olanzapine, quetiapine) was similar across the pooled treatment groups, except for a lower rate of prior quetiapine use in the lurasidone and quetiapine groups compared with the risperidone group. Across the 12-month study period, the mean modal daily doses of study medication were 90.6 mg lurasidone, 4.4 mg risperidone, and 660.6 mg quetiapine XR.

Table 2 Demographics and baseline clinical characteristics

Characteristics	Lurasidone (N=471)	Risperidone (N=89)	Quetiapine XR (N=33)
Age [mean (SD)] (years)	41.4 (11.7)	42.7 (11.3)	39.8 (9.5)
Men [n (%)]	318 (67.5)	61 (68.5)	21 (63.6)
Race [n (%)]			
White	162 (34.4)	36 (40.4)	24 (72.7)
Black	96 (20.4)	44 (49.4)	3 (9.1)
Asian	198 (42.0)	1 (1.1)	5 (15.2)
Other	15 (3.2)	8 (9.0)	1 (3.0)
Weight (kg)			
Mean (SD)	72.8 (17.8)	80.8 (18.1)	72.4 (12.8)
Median	71.2	79.1	70.9
BMI (kg/m ²)			
Mean (SD)	25.6 (5.1)	27.8 (5.6)	25.4 (4.0)
Median	24.5	27.2	24.6
BMI category [n (%)] ^a			
Underweight	14 (3.0)	1 (1.1)	0 (0)
Normal	239 (50.7)	28 (31.5)	20 (60.6)
Overweight	131 (27.8)	31 (34.8)	8 (24.2)
Obese	87 (18.5)	29 (32.6)	5 (15.2)
Waist circumference (cm) ^b			
Mean (SD)	89.7 (14.6)	96.1 (13.9)	84.8 (11.7)
Median	88.0	96.0	82.5

^aUnderweight, BMI < 18.5 kg/m²; normal weight, BMI ≥ 18.5 kg/m² and < 25.0 kg/m²; overweight, BMI ≥ 25.0 kg/m² and < 30 kg/m²; obese, BMI ≥ 30 kg/m².

^bWaist circumference was not assessed in studies 1–3; N=315 for lurasidone, N=83 for risperidone, N=33 for quetiapine XR.

Change in weight, BMI, and waist circumference during 12 months of treatment

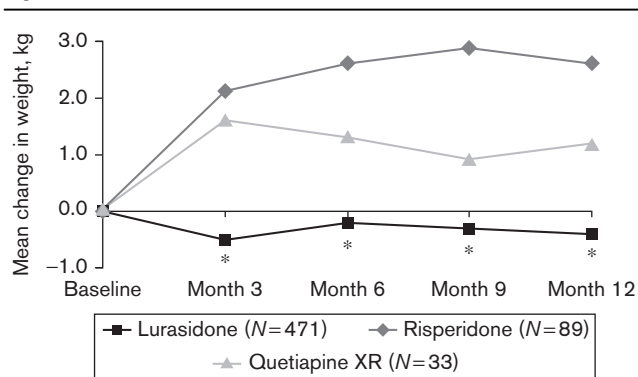
Decreases in the mean weight were observed for patients treated with lurasidone; the mean change in weight was -0.5 kg at month 3, which then remained generally stable through 12 months of treatment (-0.4 kg at month 12;

Table 3 Prior antipsychotic medications (≥10% of patients in any group)^a

Antipsychotic medication	Lurasidone (N=471) [n (%)]	Risperidone (N=89) [n (%)]	Quetiapine XR (N=33) [n (%)]
Any previous antipsychotic medication	427 (90.7)	81 (91.0)	27 (81.8)
Risperidone	181 (38.4)	0 (0)	12 (36.4)
Haloperidol	144 (30.6)	16 (18.0)	12 (36.4)
Quetiapine	115 (24.4)	59 (66.3)	0 (0)
Olanzapine	118 (25.1)	21 (23.6)	6 (18.2)
Aripiprazole	64 (13.6)	32 (36.0)	1 (3.0)
Chlorpromazine	73 (15.5)	2 (2.2)	8 (24.2)
Trifluoperazine	51 (10.8)	5 (5.6)	15 (45.5)
Ziprasidone	34 (7.2)	19 (21.3)	1 (3.0)
Paliperidone	26 (5.5)	4 (4.5)	4 (12.1)
Amisulpride	27 (5.7)	0 (0)	5 (15.2)
Promazine	1 (0.2)	9 (10.1)	0 (0)

^aTaken within 30 days before the first dose of study medication.

