Metabolic Wellness Considerations In Schizophrenia

This program is paid for by
Otsuka Pharmaceutical Development &
Commercialization, Inc. and Lundbeck, LLC.
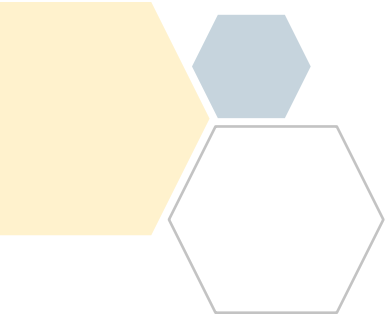
Speakers are paid consultants and/or employees of
Otsuka Pharmaceutical Development &
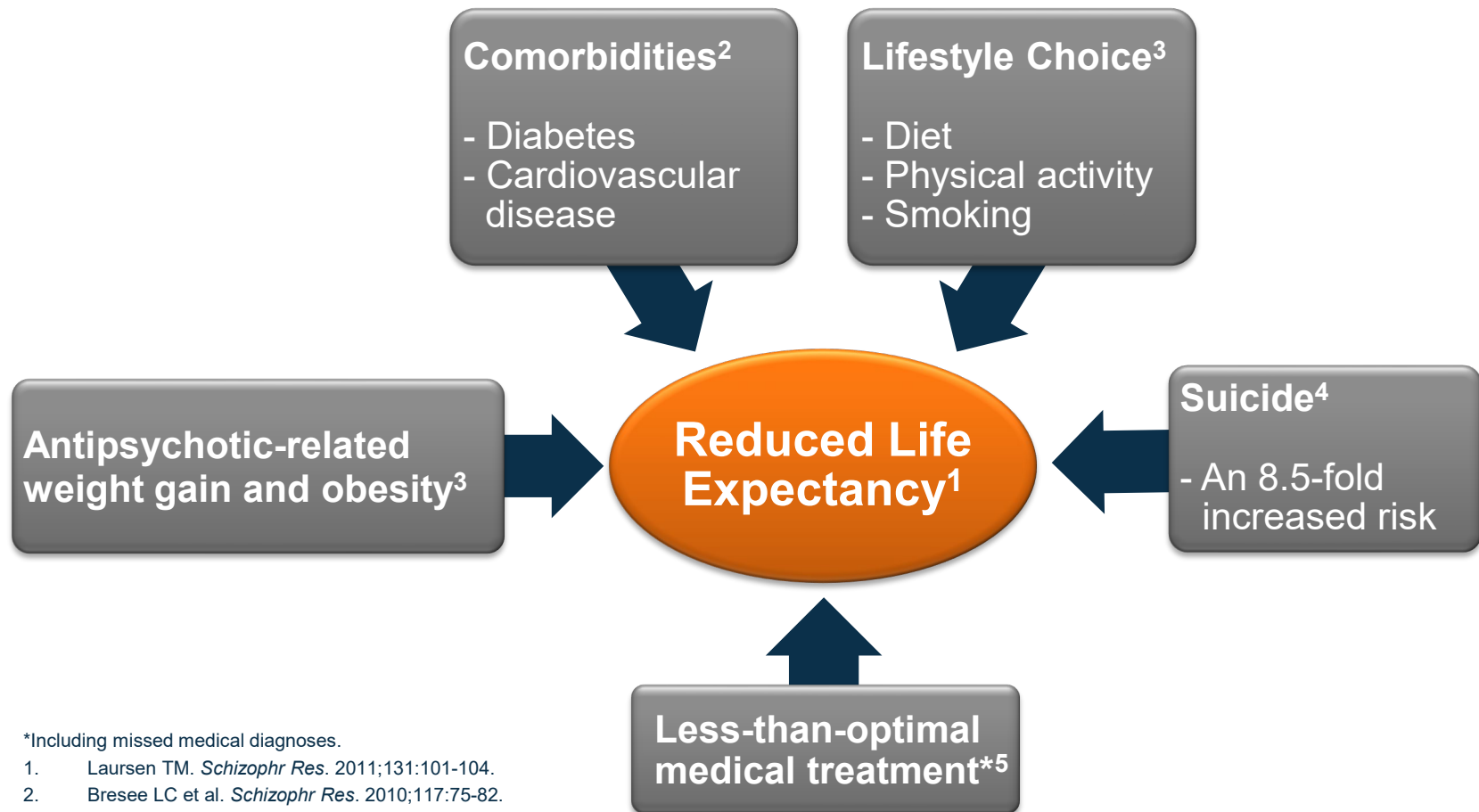Commercialization, Inc.

Objectives

- Highlight the importance of wellness in individuals with schizophrenia

- Discuss guidelines available to help maintain wellness in these patients

- Understand the importance of monitoring and treating cardiometabolic risk factors

- Explore wellness programs for those with schizophrenia and severe mental illness

Wellness in Schizophrenia: Why Is it an Issue?
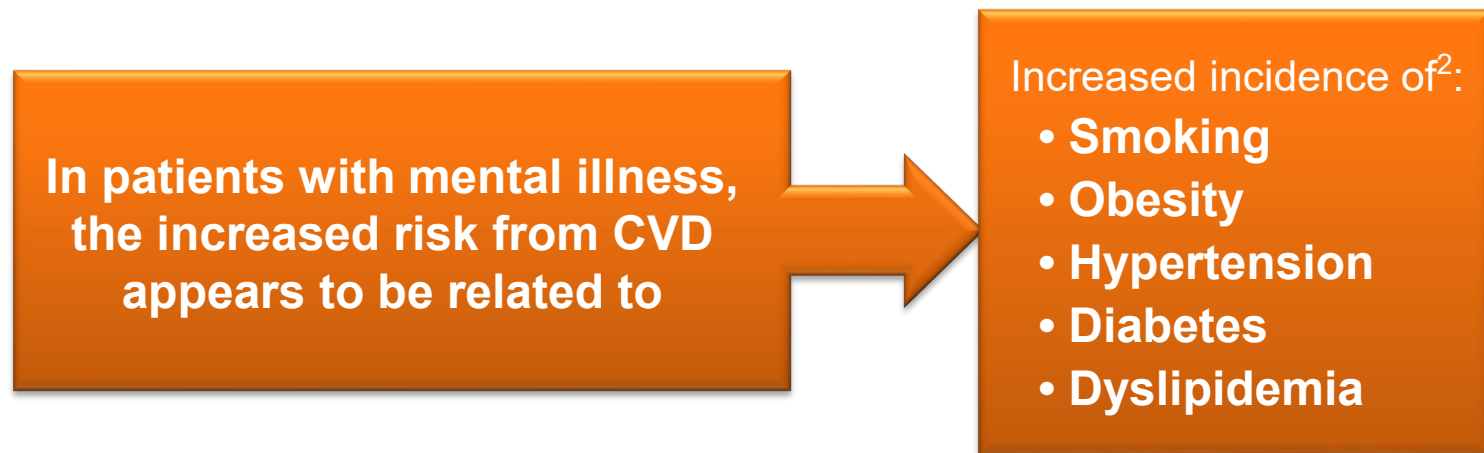
Mortality in Schizophrenia

Comorbidities[2]

- Diabetes
- Cardiovascular disease

Lifestyle Choice[3]

- Diet
- Physical activity
- Smoking

Antipsychotic-related weight gain and obesity[3]

Reduced Life Expectancy[1]

Suicide[4]

- An 8.5-fold increased risk

Less-than-optimal medical treatment*[5]

*Including missed medical diagnoses.

