

Nonfasting Screening for Cardiovascular Risk Among Individuals Taking Second-Generation Antipsychotics

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Ischemic heart disease (IHD) is the leading cause of mortality among adults with severe mental illness. Although gains in reducing mortality from IHD through screening, risk reduction, and early intervention have been realized for the general public, rates of recognition and treatment among individuals with mental illness continue to be poor. Obtaining blood samples from patients who have been fasting for eight to 12 hours is challenging for adults with severe mental illness and presents an additional obstacle to screening and treatment. This column outlines newer guidelines for cholesterol and diabetes screening that provide valid alternatives to fasting blood draws, thereby significantly reducing this common barrier to recognition of leading risk factors for IHD. (*Psychiatric Services* 65: 573–576, 2014; doi: 10.1176/appi.ps.201400015)

The leading cause of accelerated mortality among adults with serious mental illness is ischemic heart

disease (IHD) (1–3). Large-scale efforts to identify the leading modifiable risk factors for IHD—tobacco use, obesity, high blood pressure, diabetes, and dyslipidemias—and to implement early recognition of and interventions for adults with acute coronary syndrome have demonstrated benefit for the population at large (4,5). However, adults with mental illness have failed to reap the rewards of risk factor reduction or early intervention primarily because of their reduced access to high-quality preventive care, including screening and systematic treatment with evidence-based interventions (6–8).

Many adults with severe mental illness undergo therapy with second-generation antipsychotics, which have been associated with higher rates of obesity, metabolic syndrome, and diabetes (9). In 2004, a joint statement of the American Diabetes Association (ADA) and the American Psychiatric Association (APA) outlined guidelines for screening for metabolic syndrome and monitoring parameters for adults taking second-generation antipsychotics (10). Uptake of these screening guidelines by prescribers has been low (11). Recognition and treatment of dyslipidemia have remained the lowest of all the screening recommendations, despite ample evidence that interventions to lower cholesterol are safe and highly effective in preventing deaths from IHD (12,13).

A major barrier to screening and managing adults with dyslipidemia stems from guidelines that rely on

blood samples from patients who have been fasting for eight to 12 hours to accurately calculate low-density lipoprotein (LDL), the portion of total cholesterol (TC) most closely associated with atherosclerosis and cardiovascular disease (CVD). Because of their complexity, lipid profiles are also challenging to interpret. Obtaining fasting glucose values presents similar challenges to screening and diagnosing diabetes. Individuals with severe mental illness treated in safety-net settings or in community mental health centers face additional obstacles to providing fasting blood samples, such as a lack of on-site phlebotomy, transportation difficulties, erratic dietary habits, and often significant neurocognitive deficits in planning and organization. Therefore, an urgent need exists to communicate guidelines for conducting nonfasting screening for dyslipidemia and diabetes to practitioners working with individuals who are taking second-generation antipsychotics or who are otherwise at risk of suffering from premature IHD mortality because of poor access or engagement with care.

Alternatives to screening for diabetes

Adults taking second-generation antipsychotics who are overweight or obese (body mass index ≥ 25 kg/m²) or who have a history of prediabetes or gestational onset diabetes are candidates for yearly screening for diabetes (10,14). Monitoring of glycemic control among patients with

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Table 1Recommended screening guidelines and frequency for adults taking second-generation antipsychotics^a

Parameter ^b	Measurement Method	Abnormal cutoff	Measurement period					
			Baseline	4 weeks	8 weeks	12 weeks	Every 3 months	Annually
Medical or family history	Interview	na	✓					✓
Weight (BMI)	Office	>7% weight gain over baseline OR ≥ 25 kg/m ²	✓	✓	✓	✓	✓	✓
Waist circumference	Office	Men: 40 inches; women: 35 inches	✓					✓
Blood pressure ^c	Office	$\geq 140/90$ mmHg	✓				✓	✓
Nonfasting HBA1c or random plasma glucose ^{d,e}	Venipuncture	Diabetes, $\geq 6.5\%$; prediabetes, $\geq 5.7\%$; OR diabetes, ≥ 200 mg/dl; prediabetes, ≥ 140 mg/dl	✓				✓	✓
Nonfasting TC and HDL (non-HDL=TC-HDL) ^{e,f}	Venipuncture	Non-HDL, ≥ 220 mg/dl; OR 10-year risk, $\geq 7.5\%$ ^g	✓				✓	✓

^a Unless noted, guidelines are unchanged from the 2004 screening guidelines issued jointly by the American Diabetes Association and the American Psychiatric Association.

^b BMI, body mass index (kg/m²); TC, total cholesterol; HDL, high-density lipoprotein

^c Criteria for diagnosis require two measurements collected at least 1 week apart with the subject in an upright position measured over the brachial artery at the level of the heart.

^d American Diabetes Association updated classification of diabetes diagnosis and screening (15). Criteria for diagnosis require two samples collected via venipuncture on separate days. HBA1C, glycated hemoglobin.

^e Venipuncture is the preferred method of diagnosis. Finger-stick point-of-care testing has not been validated, and results should be interpreted with caution or verified with venipuncture.