Fig. 2



Mean change from baseline weight (kg) after 3, 6, 9, and 12 months of treatment with lurasidone (40–160 mg/day), risperidone (2–6 mg/day), or quetiapine XR (200–800 mg/day). * $P < 0.0001$ versus risperidone.

Fig. 2). In contrast, increases in mean weight were observed for risperidone (+2.1 kg at month 3 and +2.6 kg at month 12) and quetiapine XR (+1.6 kg at month 3 and +1.2 kg at month 12) at all assessments. Change in mean weight with lurasidone was significantly different from that with risperidone at all postbaseline assessments (all P 's < 0.001); comparisons of lurasidone with quetiapine XR were not statistically significant, despite numerical differences. Similarly, the change in mean BMI at month 12 was significantly different for lurasidone (-0.1 kg/m^2) compared with risperidone ($+0.9 \text{ kg/m}^2$, $P < 0.001$) but not for lurasidone versus quetiapine XR ($+0.5 \text{ kg/m}^2$). There was an increase in the mean waist circumference after 12 months of treatment in all three groups (+0.4 cm with lurasidone, +2.7 cm with risperidone, and +0.6 cm with quetiapine XR), with a significantly larger increase for risperidone compared with lurasidone ($P < 0.001$).

The proportion of patients with weight gain of at least 7% was 9.3% at month 3 and 16.0% at month 12 with lurasidone, 22.5% at month 3 and 25.8% at month 12 with risperidone, and 12.1% at month 3 and 15.2% at month 12 with quetiapine XR (Fig. 3). Comparisons at month 12 were not statistically significant among the treatment groups. Weight loss of at least 7% at month 12 was observed in a greater proportion of patients receiving lurasidone (18.5%) compared with risperidone (6.7%, $P < 0.001$) or quetiapine XR (9.1%, $P = \text{NS}$; Fig. 3). After 12 months of treatment with lurasidone, 10.2% of patients who were in the normal/underweight BMI category at baseline had shifted to overweight/obese compared with 27.6% of risperidone patients and 15.0% of quetiapine XR patients. Conversely, 14.3% of patients taking lurasidone had shifted from overweight/obese at baseline to normal/underweight at month 12, compared with 1.7% of patients taking risperidone and 7.7% of patients taking quetiapine XR.

Among lurasidone-treated patients, the CART analysis found no significant effect of age, sex, or duration of

illness on the proportion of patients with at least 7% weight gain at month 12, but Asian patients were significantly more likely to experience weight gain than patients of other races (Fig. 4). After 12 months of treatment with lurasidone, weight gain of at least 7% was observed in 12.4% of whites, 12.5% of blacks, and 21.2% of Asians (28.8% of Asian women and 16.8% of Asian men). In the stepwise regression analysis, age and baseline weight were found to be significant predictors of weight gain at month 12; younger age ($P = 0.040$) and lower baseline body weight ($P = 0.002$) were associated with greater weight gain.

