Managing Metabolic Wellness in the Mentally Ill: Perspectives From Both a Primary Care Physician (PCP) & a Psychiatrist

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Objectives

• Highlight the importance of wellness in individuals with schizophrenia
• Discuss guidelines available to maintain wellness in these patients
• Understand the importance of the monitoring and treating of cardiometabolic risk factors
• Explore successful wellness programs for those with schizophrenia and serious mental illness
Polling Question

In your experience, what percentage of patients with serious mental illness have been diagnosed with a comorbid cardiometabolic illness?

A. < 10%
B. 11% to 25%
C. 26% to 50%
D. 51-75%
E. >75%
Wellness in Schizophrenia: Why Is it an Issue?
In Addition to Managing Relapses, Considerations on Overall Health Are Critical

- Patients with schizophrenia have increased risks of morbidity and mortality compared with the general population\(^1\):
  - They have a 25–30 year shorter life span due primarily to premature CVD

In patients with mental illness, the increased risk from CVD appears to be related to

Increased incidence of\(^2\):
- Smoking
- Obesity
- Hypertension
- Diabetes
- Dyslipidemia

CVD, cardiovascular disease.
Mortality in Schizophrenia

Comorbidities
- Diabetes
- Cardiovascular disease

Lifestyle Choice
- Diet
- Physical activity
- Smoking

Antipsychotic-related weight gain and obesity

Reduced Life Expectancy

Suicide
- An 8.5-fold increased risk

Less-than-optimal medical treatment

*Including missed medical diagnoses.
1. Laursen TM. Schizophr Res. 2011;131:101-104.
# Wellness Issues in Schizophrenia

## Related to the Illness

<table>
<thead>
<tr>
<th>Related to the Illness</th>
<th>Related to Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine abuse¹</td>
<td>Obesity²</td>
</tr>
<tr>
<td>Obesity¹</td>
<td>Diabetes²</td>
</tr>
<tr>
<td>Diabetes¹</td>
<td>Dyslipidemia²</td>
</tr>
<tr>
<td>Dyslipidemia¹</td>
<td>Metabolic syndrome¹</td>
</tr>
<tr>
<td>Metabolic syndrome¹</td>
<td>Sexual dysfunction³</td>
</tr>
<tr>
<td>Sexual dysfunction³</td>
<td>Hyperprolactinemia³</td>
</tr>
</tbody>
</table>

Prevalence of Cardiometabolic Risk Factors in Patients With Schizophrenia or Bipolar Disorder

<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 (1.5-2)</td>
<td>21-49 (1-2)</td>
</tr>
<tr>
<td>Smoking</td>
<td>50-80 (2-3)</td>
<td>54-68 (2-3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10-15 (2)</td>
<td>8-17 (1.5-2)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>19-58 (2-3)</td>
<td>35-61 (2-3)</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>25-69 (≤5)</td>
<td>23-38 (≤3)</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>37-63 (2-3)</td>
<td>30-49 (1.5-2)</td>
</tr>
</tbody>
</table>

RR, relative risk.
Prevalence of Metabolic Dysregulation in Patients With Schizophrenia

N = 689.

HDL-C, high-density lipoprotein cholesterol.

Incentives to Participate in Wellness Management and Patient Benefits

- Symptom reduction
- Peer and staff support
- Knowledge about lifestyle issues
- Personal attributes of intervention facilitator (eg, encouraging and motivating)
- Participant attributes (eg, self-efficacy, locus of control)
- Participation of staff
- Contingency management (eg, positive reinforcement)
- Weight loss

Barriers to Patient Wellness Management

• Cognitive limitations
• Unstable mental state
• Poor motivation
• Decreased social interaction
• Sedation
• Lack of initiative
• Low self esteem/lack of confidence
• Weight gain

Discussion
Polling Question

In your experience, how many patients with serious mental illness are assessed according to metabolic monitoring guidelines in clinical practice?