1. Laursen TM. *Schizophr Res*. 2011;131:101-104.
2. Bresee LC et al. *Schizophr Res*. 2010;117:75-82.
3. Connolly M et al. *Adv Psychiatr Treat*. 2005;11:125-132.
4. Kasckow J et al. *CNS Drugs*. 2011;25:129-143.
5. Brown S et al. *Br J Psychiatry*. 2000;177:212-217.

PsychU
Improving mental health care... together®

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.
1. Newcomer JW. *Am J Manag Care*. 2007;13:S170-S177.
2. Gibson M et al. *Int J Psychiatry Med*. 2011;41:127-142.

PSYCHU
Improving mental health care... together

Metabolic Syndrome

- Pathophysiology for T2D and CVD shares underlying processes related to systemic inflammation, oxidative stress, and adipocyte dysfunction[1]

Metabolic Syndrome

- Comprised of abnormalities in central obesity, blood pressure, triglycerides, HDL cholesterol, and fasting glucose[1]*
  - Highly heritable, indicating both lifestyle and genetic underpinnings

- Prevalence among US adults: 34.7%; increases across life span[1]

- First major goal of treating metabolic syndrome is to reduce the risk of coronary heart disease; second is to prevent onset of T2D[2]
  - Prevention and early treatment involve heart-healthy lifestyle changes
    - Heart-healthy eating, healthy weight, managing stress, physical activity, and quitting smoking
  - If insufficient, medications may be used to treat and control risk factors
    - High blood pressure, high triglycerides, low HDL cholesterol, and high blood sugar

*The various diagnostic criteria require abnormalities in ≥3 components, but have different cutoff levels.

CVD, cardiovascular disease; HDL, high-density lipoprotein; T2D, type 2 diabetes; US, United States.

1. DeBoer MD, Gurka MJ. *Diabetes Metab Syndr Obes*. 2017;10:65-72.
2. National Heart, Lung, and Blood Institute. How Is Metabolic Syndrome Treated? Available at: https://www.nhlbi.nih.gov/health/health-topics/topics/ms/treatment. Accessed April 19, 2017.

PsychU®
Improving mental health care... together®

Prevalence of Cardiometabolic Risk Factors in Patients With Schizophrenia

Modifiable risk factors	Estimated prevalence, % (RR)
Obesity[1–3]*	45–55 (1.5–2)
Smoking/nicotine abuse[1,2]†	50–80 (2–3)
Diabetes[1–3]*	10–15 (2)
Hypertension[1,2]	19–58 (2–3)
Dyslipidemia[1–3]*	25–69 (≤ 5)
Metabolic syndrome[1,2]*	37–63 (2–3)

RR, relative risk.

- Additional wellness issues in schizophrenia
  - Sexual dysfunction may be related to the illness and/or the treatment[4]
  - Hyperprolactinemia may be related to treatment[4]

*Factors which may be related to the illness and/or treatment.
†Factors which may be related to the illness.

1. Correll CU. *CNS Spectr*. 2007;12(10 Suppl 17):12-20, 35.
2. De Hert M et al. *World Psychiatry*. 2009;8:15-22.
3. Marder SR et al. *Am J Psychiatry*. 2004;161:1334-1349.
4. Knegtering H et al. *PNEC*. 2003;28:109-123.

PsychU®
Improving mental health care... together®

Prevalence of Metabolic Dysregulation in Patients With First-Episode Psychosis—RAISE-ETP Study

- Patients aged 15–40 years* diagnosed with schizophrenia or related disorders† treated with <6 months of cumulative antipsychotic use (N = 394‡)

Variable	Number (%)
Weight (n = 389)	
Obese	86 (22.1)
Overweight	102 (26.2)
Dyslipidemia (n = 286)	161 (56.5)
Blood pressure (n = 389)	
Prehypertension, blood pressure 120-139/80-89 mm Hg	155 (39.9)
Hypertension, blood pressure ≥140/90 mm Hg	39 (10.0)
Metabolic syndrome, fasting glucose ≥100 mg/dL per ATP III (n = 257)	34 (13.2)
Prediabetes	
Glucose-based, 100-125 mg/dL (n = 101)	4 (4.0)
HA$_{1C}$-based, 5.7%-6.4% (n = 280)	43 (15.4)
Diabetes	
Glucose-based, >125 mg/dL (n = 101)	3 (3.0)
HA$_{1C}$-based, >6.4% (n = 280)	8 (2.9)
Smoking (n = 394)	200 (50.8)

Mean age: 23.6 years

Mean lifetime antipsychotic exposure: 47.3 days

*1 patient was 51 years old.
†Related disorders included schizophreniform disorder, schizoaffective disorder, psychotic disorder not otherwise specified, or brief psychotic disorder.
‡Enrolled patients with cardiometabolic data.
ATP III, National Cholesterol Education Program Adult Treatment Panel; HA$_{1c}$, glycosylated hemoglobin.

PSYCHU
Improving mental health care... together®

Recovery After an Initial Schizophrenia Episode-Early Treatment Program (RAISE-ETP): Psychopharmacologic Treatment Outcomes

- NAVIGATE patients as compared to Community Care patients:
  - Gained less weight (p<0.001)
  - Experienced fewer side effects (p=0.002[a])
  - Were more likely to receive an LAI (OR=1.45[b])
- NAVIGATE patients were also:
  - More likely to receive an antipsychotic (OR=3.73; p=0.005) and those prescriptions were more likely to conform to NAVIGATE prescribing principles (OR=2.19; p=0.037)
  - Less likely to receive an antidepressant (OR=0.39; p=0.037)

> Other vital signs and cardiometabolic laboratory findings did not differ between groups. Nevertheless, given the likely future duration of antipsychotic exposure, such differences are potentially important

[a]The model included treatment condition, time, and the treatment-by-time interaction; treatment-by-time interaction, F=3.86, df=5, 1143, p=0.002.
[b]Differences in LAI use were not statistically significant (p=0.645).

[c] Odds ratios greater than 1 indicate a greater likelihood of antipsychotic or antidepressant prescriptions at NAVIGATE sites; ratios less than 1 indicate a greater likelihood of antipsychotic or antidepressant prescriptions at community care sites.

LAI, long-acting injectable.
Robinson DG, et al. *Am J Psychiatry*. 2017. doi:10.1176/appi.ajp.2017.16080919. [Epub ahead of print]