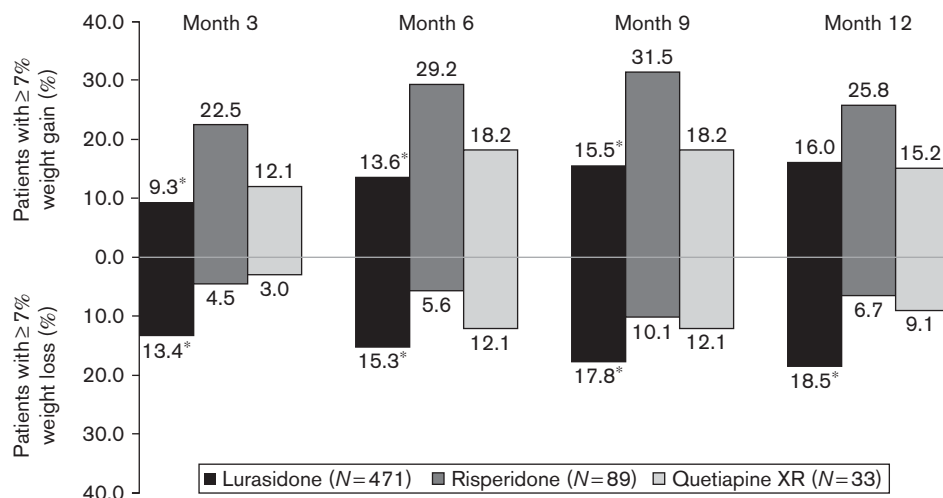
Discussion

Treatment with lurasidone was associated with a low potential for clinically significant weight gain over a 12-month period in this observed-case analysis of pooled data from six longer-term clinical trials in patients with schizophrenia. Treatment with risperidone and quetiapine XR was associated with modest weight gain (a mean change at month 12 of +2.6 kg and +1.2 kg, respectively). At month 12, a similar proportion of patients treated with lurasidone (16.0%) and quetiapine XR (15.2%) experienced weight gain of at least 7%; however, weight loss of at least 7% was observed in twice as many patients receiving lurasidone (18.5%) as those receiving quetiapine XR (9.1%). In comparison, the risperidone group had the largest proportion of patients with weight gain of at least 7% at month 12 (25.8%) and the smallest proportion of patients with weight loss of at least 7% (6.7%). We note that the baseline weight was, on average, 8 kg greater in the risperidone group compared with the lurasidone (pooled) and quetiapine XR groups; this may have reduced estimates of weight change associated with risperidone in comparison with lurasidone and quetiapine XR treatment. Patients treated with lurasidone for 12 months were more likely to experience a shift from a higher BMI category (overweight/obese) to a lower BMI category (normal/underweight) compared with patients treated with risperidone or quetiapine XR.

Results of this analysis suggest that lurasidone has a lower liability for long-term weight gain than several other atypical antipsychotic agents, which is consistent with previous pooled analyses of short-term studies on lurasidone in patients with schizophrenia (Citrome, 2012; Sunovion Pharmaceuticals Inc., 2013). Reflecting these findings, a recent comprehensive meta-analysis of short-term clinical studies on 15 antipsychotic agents in patients with schizophrenia found that lurasidone was one of only three agents (along with haloperidol and ziprasidone) that did not produce more weight gain than placebo (Leucht *et al.*, 2013).

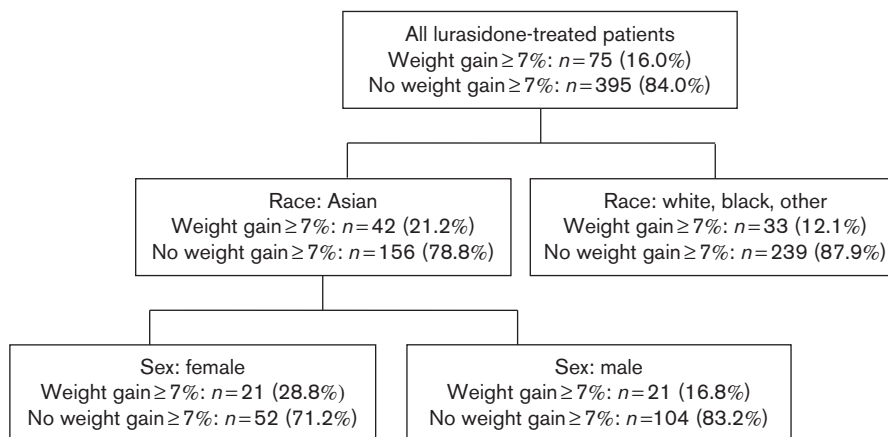
Overweight and obesity not only increase the risk for metabolic syndrome, diabetes, and cardiovascular disease (Nguyen *et al.*, 2008, 2010; Mitchell *et al.*, 2013b) but may have additional negative consequences in patients with schizophrenia, including decreased quality of life,

Fig. 3



Proportion of patients with at least 7% increase in weight and at least 7% decrease in weight from baseline after 3, 6, 9, and 12 months of treatment with lurasidone (40–160 mg/day), risperidone (2–6 mg/day), or quetiapine XR (200–800 mg/day). * $P < 0.0001$ versus risperidone.

Fig. 4



Classification and regression tree analysis of weight gain of at least 7% at month 12 in patients treated with lurasidone (40–160 mg/day).

increased stigma and social discrimination, and reduced adherence to antipsychotic treatment (Weiden *et al.*, 2004b; Kolotkin *et al.*, 2008; Monteleone *et al.*, 2009). Weight gain has been shown to be a predictor of medication nonadherence in patients with schizophrenia (Weiden *et al.*, 2004b; Velligan *et al.*, 2009; Wong *et al.*, 2011), despite the increased risk of relapse associated with discontinuing treatment (Perkins, 2002; Weiden *et al.*, 2004a).