A. < 10% of patients
B. 11% to 25% of patients
C. 26% to 50% of patients
D. > 50% of patients
Wellness in Schizophrenia: Are Clinicians Succeeding?
History of Metabolic Risk Factors in Schizophrenia

• “Diabetes is a disease which often shows itself in families in which insanity prevails.” (Henry Maudsley 1897)¹

• Introduction of first-generation antipsychotics (1950s) associated with a 2-fold to 3-fold increase in diabetes among patients with schizophrenia²

• Introduction of second-generation antipsychotics (SGAs) (1990s) associated with a further increase (of 10% to 50%)²

• In 2004, the United States Food and Drug Administration³:
  – Requested that manufacturers of SGAs include a warning and additional information about a link between SGAs and hyperglycemia
  – Recommended monitoring of blood glucose levels

# ADA/APA Monitoring Guidelines

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>4 Weeks</th>
<th>8 Weeks</th>
<th>12 Weeks</th>
<th>Quarterly</th>
<th>Annually</th>
<th>Every 5 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal/family history</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Weight (BMI)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting lipid profile</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

*If a patient gains ≥ 5% of his/her initial weight at any time during therapy, consider switching to a different antipsychotic.*

More frequent assessments may be warranted based on clinical status.

Note: These guidelines also rated available atypical antipsychotic agents according to their propensity to cause metabolic dysregulation (specifically, weight gain, risk for diabetes, and worsening lipid profile).

ADA, American Diabetes Association; APA, American Psychiatric Association; BMI, body mass index.

# Mount Sinai Monitoring Guidelines

<table>
<thead>
<tr>
<th>Issue</th>
<th>Recommendation</th>
<th>Monitoring Procedure</th>
</tr>
</thead>
</table>
| Weight gain            | • Monitor BMI  
• If BMI ≥ 25, weight-gain risk of individual antipsychotics should be considered  
• Weight gain of 1 BMI unit indicates need for intervention (unless BMI <18.5)                                                                 | BMI measurement                                           |
| Diabetes               | • Baseline plasma glucose level for all patients prior to initiating new antipsychotic  
• More frequent monitoring for those with risk factors or weight gain  
• Monitor for symptoms of new onset diabetes                                                                                                   | Fasting plasma glucose level or hemoglobin A\textsubscript{1c} value |
| Hyperlipidemia         | • Monitor lipid profiles of all patients with schizophrenia  
• Follow guidelines (National Cholesterol Education Program or US Preventive Services Task Force) for screening and treating patients at high risk for CVD  
• If LDL level is >130 mg/dL, provide referral to primary care provider or internist                                                              | Lipid screening (including total cholesterol, LDL, HDL, triglycerides) |

BMI, body mass index; CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; US, United States.  
Overall Poor Adherence to Monitoring Guidelines

- Mount Sinai Guidelines\(^1\):
  - Glucose: 53% conformance rate
  - Weight: 48% conformance rate
  - Lipids: 34% conformance rate

Approximately half of SGA users did not receive applicable monitoring for glucose or weight.
Approximately two-thirds of SGA users did not receive applicable monitoring for lipids.

- Metabolic monitoring subsequent to the ADA/APA guidelines\(^2\):
  - Glucose: 23% (baseline) and 38% (annual) testing rate of patients
  - Lipids: 8% (baseline) and 23% (annual) testing rate of patients

> 75% of SGA users did not receive baseline glucose testing.
> 90% of SGA users did not receive baseline lipids testing.

ADA, American Diabetes Association; APA, American Psychiatric Association; SGA, second-generation antipsychotics.

Overall Poor Adherence to Monitoring Guidelines

**Patient characteristics**
- Less likely to seek care
- Less likely to adhere to prescribed treatments
- Potential difficulty in communicating symptoms

**Clinician behavior**
- Primary care clinicians:
  - May lack the skills to treat this population
  - Time constraints
- Psychiatrists:
  - May not believe physical health is their responsibility
  - May lack physical medicine skills
  - Shortage of psychiatrists

**Medical system**
- Complex care systems may be difficult to navigate

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Discussion
Wellness in Schizophrenia: Best Practices
Nonwhite men treated more for diabetes ($p = 0.005$) and dyslipidaemia ($p = 0.014$).

CATIE, Clinical Antipsychotic Trials of Intervention Effectiveness.