PSYCHU
Improving mental health care... together®

Cardiometabolic Risk Factors
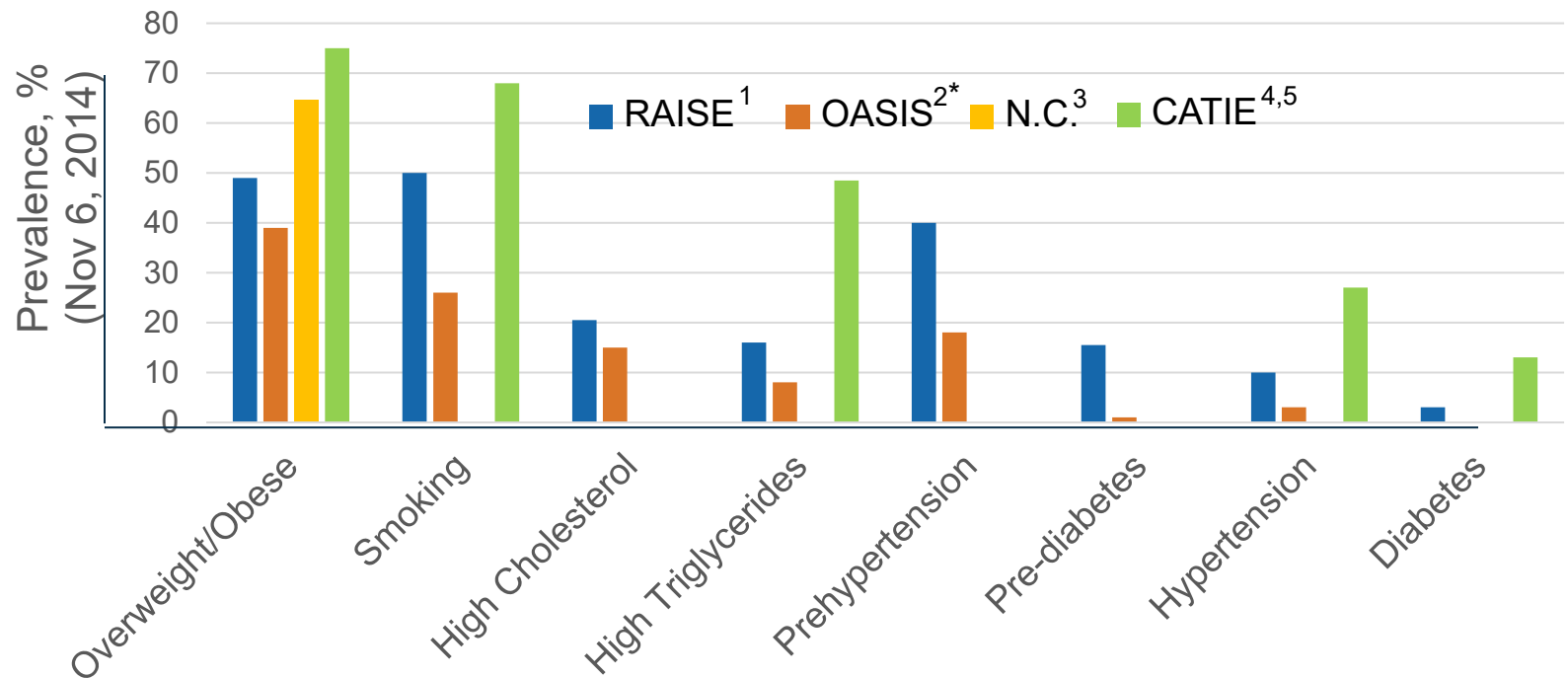
*OASIS data "snapshot" as of 6 November 2014. OASIS data on file.

N.C., North Carolina; RAISE, Recovery After an Initial Schizophrenia Episode; OASIS, Outreach and Support Intervention Services; CATIE, Clinical Antipsychotic Trials of Intervention Effectiveness.

1. Correll CU et al. *JAMA Psychiatry*. 2014;71:1350-1363; 2. OASIS: Dr. Perkins' data on file; 3. North Carolina Department of Health and Human Services. The Burden of Obesity in NC. 2009. Available at http://www.eatsmartmovemorenc.com/ObesityInNC/ObesityInNC.html. Accessed March 20, 2015; 4. McEvoy JP et al. *Schizophr Res.* 2005;80:19-32; 5. Goff DC et al. *Schizophrenia Res.* 2005;80:45-53.

Metabolic Abnormalities in Unmedicated, First-episode, and Medicated Patients With Schizophrenia

- A meta-analysis of 21 studies of unmedicated patients with schizophrenia (n = 8,593) and 26 studies of first-episode patients with schizophrenia (n = 2,548) was compared to a meta-analysis of 78 studies of medicated patients with schizophrenia* (n = 24,892)

Prevalence of MetS and its individual risk factors

Metabolic Risk Factors	Unmedicated Patients % (95% CI)	First-episode Patients % (95% CI)	Chronic Medicated Patients % (95% CI)
Waist (M>102 cm; F>88 cm)	26.6% (15.9%–38.9%)	22.0% (15.6%–29.1%)	52.7% (48.9%–56.5%)
Blood pressure (>130/85 mm Hg)	24.3% (11.2%–40.5%)	30.4% (21.3%–40.3%)	39.7% (36.4%–43.1%)
Triglycerides (>150 mg/dL)	16.9% (7.6%–29.0%)	19.6% (13.1%–27.0%)	41.1% (36.5%–45.7%)
Hyperglycemia (>100 mg/dL)	6.4% (2.2%–12.7%)	8.7% (5.2%–12.9%)	27.8% (23.0%–32.9%)
HDL (M<40 mg/dL; F<50 mg/dL)	20.4% (9.8%–33.7%)	21.9% (15.6%–28.9%)	44.7% (41.2%–48.2%)
Diabetes	2.1% (0.05%–4.8%)	1.3% (0.5%–2.4%)	12.8% (8.44%–17.9%)
Prevalence of MetS (by any definition)	**9.8% (5.3%–15.6%)**	**9.9% (6.1%–14.5%)**	**35.3% (32.8%–37.8%)**

- To minimize metabolic dysregulation, use of antipsychotics with less potential for metabolic abnormalities may be considered

*Not in their first episode of schizophrenia.
BP, blood pressure; CI, confidence interval; F, female; HDL, high-density lipoprotein; M, male; MetS, metabolic syndrome.
Mitchell AJ et al. *Schizophr Bull*. 2013;3:295-305.

PSYCHU
Improving mental health care... together®

Cardiovascular Risk Prediction Models for People With Severe Mental Illness

- **Background**
  - Established CVD risk scores (eg, Cox Framingham) dev[...] and do not consider SMI-specific exposures
- **Study objective**
  - Develop and validate risk model to predict CVD events i[...]
- **Methods**
  - Data collected from UK primary care database*
  - Compared Cox Framingham models to newly developed[...]
    - PRIMROSE models (BMI and lipid) include traditional r[...] hypertension, BMI, and dyslipidemia) and variables for[...] medication at baseline, harmful use of alcohol, use of a[...] social deprivation score
- **Results**
  - 38,824 people aged 30–90 years with a diagnosis of SM[...] years
  - PRIMROSE models predicted CVD risk more accurately[...] greater agreement between predicted and observed risk[...]
  - Superiority of PRIMROSE models was not explained by[...] populations

Conclusion: SMI-specific PRIMROSE CVD risk prediction models may offer improved prediction of CVD in people with SMI vs other CVD risk scores

BMI, body mass index; CVD, cardiovascular disease; PRIMROSE, Prediction and Management of Cardiovascular Risk in People With Severe Menta[...]
*Data collected between January 1, 1995 and December 31, 2010.
†Defined as schizophrenia/schizoaffective disorder, bipolar disorder, or other nonorganic psychoses.
Osborn DP et al. *JAMA Psychiatry*. 2015;72(2):143-151.

Figure. Calibration Plots: Prediction and Management of Cardiovascular Risk in People With Severe Mental Illnesses (PRIMROSE) Models and Published Cox Framingham Models
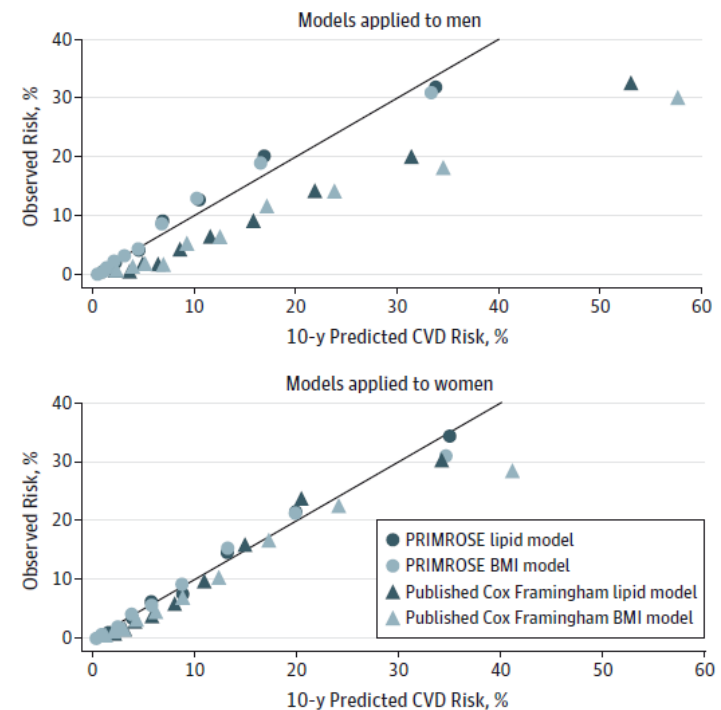
Bold line indicates perfect fit between predicted risk and observed events. In a situation of perfect calibration, the plotted points would lie on this line. Points above the line indicate underprediction; points below the line indicate overprediction. BMI indicates body mass index; CVD, cardiovascular disease.