^f American College of Cardiology and American Heart Association updated guideline on screening and diagnosis of dyslipidemia (13)

^g Risk calculators are available online (23).

diabetes was revolutionized in the 1990s with the validation of the non-fasting percentage of glycated hemoglobin, hemoglobin A1c (HBA1c), as a measure of disease control. HBA1c is highly correlated with the three-month average blood glucose reading and does not vary by fasting status. In 2010, the ADA adopted the screening cutoff of $\geq 6.5\%$ on two separate days as diagnostic of diabetes and defined prediabetes as an HBA1c value between 5.7% and 6.4% (15). Moreover, adults with two separate “random” (nonfasting) plasma glucose concentrations greater than 140 mg/dl or 200 mg/dl may be diagnosed as having prediabetes or diabetes, respectively (15). It is therefore reasonable to obtain a random plasma glucose level in addition to HBA1c when screening for diabetes, although a nonfasting HBA1c is sufficient for diagnosis.

HBA1c may be artificially low when there is a high turnover of hemoglobin, such as in anemic states or after a recent blood transfusion. Because most adults are not anemic, routinely assessing blood counts is not necessary when screening for diabetes unless

otherwise indicated or suspected. Blood venipuncture is still the recommended sample of choice for utilizing HBA1c in screening and diagnosis of diabetes (15). Point-of-care machines, which report HBA1c values from a finger-stick blood sample within five to seven minutes, are now widely available. Although these appear to have a greater margin of error (compared with blood venipuncture) and have not been empirically validated for diagnostic purposes, they may represent a very useful screening tool in settings with limited access to phlebotomy services.

Alternatives to cholesterol screening

Adults at increased risk of dyslipidemias are candidates for cholesterol screening beginning at age 20, including individuals who are obese, have high blood pressure or diabetes, use tobacco, or are taking second-generation antipsychotics (10,16). Most experts now recommend annual dyslipidemia screening of adults taking second-generation antipsychotics. Increasing numbers of researchers, epidemiologists, and practitioners are advo-

ating for the removal of traditional LDL targets in the diagnosis and management of high blood cholesterol (17–19). Mounting evidence has supported the use of non-high-density lipoprotein cholesterol (non-HDL) as the primary marker for atherogenesis, especially for adults with the metabolic syndrome phenotype commonly induced by second-generation antipsychotics (20,21).

New guidelines for screening, diagnosis, and management of dyslipidemias released jointly by the American College of Cardiology and the American Heart Association in the fall of 2013 make use of non-HDL cholesterol for defining abnormally high serum cholesterol and initiating treatment and remove LDL targets that were previously used to guide therapy or warrant treatment intensification (13). Conveniently, non-HDL cholesterol can be calculated from the common lipid profile by subtracting the HDL value from the TC value, both of which have been shown to vary by no more than 2% between fasting and nonfasting states (22).

Under the most recent guidelines, measurement of serum cholesterol

values (LDL or non-HDL) is most valuable for screening adults aged 40 to 75 without known diabetes or existing CVD (IHD, prior myocardial infarction, peripheral vascular disease, stable or unstable angina, abdominal aortic aneurysm, or ischemic stroke). Since 2010, individuals with diabetes are considered to have a risk of a subsequent cardiovascular event similar to the risk among those with preexisting CVD. For adults with existing CVD, significant evidence has demonstrated the benefit of cholesterol-lowering therapy with a statin medication regardless of serum cholesterol levels (13). Ongoing measurement of TC and HDL is useful to monitor efficacy of and adherence to cholesterol-lowering therapy among high-risk individuals. Among less high-risk individuals, TC and HDL measurement is needed to gauge the potential benefit of lowering cholesterol for persons in need of primary CVD prevention (those without diabetes or existing CVD).

Online calculators are available that utilize TC and HDL values and leading risk factors for CVD (gender, age, smoking status, most recent systolic blood pressure, presence of blood pressure treatment, and diabetes status) to approximate an individual's ten-year risk of myocardial infarction, stroke, or CVD-related death (23). Under current guidelines, individuals aged 40 to 75 with greater than a 7.5% risk warrant interventions to lower cholesterol, although controversy exists surrounding risk calculators and thresholds to initiate treatment for individuals whose risk falls between 5% and 10% (24). Individuals with random non-HDL cholesterol values greater than 220 mg/dl have such high lifetime risk of CVD that specific intervention may be warranted before the age of 40 (13). This risk can be calculated via nonfasting TC and HDL values and does not require fasting LDL measurement to screen, diagnose, or guide treatment.

Point-of-care testing is also available for cholesterol screening but has yet to be adopted into formal screening guidelines. When possible, venipuncture is the ideal method for identifying dyslipidemia, but obtaining

lipid readings from finger-stick samples may be appealing in safety-net settings for a variety of reasons, including cost, convenience, and quick turnaround (25).

Table 1 summarizes nonfasting alternatives for the current ADA-APA screening guidelines for adults prescribed second-generation antipsychotics.

Conclusions

Consensus guidelines for the screening, diagnosis, and management of major leading risk factors for CVD have changed dramatically in the past several years. As a result, practitioners are now able to rely on validated nonfasting lipid profiles via non-HDL values and blood glucose markers, such as HBA1c, to screen and diagnose dyslipidemia and diabetes among adults with severe mental illness treated with second-generation antipsychotics in safety-net settings. The use of nonfasting values to detect and manage common risk factors should lead to higher rates of screening and recognition of individuals at risk for CVD, a crucial first-step to shortening the mortality gap for adults with severe mental illness.

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