Younger, treatment-naïve patients and patients belonging to certain racial and ethnic groups (e.g. black and Hispanic patients) appear to be at greater risk for antipsychotic-related weight gain (Meyer *et al.*, 2009; Salimi *et al.*, 2009; Maayan and Correll, 2011). In the present analysis, younger age was

significantly associated with weight gain during lurasidone treatment; however, weight gain of at least 7% was observed in a similar proportion of white patients and black patients taking lurasidone for 12 months. Asian patients (particularly Asian women) were significantly more likely than patients of other races to experience at least 7% weight gain, which is consistent with previous reports that Asian patients may be more likely to experience adverse effects of antipsychotic medications (Bond, 1991). Genetic factors may account for differences in medication-related weight gain based on race or ethnicity (Lett *et al.*, 2012). A recent meta-analysis found a significant association between the leptin – 2548A allele and the risk for antipsychotic-induced weight gain in Asian patients with schizophrenia (Shen *et al.*, 2014).

The development of antipsychotic agents with lower metabolic risk, an increased clinical awareness of antipsychotic-related metabolic problems, and the incorporation of physical health management concerns into treatment guidelines (American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity, 2004; De Hert *et al.*, 2009a) have provided greater impetus for clinicians to consider switching medication to reduce the likelihood of metabolic adverse effects. Studies investigating the effects of a medication switch have shown that switching patients to atypical antipsychotic agents with lower metabolic liability (e.g. aripiprazole, lurasidone, or ziprasidone) generally resulted in weight loss and improvement in metabolic indices, without compromising treatment efficacy (Casey *et al.*, 2003; Weiden *et al.*, 2003a, 2003b, 2008; Newcomer *et al.*, 2008; Alptekin *et al.*, 2009; Barak and Aizenberg, 2011; Ganguli *et al.*, 2011; Stroup *et al.*, 2011; Stahl *et al.*, 2013). In an open-label study of patients with schizophrenia or schizoaffective disorder who were transitioned to lurasidone from other antipsychotic agents, improvement was observed in weight and metabolic parameters after 6 weeks (McEvoy *et al.*, 2013) and 6 months (Citrome *et al.*, 2014) of treatment. Similarly, patients with schizophrenia who were treated with open-label lurasidone for up to 6 months after completing 6 weeks of double-blind treatment with olanzapine experienced a mean weight loss of 1.9 kg after switching to lurasidone, with sustained therapeutic efficacy (Stahl *et al.*, 2013).

This analysis has several limitations, including its post-hoc nature and the lack of a placebo control group. This observed-case analysis included only patients who completed 12 months of treatment. The number of patients treated with quetiapine XR for 12 months ($N=33$) was relatively small compared with the other treatment groups. Between-group differences in dropout rates could have influenced the magnitude of weight change observed at month 12, to the extent that treatment discontinuation was associated with weight change; however, the proportion of patients in the underlying studies who discontinued study medication was similar for lurasidone, risperidone, and quetiapine XR. In addition, detailed information was not collected with regard to prior antipsychotic treatment (e.g. dose, duration of treatment, impact on weight). Thus, the magnitude of antipsychotic-induced weight gain that may have occurred before the patients' enrollment in the studies included in this analysis is unknown. The effect of antipsychotic medication dose on weight gain was not evaluated in this analysis because five of six longer-term studies used flexible dosing.

In summary, the results of this post-hoc, pooled analysis of 593 patients with schizophrenia who completed 12 months of study treatment suggest that lurasidone, in the dose range of 40–160 mg/day, is associated with a low potential for long-term weight gain. Consistent with prior reports, Asian patients appeared to be more susceptible

to weight gain during antipsychotic therapy. The findings of this analysis suggest that lurasidone may be an important treatment option for patients judged to be at higher risk for weight gain, those who present with cardiovascular risk factors, or those who have experienced weight gain or metabolic disturbances on their current treatment regimen. Regular monitoring of metabolic parameters (including weight, lipid levels, and glycemic control) is now considered the standard of care for patients with schizophrenia and may help limit the effects of long-term antipsychotic treatment on weight and metabolic parameters.

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Conflicts of interest

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