Cardiovascular and Cerebrovascular Risk Factors Associated With SGAs

- A study that examined associations between metabolic, CVD, and cerebrovascular outcomes and use of SGAs vs ADs in a large sample of non-elderly adults* (N = 284,234) found that:
  - When compared with AD use, SGA exposure was associated with significantly increased risk for all outcomes (HR 1.24 – 2.12; all *P* ≤ 0.0017)
  - Among 5 commonly used SGAs, the hazard ratios for significant adverse outcomes varied from 0.40 – 2.02

- **Conclusion**: Care should be exercised in monitoring and mitigating adverse metabolic consequences of SGAs, even in a younger population

*Age <18 or >65 years.
AD, antidepressant; CVD, cardiovascular; HR, hazard ratio; SGA, second-generation antipsychotic.
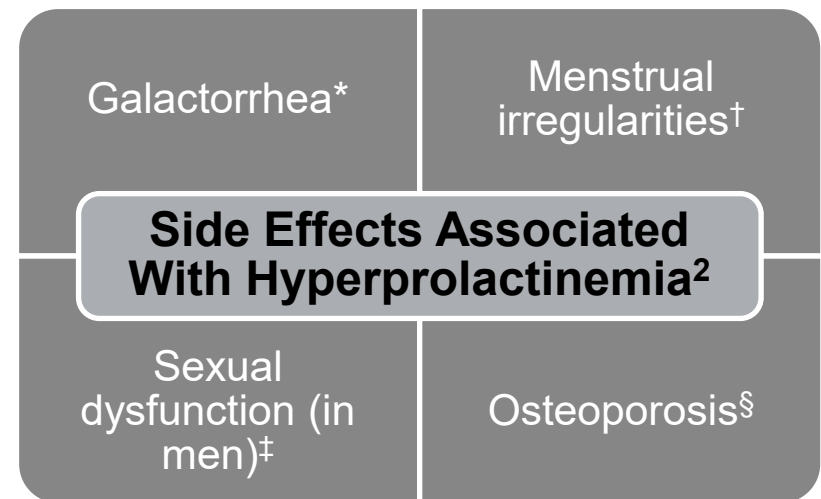Correll CU, et al. *World Psychiatry*. 2015;14(1):56-63.

Metabolic/Cardiovascular Risk Associated With SGA Exposure at 1 Year

Essential hypertension	Diabetes Mellitus
Obesity	Hyperlipidemia
Myocardial Infarction	Stroke
Angina	Hypertensive Heart Disease
Coronary Artery Disease	Transient Ischemic Attack

Dark blue boxes = Well-established proximal metabolic risks of SGAs
Light blue boxes = Distal cardiovascular and cerebrovascular outcomes

PSYCHU®
Improving mental health care... together®

Endocrine Dysfunction: Hyperprolactinemia

- **Prolactin regulation**: Several neurotransmitters may be involved, but modulation by dopaminergic mechanisms is likely the most important[1]

- **Antipsychotics**: First-generation and certain second-generation antipsychotics can cause hyperprolactinemia[2]
  - Due to dopamine D_2 blockade

Galactorrhea*	Menstrual irregularities†
Side Effects Associated With Hyperprolactinemia[2]	
Sexual dysfunction (in men)‡	Osteoporosis§

*Can occur in men or women. †Can occur in women. ‡Can occur in men. §Can occur if hyperprolactinemia impairs sex steroid production.[2]

1. Knegtering H et al. *Psychoneuroendocrinology*. 2003;28:109-123.
2. Marder SR et al. *Am J Psychiatry*. 2004;161:1334-1349.

PSYCHU
Improving mental health care... together®

Hyperprolactinemia: Clinical Recommendations

Situation	Clinical Recommendations
All patients	Provide information about the risks of elevated prolactin (especially risk of osteoporosis, reduced fertility, abnormal menstruation, and sexual dysfunction)
If prolactin elevation is an important treatment consideration	Consider an antipsychotic drug with a lower potential to elevate prolactin levels
Prior to initiating antipsychotic treatment	Obtain baseline prolactin level as part of an overall assessment of physical health
Patients who have not yet reached peak bone mass (<25 years old)	Avoid antipsychotics associated with increased prolactin level
Women planning to become pregnant	
Patients with history of breast (and possibly prostate) cancer or prolactinoma	
Patients diagnosed with osteoporosis	

Peveler RC et al. *J Psychopharmacol*. 2008;22 (2 suppl):98-103.

PsychU
Improving mental health care... together®

Wellness in Schizophrenia: Why Is it Important to Clinicians and Patients?
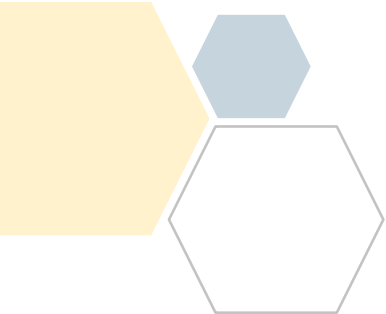
Incentives to Participate in Wellness Management and Patient Benefits

- 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

Roberts SH et al. *J Adv Nurs*. 2011;67:690-708.

PSYCHU®
Improving mental health care... together®

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

Roberts SH et al. *J Adv Nurs*. 2011;67:690-708.

PSYCHU®
Improving mental health care... together®

Quality of Care in Schizophrenia

- Patients with mental illness have been reported to experience worse quality of care than those without:[1]
  - In a review of 27 studies, worse quality of medical care was observed in 70% of studies[1]
  - May be due to communication difficulties, cognitive impairment, lack of social support, and/or fragmentation of behavioral and medical health delivery services[2]

Comorbidities for Which Patients With Serious Mental Illness Have Been Reported to Receive Worse Healthcare

Cardiovascular Disease[1,3]	**Diabetes Mellitus**[1]
Respiratory Illness[3]	**Cancer**[3]

"A human rights argument could be made that people with a higher burden of physical illness, such as people with serious mental illness, should be entitled to higher use of healthcare given the higher level of health need"[3]

1. Mitchell AJ et al. *Br J Psychiatry*. 2009;194(6):491-499.
2. Cahoon EK et al. *BMC Psychiatry*. 2013;13:37.
3. Lawrence D et al. *J Psychopharmacol*. 2010;24 (suppl 4):61-68.

PsychU
Improving mental health care... together®

Aspects of the PPACA That May Impact Mental Health Services in the United States

Title I — Quality, affordable healthcare for all Americans

Title II — The role of public programs

Title III — Improving the quality and efficiency of healthcare

Title IV — Preventing chronic disease and improving public health

Title VIII — Community living assistance services and supports

PPACA, Patient Protection and Affordable Care Act.
Affordable Care Act Summary. Available at: http://obamacarefacts.com/affordablecareact-summary.php. Accessed April, 2017.

