Minimising the Impact of Medication on Physical Health in Schizophrenia

"Imagination is more important than knowledge"

Albert Einstein
Choosing Health
Making healthy choices easier

Lifestyle ↔ Making choices ↔ Treatment

NHS
General course of schizophrenia

- Prodrome
- 1st psychotic episode
- Remitting & relapsing chronic schizophrenia
- Residual

Psychopathology, Function & outcome

Better

Worse

Chronic disability

Life expectancy 20 years less than general population

Age (years)

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CHALLENGING THINKING IN SCHIZOPHRENIA CARE

- Side effects & iatrogenic disease
- Poor physical health
- Psychiatric comorbidities
- Poor adherence
- Failure to engage
- Cognitive impairment
- Drug misuse
- Homelessness

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Adverse effects have a pervasive impact

ADVERSE EFFECTS

MORTALITY
PHYSICAL HEALTH
QUALITY OF LIFE
STIGMA
ADHERENCE
RELAPSE
CHRONIC ILLNESS
3.6 Individuals with schizophrenia consider the most troublesome side effects to be EPS, weight gain, sexual dysfunction and sedation.
Antipsychotic induced iatrogenic disease in schizophrenia

- Parkinsonism
- Akathisia
- Dystonia
- Tardive dyskinesia
- Hyperprolactinaemia
- Sexual dysfunction
- Osteoporosis
- Breast cancer

- Obesity
- Type 2 diabetes
- Dyslipidaemia
- Hypertension

Neurological disorders
Endocrine disorders
Metabolic disorders
Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis

Stefan Leucht, Andrea Cipriani, Loukia Spinei, Dimitris Mavridis, Deniz Örey, Franziska Richter, Myrto Samara, Corrado Barbui, Rolf R Engel, John R Geddes, Werner Kissling, Marko Paul Stapf, Bettina Lässig, Georgia Salanti, John M Davis

Summary
Background The question of which antipsychotic drug should be preferred for the treatment of schizophrenia is controversial, and conventional pairwise meta-analyses cannot provide a hierarchy based on the randomised evidence. We aimed to integrate the available evidence to create hierarchies of the comparative efficacy, risk of all-cause discontinuation, and major side-effects of antipsychotic drugs.

www.thelancet.com Published online June 27, 2013 http://dx.doi.org/10.1016/S0140-6736(13)60733-3
Impact of extrapyramidal symptoms (EPS)

- Effectiveness of antipsychotic treatment reduced
- Interferes with therapeutic alliance
- Contributes to cognitive impairment
- Markedly impaired quality of life
- Simulates depressive or negative symptoms
- Contributes to non-adherence

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)

More extrapyramidal side-effects with placebo
More extrapyramidal side-effects with active drug
Impact of prolactin elevation

Antipsychotic-induced hyperprolactinaemia

- Dysthymia
- Sexual dysfunction
- Risk of breast cancer
- Reduction in bone mineral density
Sexual dysfunction: the secret side effect?

50% of patients ‘never or infrequently’ discuss sexual functioning with their mental healthcare providers

62.5% of men and 38.5% of women felt that their medication was causing sexual side effects

80% of women with sexual side effects never discuss sexual dysfunction with their mental healthcare providers

41.7% of men and 15.4% of women admitted stopping their medications because of sexual side effects

Rosenberg K, Bleiberg K, Koscis J, et al
A survey of sexual side effects among severely mentally ill patients taking psychotropic medications: impact on compliance.
J of Sex and Marital Therapy, 2003;29:289–296
Osteoporosis

Effects on bone mineral density:

- Premature bone loss in both women and men

Haddad PM, Wieck A. Drugs 2004;64:2291-314

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Breast Cancer

- Use of antipsychotics associated with increased risk of breast cancer\(^1\)

- Excess mortality from breast cancer reported in female schizophrenic patients\(^2\)

- Aripiprazole: -0.22 (95% CI: -0.46 to 0.03)
- Quetiapine: -0.05 (95% CI: -0.23 to 0.13)
- Asenapine: 0.12 (95% CI: -0.12 to 0.37)
- Olanzapine: 0.14 (95% CI: +0.00 to 0.28)
- Chlorpromazine: 0.16 (95% CI: -0.48 to 0.8)
- Iloperidone: 0.21 (95% CI: -0.09 to 0.51)
- Ziprasidone: 0.25 (95% CI: 0.01 to 0.49)
- Lurasidone: 0.34 (95% CI: 0.11 to 0.57)
- Sertindole: 0.45 (95% CI: 0.16 to 0.74)
- Haloperidol: 0.70 (95% CI: 0.56 to 0.85)
- Risperidone: 1.23 (95% CI: 1.06 to 1.40)
- Paliperidone: 1.30 (95% CI: 1.08 to 1.51)