Medical Risk Management Strategies of Antipsychotic-treated Patients

**Treatment Initiation**
- Healthy lifestyle counseling
- Healthy lifestyle intervention
- Start with lower-risk antipsychotic

**If Adverse Effect Is Present**
- Healthy lifestyle counseling/intervention
- Consider changing to lower-risk antipsychotic
- Consider weight loss intervention

**If Adverse Effect Progresses/Serious**
- Healthy lifestyle counseling/intervention
- Considering changing to lower-risk antipsychotic
- Add targeted treatment for pathological values
- Consider referral to specialist

Correll CU. CNS Spectr. 2007;12(10) (suppl 17):12–20,35.
Wellness Programs

Education and Activity + Nutrition and Exercise + ≥ 3 Months’ Duration = Success

Note: Programs that are less likely to be successful include briefer duration interventions, general wellness or health promotion or education-only programs, non-intensive, unstructured, or non-manualized interventions and programs limited to nutrition only or exercise only (as opposed to combined nutrition and exercise).

Effect of Interventions to Reduce Coronary Heart Disease Risk

-8

-16

-27

-30

-30

-45

-45

-60

BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol.

Correll CU. CNS Spectr. 2007;12(10) (suppl 17):12–20,35.
## Hypertension Treatment: Eighth Joint National Committee

<table>
<thead>
<tr>
<th>Population</th>
<th>When to Treat (mmHg)</th>
<th>Pharmacotherapy</th>
<th>Goal (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population ≥ 60 y</td>
<td>SBP ≥ 150 or DBP ≥ 90</td>
<td>THZ, CCB, ACEI, or ARB</td>
<td>THZ or CCB</td>
</tr>
<tr>
<td>General population &lt; 60 y</td>
<td>SBP ≥ 140 or DBP ≥ 90</td>
<td>THZ, CCB, ACEI, or ARB</td>
<td>THZ or CCB</td>
</tr>
</tbody>
</table>

If goal blood pressure not reached within 1 month, increase the dose or add a second drug (THZ, CCB, ACEI, or ARB).

Do not use an ACEI and an ARB together in the same patient.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CKD, chronic kidney disease; DBP, diastolic blood pressure; SBP, systolic blood pressure; THZ, thiazide-type diuretic.


Type 2 Diabetes Treatment for Nonpregnant Adults: American Diabetes Association

### When to Treat
- A1C ≥ 6.5%** or
- FPG ≥ 126 mg/dL** or
- 2–h PG ≥ 200 mg/dL during an OGTT** or
- Random PG ≥ 200 mg/dL in patients with classic symptoms of hyperglycemia or hyperglycemic crisis

### Pharmacotherapy
- Oral antihyperglycemic biguanidines (preferred initial agent)
- GLP–1 receptor agonist, basal insulin, or second oral agent
- Insulin (with or without additional agents)

### Goal*
- A1C < 7.0%
- Preprandial glucose 80–130 mg/dL
- Postprandial glucose < 180 mg/dL (1–2 hrs after meal)

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In addition to pharmacotherapy, include medical nutrition therapy, self-management education and support, and physical activity.

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*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

**More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.

CVD, cardiovascular disease; DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; GLP-1, glucagon-like peptide 1; A1c; glycosylated hemoglobin; MTD, maximum tolerated dose; OGTT, oral glucose tolerance test; PG, plasma glucose; T2D, type 2 diabetes; 2-h PG, 2-hour PG.

Evaluating Risk for Atherosclerotic Cardiovascular Disease

- In addition to lipoprotein lipid levels, ASCVD risk assessment includes evaluation of major risk factors and other conditions associated with ≥ high risk for an ASCVD event, such as:
  - Diabetes mellitus, chronic kidney disease stage ≥ 3B, LDL-C ≥ 190 mg/dL (severe hypercholesterolemia phenotype), ASCVD:
    - Patients in these categories are all at “high” or “very high” risk for an ASCVD event and should be treated accordingly

<table>
<thead>
<tr>
<th>Major risk factors for ASCVD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Male ≥ 45 years</td>
</tr>
<tr>
<td>Female ≥ 55 years</td>
</tr>
<tr>
<td>Family history of early CHD†</td>
</tr>
<tr>
<td>&lt; 55 years of age in a male first-degree relative or &lt; 65 years of age in a female first-degree relative</td>
</tr>
<tr>
<td>Current cigarette smoking</td>
</tr>
<tr>
<td>High blood pressure (≥ 140 / ≥ 90 mm Hg, or on blood pressure medication)</td>
</tr>
<tr>
<td>Low HDL-C</td>
</tr>
<tr>
<td>Male &lt; 40 mg/dL</td>
</tr>
<tr>
<td>Female &lt; 50 mg/dL</td>
</tr>
</tbody>
</table>

*Levels of non–high-density lipoprotein cholesterol and low-density lipoprotein cholesterol are not listed, because these risk factors are used to assess risk category and treatment goals for atherogenic lipoprotein cholesterol levels. Diabetes mellitus is not listed because it is considered a high- or very high–risk condition for ASCVD risk assessment purposes.