PsychU®
Improving mental health care... together®

PPACA: Paying for Performance

Medicare Shared Savings Program	Hospital Value-based Purchasing Program	Physician Quality Reporting System	Other Programs With Incentives
• Groups of providers come together as accountable care organizations to improve care coordination • ACOs may share in savings if they meet certain quality improvement measures	• Participating hospitals are paid based on whether they meet performance standards and their degree of improvement	• Provides physicians with incentives to voluntarily report quality measurement data	• Medicare Advantage Plans • Medicare Home Health Pay for Performance

ACO, accountable care organization; PPACA, Patient Protection and Affordable Care Act.
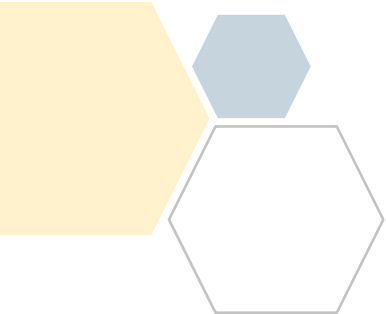CMS.gov. The Affordable Care Act: Lowering Medicare Costs by Improving Care. Available at: http://www.cms.gov/apps/files/aca-savings-report-2012.pdf. Accessed April, 2017.

PsychU
Improving mental health care... together®

Quality Measures: Healthcare Effectiveness Data and Information Set (HEDIS)

- HEDIS measures relevant to patients with schizophrenia on Medicaid include:
  - Adherence to antipsychotic medications for individuals with schizophrenia
  - Cardiovascular monitoring for people with cardiovascular disease and schizophrenia
  - Diabetes monitoring for people with diabetes and schizophrenia
  - Diabetes screening for people with schizophrenia or bipolar disorder who are using antipsychotic medications
  - Follow-up after hospitalization for mental illness (applies to Medicare and the commercially insured as well)

HEDIS. Summary Table of Measures, Product Lines, and Changes. 2013; vol 2. Available at:
http://www.ncqa.org/Portals/0/HEDISQM/HEDIS2014/List%20of%20HEDIS%202014%20Measures.pdf. Accessed April, 2017.

PSYCHU
Improving mental health care... together®

Wellness Guidelines

Hypertension Treatment: Eighth Joint National Committee

Population	When to Treat (mmHg)	Pharmacotherapy		Goal (mmHg)
		Nonblack	Black	
General population ≥ 60 y	SBP ≥ 150 or DBP ≥ 90	THZ, CCB, ACEI, or ARB	THZ or CCB	SBP < 150 DBP < 90
General population < 60 y	SBP ≥ 140 or DBP ≥ 90	THZ, CCB, ACEI, or ARB	THZ or CCB	SBP < 140 DBP < 90

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; DBP, diastolic blood pressure; SBP, systolic blood pressure; THZ, thiazide-type diuretic.

Guidelines available at: http://jama.jamanetwork.com/article.aspx?articleid=1791497.

James PA et al. *JAMA*. 2014;311:507-520.

PsychU®
Improving mental health care... together®

Diabetes Testing in Asymptomatic Individuals: American Diabetes Association

- Testing is recommended for adults of any age who are overweight or obese (BMI ≥ 25 kg/m^2) with ≥1 additional risk factor

    - If no risk factor, testing should begin at 45 years of age

- Tests for diabetes/prediabetes include HA$_{1C}$, FPG, or 2-hour 75-g OGTT

    - In those with prediabetes, identify and, if appropriate, treat other CVD risk factors

- If tests are normal, repeat at least every 3 years

BMI, body mass index; CVD, cardiovascular disease; FPG, fasting plasma glucose; HA$_{1c}$; glycosylated hemoglobin; OGTT, oral glucose tolerance test.
Guidelines available at: http://care.diabetesjournals.org/content/37/Supplement_1/S14.full.pdf+html.
American Diabetes Association. *Diabetes Care*. 2017;40 (suppl 1):S11-S24.

Type 2 Diabetes Treatment for Nonpregnant Adults: American Diabetes Association

When to Treat	Pharmacotherapy	Goal**
• A1C ≥ 6.5% (48 mmol/mol)* or • FPG ≥ 126 mg/dL (7.0 mmol/L)* or • 2-h PG ≥ 200 mg/dL (11.1 mmol/L) during an OGTT* or • Random PG ≥ 200 mg/dL (11.1 mmol/L) in patients with classic symptoms of hyperglycemia or hyperglycemic crisis	• Oral antihyperglycemic biguanidines (preferred initial agent)† • Insulin therapy (with or without additional agents) in newly diagnosed patients with T2D who are symptomatic and/or have A1C ≥ 10% (86 mmol/mol) and/or blood glucose levels ≥ 300 mg/dL (16.7 mmol/L) • If noninsulin monotherapy at MTD does not achieve or maintain HA_{1C} target after 3 months, add second oral agent, a glucagon-like peptide 1 receptor agonist, or basal insulin	• A1C < 7.0% (53 mmol/mol) • Preprandial capillary plasma glucose 80–130 mg/dL (4.4–7.2 mmol/L) • Peak postprandial capillary plasma glucose < 180 mg/dL (10.0 mmol/L; 1–2 hrs after meal)‡

Lifestyle management, including diabetes self-management education, diabetes self-management support, nutrition therapy, physical activity, smoking cessation counseling, and psychosocial care should also be pursued

*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.
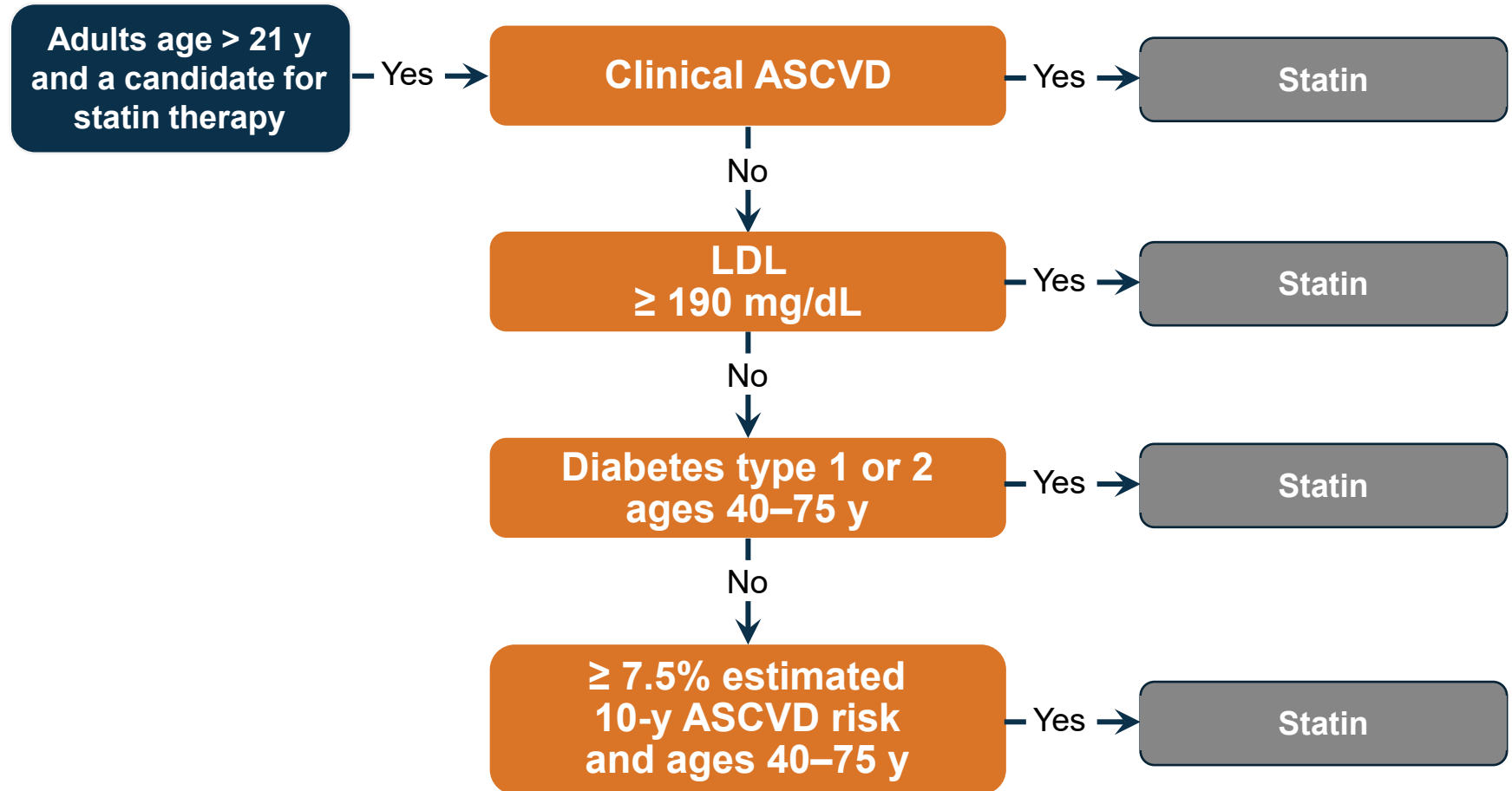
†Long-term use of metformin may be associated with biochemical vitamin B12 deficiency, and periodic measurement of vitamin B12 levels should be considered in metformin-treated patients, especially in those with anemia or peripheral neuropathy.