Amisulpride: NA
Clozapine: NA
Zotepine: NA
Weight increase, Metabolic disease & Cardiovascular risk
Growing awareness of need to improve CV health in severe mental illness

- CV mortality and morbidity in people with severe mental illness is a growing concern
- Life expectancy in schizophrenia is 20 years less than that of the general population
- Decreased access to care
- Poverty
- Limited insight

Standardised Mortality Ratio (SMR) is high in schizophrenia

- All causes of death: 2.98
- Cardiovascular disease: 2.01

SMR = (observed number of deaths / expected number of deaths)
Weight status of general population

- **Healthy Males**: 40.6%
- **Healthy Females**: 36.4%
- **Overweight Males**: 32.1%
- **Overweight Females**: 37.1%
- **Obese Males**: 25.1%
- **Obese Females**: 24.7%

Public Health England. Adult Weight Factsheet
August 2014

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### Estimated Prevalence and RR of Modifiable Cardiovascular Disease Risk Factors in Schizophrenia and Bipolar Disorder Compared to the General Population\textsuperscript{45-67}

<table>
<thead>
<tr>
<th>Modifiable Risk Factors</th>
<th>Schizophrenia</th>
<th>Bipolar Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>45%–55%</td>
<td>21%–49%</td>
</tr>
<tr>
<td></td>
<td>RR: 1.5–2</td>
<td>RR: 1–2</td>
</tr>
<tr>
<td>Smoking</td>
<td>50%–80%</td>
<td>54%–68%</td>
</tr>
<tr>
<td></td>
<td>RR: 2–3</td>
<td>RR: 2–3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10%–15%</td>
<td>8%–17%</td>
</tr>
<tr>
<td></td>
<td>RR: 2</td>
<td>RR: 1.5–2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>19%–58%</td>
<td>35%–61%</td>
</tr>
<tr>
<td></td>
<td>RR: 2–3</td>
<td>RR: 2–3</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>25%–69%</td>
<td>23%–38%</td>
</tr>
<tr>
<td></td>
<td>RR: ≤5</td>
<td>RR: ≤3</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>37%–63%</td>
<td>30%–49%</td>
</tr>
<tr>
<td></td>
<td>RR: 2–3</td>
<td>RR: 1.5–2</td>
</tr>
</tbody>
</table>

RR=relative risk.
Cardiovascular care in schizophrenia

1.5.3.2 GPs and other primary healthcare professionals should monitor the physical health of people with psychosis or schizophrenia when responsibility for monitoring is transferred from secondary care, and then at least annually. The health check should be comprehensive, focusing on physical health problems that are common in people with psychosis and schizophrenia. Include all the checks recommended in 1.3.6.1 and refer to relevant NICE guidance on monitoring for cardiovascular disease, diabetes, obesity and respiratory disease. A copy of the results should be sent to the care coordinator and psychiatrist, and put in the secondary care notes. [new 2014]

1.5.3.3 Identify people with psychosis or schizophrenia who have high blood pressure, have abnormal lipid levels, are obese or at risk of obesity, have diabetes or are at risk of diabetes (as indicated by abnormal blood glucose levels), or are physically inactive, at the earliest opportunity following relevant NICE guidance (see Lipid modification [NICE clinical guideline 67], Preventing type 2 diabetes [NICE public health guidance 38], Obesity [NICE clinical guideline 43], Hypertension [NICE clinical guideline 127], Prevention of cardiovascular disease [NICE public health guidance 25] and Physical activity [NICE public health guidance 44]). [new 2014]
1.5.3.5 Healthcare professionals in secondary care should ensure, as part of the care programme approach, that people with psychosis or schizophrenia receive physical healthcare from primary care as described in recommendations 1.5.3.1–1.5.3.4.
Patients with schizophrenia have complex cardiovascular needs

- Obesity
- Hypertension
- Dyslipidaemia
- Diabetes

Assess risk

Lifestyle advice

Manage comorbidities

Address risk factors

Control glucose levels

Prescribe:
- Metformin
- Antithrombotic
- Statin
- Antihypertensive
- etc

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Positive Cardiometabolic Health Resource

An intervention framework for people experiencing psychosis and schizophrenia

This clinical resource supports the implementation of the physical health CQUIN
which aims to improve collaborative and effective physical health monitoring of patients experiencing severe mental illness. It focusses on antipsychotic medication for adults, but many of the principles can be applied to other psychotropic medicines given to adults with long term mental disorders, e.g. mood stabilisers.