†CHD is defined as myocardial infarction, coronary death, or a coronary revascularization procedure.

ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Criteria</th>
<th>Treatment goal (mg/dL)</th>
<th>Consider drug therapy (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Non-HDL-C</td>
<td>LDL-C</td>
</tr>
<tr>
<td>Low</td>
<td>• 0–1 major ASCVD risk factors</td>
<td>&lt; 130</td>
<td>&lt; 100</td>
</tr>
<tr>
<td></td>
<td>• Consider other risk indicators, if known</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 190 non-HDL-C ≥ 160 LDL-C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>• 2 major ASCVD risk factors</td>
<td>&lt; 130</td>
<td>&lt; 100</td>
</tr>
<tr>
<td></td>
<td>• Consider quantitative risk scoring</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Consider other risk indicators</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>• ≥3 major ASCVD risk factors</td>
<td>&lt; 130</td>
<td>&lt; 100</td>
</tr>
<tr>
<td></td>
<td>• Diabetes mellitus (type 1 or 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 0–1 other major ASCVD risk factors and no evidence of end-organ damage</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Chronic kidney disease stage 3B or 4</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• LDL-C of ≥190 mg/dL (severe hypercholesterolemia)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Quantitative risk score reaching high-risk threshold</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very High</td>
<td>• ASCVD</td>
<td>&lt; 100</td>
<td>&lt; 70</td>
</tr>
<tr>
<td></td>
<td>• Diabetes mellitus (type 1 or 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ≥2 other major ASCVD risk factors or evidence of end-organ damage</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

National Lipid Association Guidelines: Treatment Considerations and Goals

- Unless contraindicated, first-line drug therapy for treatment of elevated atherogenic cholesterol levels is a moderate- or high-intensity statin.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Decreased Lipid/Lipoproteins</th>
<th>Increased Lipid/Lipoproteins</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statins</strong></td>
<td>LDL-C (18%-55%) Non-HDL-C (15%-51%)</td>
<td>HDL-C (5%-15%) TG (7%-30%)</td>
</tr>
<tr>
<td><strong>Bile Acid Sequestrants</strong></td>
<td>LDL-C (15%-30%) Non-HDL-C (4%-16%)</td>
<td>HDL-C (3%-5%) TG (0%-10%)</td>
</tr>
<tr>
<td><strong>Fibric Acids</strong></td>
<td>TG (20%-50%) Non-HDL-C (5%-19%) LDL-C (5%-↑20%)</td>
<td>HDL-C (10%-20%)</td>
</tr>
<tr>
<td><strong>Cholesterol Absorption Inhibitors</strong></td>
<td>Non-HDL-C (14%-19%) LDL-C (13%-20%) TG (5%-11%)</td>
<td>HDL-C (3%-5%)</td>
</tr>
<tr>
<td><strong>Nicotinic Acid</strong></td>
<td>TG (20%-50%) Non-HDL (8%-23%) LDL-C (5%-25%)</td>
<td>HDL-C (15%-35%)</td>
</tr>
<tr>
<td><strong>Long-chain Omega-3 Fatty Acid Drugs</strong></td>
<td>TG (19%-44%) Non-HDL (5%-14%) LDL-C (6%-↑25%) HDL-C (5%-↑7%)</td>
<td></td>
</tr>
</tbody>
</table>

LDL-C, low density lipoprotein cholesterol; Non-HDL-C, Non-high density lipoprotein cholesterol; TG, triglycerides;
Summary

- Wellness is extremely important for individuals with schizophrenia, due to increased incidence of cardiometabolic risk factors (both disease- and treatment-related)\(^ {1-5}\)
- Despite cardiometabolic guidelines specific to schizophrenia, the majority of patients are not monitored appropriately\(^ {6,7}\)
- Wellness programs can be successful in those with severe mental illness, with programs of at least 3 months’ duration that include education- and activity-based approaches, nutrition, and exercise demonstrating the best results\(^ {8,9}\)

References:

Questions
CLOSING