‡Postprandial glucose may be targeted if HA_{1C} goals are not met despite reaching preprandial glucose goals.

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

American Diabetes Association. *Diabetes Care*. 2017;40 (suppl 1):S1-S135.

PSYCHU
Improving mental health care... together®

Statin Treatment in Atherosclerotic Cardiovascular Disease Risk Group: American College of Cardiology/American Heart Association

Adults age > 21 y and a candidate for statin therapy — Yes → **Clinical ASCVD** — Yes → **Statin**

↓ No

LDL ≥ 190 mg/dL — Yes → **Statin**

↓ No

Diabetes type 1 or 2 ages 40–75 y — Yes → **Statin**

↓ No

≥ 7.5% estimated 10-y ASCVD risk and ages 40–75 y — Yes → **Statin**

ASCVD, atherosclerotic cardiovascular disease; LDL, low-density lipoprotein; y, years.
Guidelines available at: http://annals.org/article.aspx?articleid=1818923.
Stone NJ et al. *Circulation*. 2014;129:S1-45.

PsychU®
Improving mental health care… together®

Treatment Considerations and Goals by Risk Category: National Lipid Association Guidelines

| Risk Category	Criteria	Treatment goal (mg/dL)			Consider drug therapy (mg/dL)
		Non-HDL-C	LDL-C	Apo-B*	
Low	• 0–1 major ASCVD risk factors • Consider other risk indicators, if known	< 130	< 100	< 90	≥ 190 non-HDL-C ≥ 160 LDL-C
Moderate	• 2 major ASCVD risk factors • Consider quantitative risk scoring • Consider other risk indicators	< 130	< 100	< 90	≥ 160 non-HDL-C ≥ 130 LDL-C
High	• ≥ 3 major ASCVD risk factors • Diabetes mellitus (type 1 or 2) ○ 0–1 other major ASCVD risk factors and no evidence of end-organ damage • Chronic kidney disease stage 3B or 4 • LDL-C of ≥ 190 mg/dL (severe hypercholesterolemia) • Quantitative risk score reaching high-risk threshold	< 130	< 100	< 90	≥ 130 non-HDL-C ≥ 100 LDL-C
Very High	• ASCVD • Diabetes mellitus (type 1 or 2) ○ ≥ 2 other major ASCVD risk factors or evidence of end-organ damage	< 100	< 70	< 80	≥ 100 non-HDL-C ≥ 70 LDL-C

For patients with ASCVD or diabetes mellitus, consideration should be given to use of moderate- or high-intensity statin therapy, irrespective of baseline atherogenic cholesterol levels.

*Apo B is a secondary, optional target of treatment. Elevated triglyceride level is not a target of therapy, except when very high (≥500 mg/dL).

ASCVD, atherosclerotic cardiovascular disease; apo B, apolipoprotein B; HDL-C, high density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Jacobson TA et al. *J Clin Lipidol*. 2015;8(5):473-488.

PSYCHU
Improving mental health care... together®

Metabolic Monitoring Guidelines For Schizophrenia
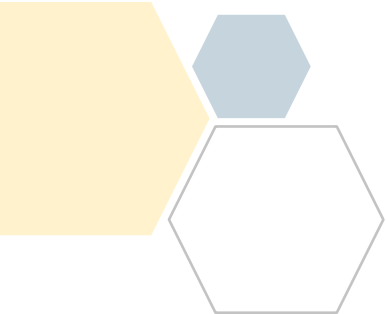
Treatment of Hypertriglyceridemia: Endocrine Society

Severity of Hypertriglyceridemia[1]	Treatment Recommendations[1]
Mild to moderate	Lifestyle therapy (eg, dietary counseling, exercise, weight management) as initial treatment
Moderate to severe	Fibrates, nicotinic acid, and omega-3 fatty acids alone or in combination with statins*

NCEP ATP guidelines recommend treatment for triglycerides ≥150 mg/dL. If ≥ 200 mg/dL, fibrates or nicotinic acid may be added.[2]

*Moderate hypertriglyceridemia treatment goal: non-HDL cholesterol level in agreement with NCEP ATP guidelines.[1]

HDL, high-density lipoprotein; NCEP ATP, National Cholesterol Education Program Adult Treatment Panel.

1. Berglund L et al. *J Clin Endocrinol Metab*. 2012;97:2969-2989. Available at: http://press.endocrine.org/doi/pdf/10.1210/jc.2011-3213. Accessed April, 2017.
2. US Dept of Health and Human Services. NIH Publication No. 01-3670. May 2001. Available at: https://www.nhlbi.nih.gov/files/docs/guidelines/atp3xsum.pdf. Accessed April, 2017.

PSYCHU
Improving mental health care... together®

BAP Guidelines: Management of Weight Gain, Metabolic Disturbances, and CV Risk Associated With Psychosis and Antipsychotic Usage

	Before starting antipsychotic	Week 4	Week 8	Week 12	6 months	Annually
BMI and weight*	X	X	X	X	X	X
Fasting or random plasma glucose†	X			X	X	X
Fasting or random lipid profile‡	X			X	X	X
Blood pressure	X			X	X	X

- If antipsychotic medication changes, it may be appropriate to revisit all steps
- Tobacco smoking and alcohol use should be inquired about at all opportunities
- Ethnicity should be taken into account when evaluating BMI results

*Minimum monitoring schedule shown. Ideal monitoring schedule is weekly for the first 4–6 weeks and then every 2–4 weeks up to 12 weeks.

†In the long term, blood glucose control should be monitored using glycated hemoglobin (HA_{1c}).

‡In order to assess cardiovascular risk, for example using the QRISK2 cardiovascular risk model, the total cholesterol/high-density lipoprotein (HDL) cholesterol ratio will be required.

BAP, British Association for Psychopharmacology; BMI, body mass index; CVD, cardiovascular.

Cooper SJ et al *J Psychopharmacol*. 2016;30(8):717-748.