For all patients in the “red zone” (see center page spread): The general practitioner, psychiatrist and patient will work together to ensure appropriate monitoring and interventions are provided and communicated. The general practitioner will usually lead on supervising the provision of physical health interventions. The psychiatrist will usually lead on decisions to significantly change antipsychotic medication.

Download Lester UK Adaptation: www.rcpsych.ac.uk/quality/NAS/resources
Positive Cardiometabolic Health Resource

**Smoking**
- Current smoker

**Lifestyle and Life Skills**
- Poor diet AND/OR Sedentary lifestyle

**Body Mass Index (BMI) Weight**
- BMI ≥25 kg/m²
  - (≥23 kg/m² if South Asian or Chinese)
  - AND/OR
  - Weight gain >5kg over 3 month period

**Blood Pressure**
- >140 mm Hg systolic AND/OR >90 mm Hg diastolic

**Glucose Regulation**
- HbA1c >42 mmol/mol (≥6%)
- AND/OR
- FPG ≥5.5 mmol/l
- OR
- RPG ≥11.1 mmol/l

**Blood Lipids**
- Total chol/HDL ratio to detect high (>10%) risk of CVD based on QRISK-2 Tool
  - http://qrisk.org/
  - Note: CVD risk scores can underestimate risk in those with psychosis

**Medication review and lifestyle advice to include diet and physical activity**

- NB Family history of diabetes and/or premature heart disease heightens cardiometabolic risk.

Refer for investigation, diagnosis and treatment by appropriate clinician if necessary.

**Interventions**

**Brief intervention**
- Combined NRT and/or varenicline
  - Individual/group behavioral support or specialist support if high dependency
  - Referral to Smoking Cessation service

**Follow NICE guidelines for obesity**
- http://www.nice.org.uk/CG43

**At High Risk of Diabetes**
- HbA1c 42-47 mmol/mol (6.0% - 6.4%)
- FPG 5.5 - 6.9 mmol/l
- RPG ≥11.1 mmol/l
- i) Offer intensive structured lifestyle education programme
- ii) If ineffective consider metformin

**Diabetes**
- HbA1c ≥48 mmol/mol (≥6.5%)
- FPG ≥7.0 mmol/l
- RPG ≥11.1 mmol/l
- Endocrine review
- Follow NICE diabetes guidelines
  - http://www.nice.org.uk/CG87

- Consider lipid modification for those with CVD or Diabetes

**TARGET**

- Stop smoking
- Improve quality of diet
  - Contain calorie intake
  - Daily exercise of 30 mins/day

- BMI 18.5-24.9 kg/m²
  - (18.5-22.9 kg/m² if South Asian or Chinese)

- <140/90 mm Hg
  - (<130/80 mm Hg for those with CVD or diabetes)

- Prevent or delay onset of diabetes
  - HbA1c <42 mmol/mol (≤6%)
  - FPG <5.5 mmol/l

- HbA1c ≥47-58 mmol/mol (6.5-7.5%)

**FPG** = Fasting Plasma Glucose | **RPG** = Random Plasma Glucose | **BMI** = Body Mass Index | **Total Chol** = Total Cholesterol | **HDL** = High Density Lipoprotein | **TRIG** = Triglycerides
Of all the pharmacologic strategies, choice of psychotropic medication may have the greatest influence on weight gain and associated metabolic disturbance.

There is good evidence for a range of weight-gain liability among antipsychotic medications.
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)
- Chlorpromazine 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)

More weight gain with placebo  More weight gain with active drug
Clinical Study Summary: Study F1D-US-HGLS

Olanzapine Versus Aripiprazole in the Treatment of Acutely Ill Patients with Schizophrenia

Date summary approved by Lilly: 16 July 2007

Brief Summary of Results

This was a 5-day, Phase 4, multicenter, parallel, double-blind, randomized, controlled study to evaluate olanzapine (20 mg/day) versus aripiprazole (15 or 30 mg/day) in the treatment of acutely ill patients meeting Diagnostics and Statistics Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for schizophrenia, schizoaffective disorder, or schizophreniform disorder. The results of the study are as follows:

- Out of 604 patients who entered the study, 306 patients were randomly assigned to the olanzapine group out of which 234 (76.5%) patients completed the study. Two hundred ninety-eight patients were assigned to the aripiprazole group out of which 237 (79.5%) completed the study. There was no statistically significant difference (p=.378) between the groups on the proportion of patients who completed the study.