PsychU
Improving mental health care... together®

ADA/APA Monitoring Guidelines

	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Every 5 Years
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X			X

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.

American Diabetes Association et al. *Diabetes Care*. 2004;27:596-601.

PsychU®
Improving mental health care... together®

Mount Sinai Monitoring Guidelines

Issue	Recommendation	Monitoring Procedure
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_{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.
Marder SR et al. *Am J Psychiatry*. 2004;161:1334-1349.

PsychU
Improving mental health care... together®

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 antipsychotic.
1. Keller WR et al. *J Nerv Ment Dis*. 2014;202:6-12.
2. Morrato EH et al. *Diabetes Care*. 2009;32:1037-1042.

PSYCHU®
Improving mental health care... together®

Overall Poor Adherence to Monitoring Guidelines

Patient characteristics[1]:

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

Clinician behavior[1,2]:

- 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
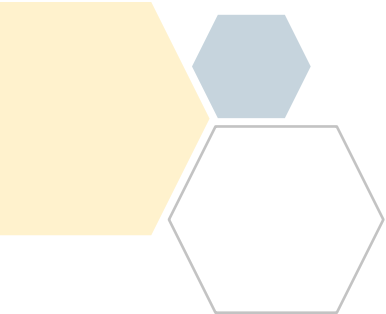 - Shortage of psychiatrists

Medical system[1]:

- Complex care systems may be difficult to navigate

Adequate Care

1. Morden NE et al. *J Am Board Fam Med*. 2009;22:187-195.
2. Insel T. 2011; Available at: http://www.nimh.nih.gov/about/director/2011/psychiatry-where-are-we-going.shtml.

PsychU
Improving mental health care... together

Wellness in Schizophrenia: Best Practices

Models to Improve Care in Schizophrenia/Severe Mental Illness

Model	Description	Limitations
Dually trained physicians	Physician trained in both psychiatric and physical medicine manages all care	Few available; may not maintain sufficient skills for complex medical care
Physical medicine on-site consultation	Physical medicine clinician provides consultation and care within psychiatric clinic or inpatient setting	Expensive, unless volume is sufficient to fill consultant's schedule
Collaborative care	Frequent communication between mental and physical healthcare teams	Requires unreimbursed communication time, added attention to HIPAA compliance
Case manager	Often a registered nurse who coordinates transportation and appointments	Time intensive for nurse; potentially expensive
Facilitated referral to primary care	Psychiatric care team facilitates access to primary care team	Requires sufficient primary care access in community

HIPAA, Health Insurance Portability and Accountability Act.

Morden NE et al. *J Am Board Fam Med*. 2009;22:187-195.

PsychU
Improving mental health care... together®

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).

Bartels S et al. Health Promotion Programs for People with Serious Mental Illness. Wash DC SAMHSA-HRSA Center for Integrated Health Solutions. Jan 2012. Available at: http://www.integration.samhsa.gov/Health_Promotion_White_Paper_Bartels_Final_Document.pdf. Accessed July 22, 2014.

PsychU
Improving mental health care... together®

Wellness Programs in Patients with SMI

Program	Description	Results
Canadian Study[1]	Outpatient program One 90-minute educational session (dietary and physical activity counseling) at beginning of study; twice-weekly, 60-minute exercise sessions for 18 months Active treatment: N = 59	Significant improvement in BMI, weight, waist circumference, triglycerides, total cholesterol, HDL, LDL, glucose, HA_{1c} No significant improvement in prolactin or thyrotropin-stimulating hormone
Healthy Living[2]	Day treatment program 12-week intensive weight control program (including basic nutrition principles, principles of physical fitness and behavioral management), followed by a 12-week step-down program and a 6-month maintenance program Active treatment: N = 31	Significant improvement in BMI, weight, waist circumference, HA_{1c}, SBP, DBP No significant improvement in total cholesterol, HDL, LDL, or triglycerides

BMI, body mass index; DBP, diastolic blood pressure; HA_{1c}, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.

1. Poulin MJ et al. *Aust NZ J Psychiatry*. 2007;41:980-989;
2. Menza M et al. *J Clin Psychiatry*. 2004;65:471-477.

PSYCHU®
Improving mental health care... together®

Wellness Programs in Patients with SMI (cont'd)

Program	Description	Results
Solutions for Wellness/Team Solutions[1]	Psychiatric inpatient setting 4 hours per day, 5 days/week, for 36 weeks Solutions for Wellness program: tips on nutrition and fitness, with an exercise component Team Solutions program: patients learned about symptoms of mental illness, promotion of recovery, and prevention of relapse N = 275	Significant improvement in BMI, weight, glucose, triglycerides, blood pressure (% of patients with SBP ≥ 140 mmHg or DBP ≥ 90 mmHg) No significant improvement in cholesterol, HDL, LDL, HA_{1c}
Well-being Support[2]	Outpatient setting Healthy living education In addition, patients could participate in a group for weight management or physical activity; minimum of 6 consultations over 2 years N = 966	Significant improvement in cigarette smoking, alcohol use, physical activity, diet No significant improvement in BMI, DBP, SBP

BMI, body mass index; DBP, diastolic blood pressure; HA_{1c}, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.

1.   Lindenmayer J-P et al. *J Clin Psychiatry*. 2009;70:1385-1396.
2.   Smith S et al. *Eur Psychiatry*. 2007;22:413-418.

PSYCHU®
Improving mental health care... together®

Wellness Programs in Patients with SMI (cont'd)

Program	Description	Results
In SHAPE[1]	Fitness/health promotion community-integrated program consisting of weekly sessions with a health mentor/fitness trainer (45–60 minutes) and free fitness club membership for up to 12 months; weekly sessions included review of progress, individualized exercise instruction, and education about healthy eating (N = 67)	Compared with fitness club membership and education, In SHAPE was associated with greater fitness club attendance, more participation in physical exercise, increased vigorous physical activity, and greater improvement in dietary habits No differences in mean weight and BMI among participants from baseline to 12-month follow-up*
Keeping the Body in Mind (KBIM)[2]	12-week holistic, individualized lifestyle and life skills intervention program for the prevention of weight gain in youth aged 14–25 years with FEP recently commenced on antipsychotic medications. Components included health coaching, weekly dietetic support and supervised exercise prescription, individualized based on best-practice recommendations. Involved youth peer wellness coaches and medication review** (N = 16)	Compared with standard care, KBIM intervention resulted in substantially lower weight gain (1.8 kg vs 7.8 kg; $P < 0.001$), significantly less change in BMI (0.4 kg/m^2 vs 2.6 kg/m^2; $P < 0.001$), and significantly less change in waist circumference (0.1 cm vs 7.1 cm; $P < 0.001$). The rate of clinically significant weight gain† was 13% vs 75% in standard care ($P = 0.001$). There was no significant change in fasting lipids or glucose in either group

*Or as compared with fitness club membership and education participants. **Clients who gained >5 kg following initiation of antipsychotic treatment were reviewed to consider switching to more weight neutral medication. †Defined as >7% of baseline weight. BMI, body mass index; DBP, diastolic blood pressure; FEP, first-episode psychosis; HA$_{1c}$, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; YPAS, Yale Physical Activity Scale.

1. Bartels SJ, et al. *Psychiatr Serv*. 2013;64(8):729-36.
2. Curtis J, et al. *Early Interv Psychiatry*. 2016;10(3):267-76.