- There were statistically significant decreases from baseline in Positive and Negative Syndrome Scale-Excited Component (PANSS-EC) to each visit over 5 days of treatment for both treatment groups (p<.001). There were no statistically significant between-group treatment differences over 5 days of treatment.

- There were no statistically significant between-group treatment differences in the PANSS-EC, from baseline to endpoint, in the proportions of patients with varying percentages of reduction (between 10% and 40%).
Metabolic changes during 5-Day RCT of Olanzapine vs Aripiprazole in agitation in schizophrenia

Change from baseline, mg/dL

- Olanzapine 20mg/day N=306
- Aripiprazole 15-30mg/day N=298

* p=0.01 vs baseline value  ** p<0.001 vs. baseline value


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Risk factors for metabolic syndrome

1. Abdominal obesity
   Waist circumference
   ≥102cm in men
   ≥88cm in women

2. Fasting plasma triglycerides
   ≥150mg/dL

3. Low HDL cholesterol
   <40mg/dL in men
   <50mg/dL in women

4. Elevated blood pressure
   ≥130/85 mm Hg

5. Elevated fasting plasma glucose
   ≥100mg/dL

Grundy SM, Cleeman JI, Daniels SR et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation 2005;112;2735-2752
Risk factors for metabolic syndrome

Metabolic changes with Olanzapine during 5-Day RCT in agitation in schizophrenia

2. Fasting plasma triglycerides
   Baseline 144.4 mg/dL
   5 days: 200.44 mg/dL

5. Elevated fasting plasma glucose
   Baseline 92.1 mg/dL
   5 days: 102.4 mg/dL


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Antipsychotics and **long-term** weight and metabolic change

- **Oral?**
- **LAIs?**
### Long-term weight change

#### Aripiprazole (oral)

Weight change at 1 year categorized by BMI at baseline

<table>
<thead>
<tr>
<th>Baseline BMI</th>
<th>BMI &lt;23</th>
<th>BMI 23-27</th>
<th>BMI &gt;27</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change from baseline (kg)</td>
<td>2.6</td>
<td>1.4</td>
<td>-1.2</td>
</tr>
<tr>
<td>% with &gt;/=7% weight increase</td>
<td>30%</td>
<td>19%</td>
<td>8%</td>
</tr>
</tbody>
</table>

Adapted from Physician's Desk Reference 2008 (USA)

BMI <20 underweight
BMI 20-25 ideal
BMI 25-30 overweight
BMI 30-35 obese
BMI >35 severely obese

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Long-term weight change

Olanzapine (oral)

• In long-term (≥6 months) treatment
  – 64% of patients gain ≥ 7% of baseline weight
  – Average weight gain 5.6kg (12lb)

Zyrex US Data Sheet 2009

• At 12 months, mean weight gain (12.5mg/day-17.5mg/day)
  – 12kg (26.4lb)

Beasley CM. Safety of Olanzapine.
Meta-analysis of 4 long-term studies
# Long-term weight change

## Quetiapine

<table>
<thead>
<tr>
<th>Baseline BMI</th>
<th>&lt;18.5</th>
<th>18.5-&lt;25</th>
<th>25-&lt;30</th>
<th>30-&lt;35</th>
<th>&gt;35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight change (kg)</td>
<td>10.5</td>
<td>4</td>
<td>2</td>
<td>1.7</td>
<td>0</td>
</tr>
</tbody>
</table>

- > 7% weight **loss** = 12.8%
- > 7% weight **gain** = 37.2%

Long-term weight change

Risperidone (oral)

$2.3kg^a - 3.3kg^b$ at 12 months

---


Antipsychotics and long-term weight and metabolic change

Oral?

LAIs?
### Incidence of new-onset metabolic abnormalities*

<table>
<thead>
<tr>
<th>Metabolic Parameter</th>
<th>Aripiprazole LAI monthly</th>
<th>Placebo IM monthly</th>
<th>Number Needed to Harm (NNH)</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;7% weight increase</td>
<td>6.4%</td>
<td>5.2%</td>
<td>83</td>
<td>16-infinity</td>
</tr>
<tr>
<td>Glucose</td>
<td>4.5%</td>
<td>2.5%</td>
<td>50</td>
<td>14-infinity</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td>0.0%</td>
<td>0.0%</td>
<td>∞</td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>7.7%</td>
<td>9.0%</td>
<td>77†</td>
<td>11-infinity</td>
</tr>
</tbody>
</table>

* NNT for aripiprazole LAI vs placebo

IM=intramuscular; LDL=low-density lipoprotein.