PSYCHU
Improving mental health care... together®

Wellness Programs in Patients with SMI (cont'd)

Program	Description[1]	Results[2]
STRIDE[1,2]	Community outpatient settings 12-month program including usual care or a weight loss and lifestyle intervention program consisting of weekly group participation for 6 months covering topics on nutrition, physical activity and lifestyle changes + monthly group participation for an additional 6-month maintenance period + individual monthly contacts from intervention group facilitators during the second 6-month phase N = 200	Intervention participants lost 4.4 kg more than control participants from baseline to 6 months and 2.6 kg more than controls from baseline to 12 months At 12 months, fasting glucose levels had increased in the control group (from 106.0 mg/dL to 109.5 mg/dL) and decreased in the intervention group (from 106.3 mg/dL to 100.4 mg/dL) Medical hospitalizations were lower in the intervention group vs control group (6.7% vs 18.8%)

BMI, body mass index; DBP, diastolic blood pressure; HA_{1c}, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.

1. Yarborough BJH et al. *BMC Psychiatry*. 2013;13:238.
2. Green CA et al. *Am J Psychiatry*. 2015;172(1):71-81.

PsychU®
Improving mental health care... together®

Wellness Programs in Patients with SMI (cont'd)

Program	Description	Results
Diabetes Prevention Program[1]*	Outpatient program 12-month program (includes weekly classes, dietary monitoring, and individual coaching on nutrition and healthy lifestyles for 8 weeks and monthly booster classes and counseling for 1 year) Active treatment: N = 60	Significant improvement in BMI, weight, and body fat No significant improvement in glucose or lipid levels
Danish Study[2]	Outpatient program 30-month intervention program consisting of individual consultations, group sessions, and focus groups centered on diet and physical health; voluntary walking/running Active treatment: N = 54	Significant reduction in consumption of fast food, soft drinks, and number of daily cigarettes Improvements in WC, average cholesterol, triglycerides and HA_{1c} for women Improvements in LDL and cholesterol for men

*Mean weight change, BMI, body fat, glucose and lipid level trajectories were determined using a general linear mixed model (GLMM) approach.

BMI, body mass index; HA_{1c}, glycosylated hemoglobin; LDL, low-density lipoprotein; WC, waist circumference.

1. Erickson ZD, et al. *J Clin Psychiatry*. 2016;77(2):e183-9.
2. Hjorth P, et al. *Archives of Psychiatric Nursing*. 2017.

PsychU®
Improving mental health care... together®

Wellness Programs in Patients with SMI (cont'd)

Program	Description	Results
ACHIEVE Study[1]	Community outpatient settings 18-month behavioral weight loss intervention program composed of group weight-management, individual weight-management, and group exercise sessions Active treatment: N = 144	Significant improvement in BMI and weight (at 18 months, the mean between-group difference in weight was −3.2 kg)
McLean Study[2]	Intensive 24-week program of diet, exercise, and counseling followed by an additional 24-week, less intensive extension phase Active treatment: N = 12	By 24 weeks, weight loss per patient averaged 6.0 kg (5.7%); BMI decreased to 34.5 (by 5.7%); blood pressure decreased from 130/83 to 116/74 (11% improvement) With less intensive management for another 24 weeks, subjects regained minimal weight (0.43 kg) No significant improvement in serum cholesterol and triglyceride concentrations

BMI, body mass index.

1. Daumit GL, et al. *N Engl J Med*. 2013;368(17):1594-602.
2. Centorrino F, et al. *Int J Obes (Lond)*. 2006;30(6):1011-6.

PsychU®
Improving mental health care... together®

Integrating Mental and Physical Healthcare Services: Impact on Outcomes

- 10-year retrospective longitudinal study on the impact of delivering integrated mental and physical healthcare in team-based primary care vs traditional practices
  - Study included 113,452 adult patients, including 27 team-based medical practices and 75 traditional practices

- Compared to care in traditional practices, receipt of care in team-based practices was associated with:
  - Significantly higher rates of quality measures
  - Increased proportion of patients with an annual visit to PCP (OR, 1.09; 95% CI, 1.03 to 1.15; P = 0.002)
  - Lower rates of healthcare utilization
    - Emergency visits per 100 person-years: IRR, 0.77 [95% CI, 0.74 to 0.80], $P < 0.001$
    - Hospital admissions per 100 person-years: IRR, 0.89 [95% CI, 0.85 to 0.94], $P < 0.001$

Suggests the value of coordinated team relationships within a delivery system emphasizing the integration of physical and mental healthcare

CI, confidence interval; IRR, incidence rate ratio; OR, odds ratio; PCP, primary care physician.

Reiss-Brennan B et al. *JAMA*. 2016;316(8):826-834.

PsychU
Improving mental health care... together®

Selected Wellness Program Resources

- Wellness program materials available online:
  - Simplified Intervention to Modify Physical activity, Lifestyle, and Eating behavior (SIMPLE) program:
    - A weight loss program designed to be used to assist individuals with severe mental illness; developed by Yale University Department of Psychiatry
  - Enhancing Quality and Utilization in Psychosis (EQUIP) wellness program for patients with severe mental illness:
    - Implemented at the Greater Los Angeles Healthcare System and the Long Beach Healthcare System in close collaboration with the VA Desert Pacific Mental Illness Research, Education and Clinical Center
  - Outreach and Support Intervention Services (OASIS)
    - Emphasizes early identification and treatment of young people and their families at the start of a psychotic disorder; developed by the Department of Psychiatry at University of North Carolina – Chapel Hill School of Medicine

PSYCHU
Improving mental health care... together®

Summary

- Wellness is extremely important for individuals with schizophrenia, due to increased incidence of cardiometabolic risk factors (both disease- and treatment-related)[1-5]

  – In fact, metabolic syndrome, a cluster of conditions that increase the risk of cardiovascular disease and diabetes, occurs at increased frequency in patients with schizophrenia who are chronically medicated[6,7]

- Despite cardiometabolic guidelines specific to schizophrenia, the majority of patients are not monitored appropriately[8,9]

- Wellness programs may 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[10,11]

1. Newcomer JW. *Am J Manag Care*. 2007;13:S170-S177.
2. Gibson M et al. *Int J Psychiatry Med*. 2011;41:127-142.
3. De Hert M et al. *World Psychiatry*. 2009;8:15-22.
4. Marder SR et al. *Am J Psychiatry*. 2004;161:1334-1349.
5. Knegtering H et al. *PNEC*. 2003;28:109-123.
6. DeBoer MD, Gurka MJ. *Diabetes Metab Syndr Obes*. 2017;10:65-72.
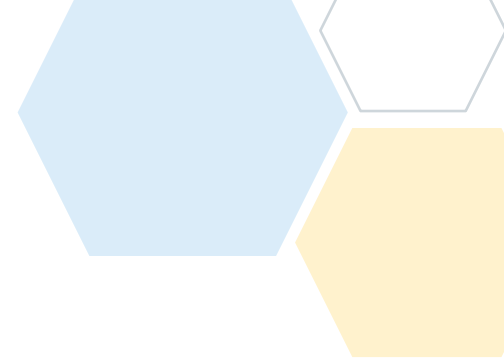7. Mitchell AJ et al. *Schizophr Bull*. 2013;3:295-305.
8. Keller WR et al. *J Nerv Ment Dis*. 2014;202:6-12.
9. Morrato EH et al. *Diabetes Care*. 2009;32:1037-1042.
10. Bartels S et al. Health Promotion Programs for People with Serious Mental Illness. Wash DC SAMHSA-HRSA Center for Integrated Health Solutions. Jan 2012. Available at: http://www.integration.samhsa.gov/Health_Promotion_White_Paper_Bartels_Final_Document.pdf. Accessed July 22, 2014.
11. Menza M et al. *J Clin Psychiatry*. 2004;65:471-477.

MRC2.PSY.D.00020

PSYCHU®
Improving mental health care... together®

Metabolic Wellness Considerations in Schizophrenia