* Defined as the following changes:
  - Glucose, <100 mg/dL to ≥126 mg/dL;
  - LDL-cholesterol, <100 to ≥160 mg/dL;
  - Triglycerides, <150 mg/dL to ≥200 mg/dL.


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Olanzapine LAI

Weight change in Olanzapine LAI adult monotherapy studies of ≥ 48 weeks exposure

% of patients

- Zero
- >10kg
- >15kg
- >20kg

Adapted from Olanzapine LAI US data sheet

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Olanzapine LAI

Incidence of new-onset metabolic abnormalities* in Olanzapine LAI adult monotherapy studies of ≥ 48 weeks exposure

% of patients

<table>
<thead>
<tr>
<th>Metabolic Parameter</th>
<th>Normal to high</th>
<th>Borderline to high</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose</td>
<td>12.8</td>
<td>26</td>
<td>38.8</td>
</tr>
<tr>
<td>Fasting triglycerides</td>
<td>32.4</td>
<td>70.7</td>
<td>103.1</td>
</tr>
<tr>
<td>Fasting LDL cholesterol</td>
<td>7.3</td>
<td>31</td>
<td>38.3</td>
</tr>
</tbody>
</table>

*GLUCOSE: Normal to high: <100mg/dL to ≥126mg/dL
Borderline to high: ≥100mg/dL & <126mg/dL to ≥126mg/dL
*TRIGLYCERIDES: Normal to high: <150mg/dL to ≥200mg/dL
Borderline to high: ≥150mg/dL & <200mg/dL to ≥200mg/dL
*LDL CHOLESTEROL: Normal to high: <100mg/dL to ≥160mg/dL
Borderline to high: ≥100mg/dL & <160mg/dL to ≥160mg/dL

Source: Olanzapine LAI US data sheet

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Paliperidone LAI

Long-term mean weight & fasting metabolic changes at a dose of 234mg/4 weekly

<table>
<thead>
<tr>
<th></th>
<th>Week 29</th>
<th>Week 53</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>-0.4 mg/dL</td>
<td>6.8 mg/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>16.2 mg/dL</td>
<td>37.4 mg/dL</td>
</tr>
<tr>
<td>LDL Cholesterol</td>
<td>-2.7 mg/dL</td>
<td>-2.3 mg/dL</td>
</tr>
<tr>
<td>Weight</td>
<td>2.4Kg</td>
<td>4.3Kg</td>
</tr>
</tbody>
</table>

Source: Paliperidone LAI US data sheet

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Risperidone LAI

12-week RCT in patients with schizophrenia
  • 9% of risperidone-treated patients increased weight by ≥7%

24-month study in patients with bipolar disorder
  • 11.6% of risperidone-treated patients increased weight by ≥7%

No data on changes to glucose or lipid profile

Source: Risperdal Consta US data sheet
Switching to a different antipsychotic medication, which evidence suggests may have a lower liability for weight gain, commends itself as an appropriate and worthwhile treatment option for consideration.
• 4 studies, N=636; all but one duration <26 weeks
• Switch from olanzapine to aripiprazole or quetiapine
• No significant changes in mental state on switching
• Mean weight loss 1.94 kg
• Significant decrease in fasting blood glucose
• Aripiprazole: improvement in lipid profile

“switching antipsychotic medication to one with lesser potential for causing weight gain or metabolic problems could be an effective way to manage these side effects”
Antipsychotics & Iatrogenic Disease

**HIGH RISK:**
- 1st generation antipsychotics
- Some 2nd generation antipsychotics
  - Amisulpride, Risperidone, Paliperidone

**LOW RISK:**
- Aripiprazole, Quetiapine

**HIGH RISK:**
- Olanzapine, Clozapine

**LOW RISK:**
- Aripiprazole, Haloperidol

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Summary: Antipsychotics & Iatrogenic Disease

Neurological disorders

HIGH RISK:
1\textsuperscript{st} generation antipsychotics

Lower risk:
2\textsuperscript{nd} generation antipsychotics

Endocrine disorders

HIGH RISK:
1\textsuperscript{st} generation antipsychotics and some 2\textsuperscript{nd} generation antipsychotics
- Amisulpride, Risperidone, Paliperidone

Low risk:
- Aripiprazole, Quetiapine

Metabolic disorders

HIGH RISK:
- Olanzapine
- Clozapine

Low risk:
- Aripiprazole
- Haloperidol
Improving the use of medicines in severe mental illness

Medicines in Mental Health Ltd offers a range of services designed to obtain maximum benefit from medicines in the treatment of severe mental illness.

Thank you

www.mentalmeds.co.uk