Depressive Symptoms, Insulin Resistance, and Risk of Diabetes in Women at Midlife

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OBJECTIVE — To examine depression and 3-year change in insulin resistance and risk of diabetes and whether associations vary by race.

RESEARCH DESIGN AND METHODS — We analyzed data from 2,662 Caucasian, African-American, Hispanic, Japanese-American, and Chinese-American women without a history of diabetes from the Study of Women's Health Across the Nation. We estimated regression coefficients and odds ratios to determine whether depression (Center for Epidemiological Studies Depression Scale score ≥16) predicted increases in homeostasis model assessment of insulin resistance (HOMA-IR) and greater risk of incident diabetes, respectively, over 3 years.

RESULTS — Mean baseline HOMA-IR was 1.31 (SD 0.86) and increased 0.05 units per year for all women ($P < 0.0001$). A total of 97 incident cases of diabetes occurred. Depression was associated with absolute levels of HOMA-IR ($P < 0.04$) but was unrelated to changes in HOMA-IR; associations did not vary by race. The association between depression and HOMA-IR was eliminated after adjustment for central adiposity ($P = 0.85$). Depression predicted a 1.66-fold greater risk of diabetes ($P < 0.03$), which became nonsignificant after adjustment for central adiposity ($P = 0.12$). We also observed a depression-by-race interaction ($P < 0.05$) in analyses limited to Caucasians and African Americans, the only groups with enough diabetes cases to reliably test this interaction. Race-stratified models showed that depression predicted 2.56-fold greater risk of diabetes in African Americans only, after risk factor adjustment ($P = 0.008$).

CONCLUSIONS — Depression is associated with higher HOMA-IR values and incident diabetes in middle-aged women. These associations are mediated largely through central adiposity. However, African-American women with depression experience increased risk of diabetes independent of central adiposity and other risk factors.

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Several lines of evidence suggest that depression influences glucose metabolism and risk of diabetes (1). Prevalence of clinically significant depression is twice as high in individuals with diabetes than in those without diabetes (2). Depression is associated with poor glycemic control and hyperglycemia in patients with type 1 or type 2 diabetes (3), impaired insulin sensitivity, and hyperinsulinemia (4). Three recent studies (5–7) reported that depressive symptoms were associated with increased incidence of diabetes, although each study used a nonstandard measure of depressive symptoms; in one study, the association was limited to respondents with less than a high school education (5). Two studies found that diabetes was twice as likely to develop in depressed individuals compared with nondepressed individuals over 13 and 8 years of follow-up, respectively, but both studies were limited by low incidence rates of diabetes in their samples (8,9). Depression may contribute to metabolic abnormalities preceding the development of diabetes (10), although evidence is conflicting. Depressed patients with normal glucose tolerance had lower insulin sensitivity and higher insulin resistance relative to nondepressed control subjects (11). In another study, prevalence of depression was lowest at the highest levels of insulin resistance among nondiabetic women (12).

Few studies examining depression and risk of diabetes have included African Americans or other minorities (5,13), although prevalence and incidence of diabetes are highest in these populations (14).

We examined the relationship between depressive symptoms and insulin resistance and risk of diabetes in a multiethnic community sample of middle-aged women participating in a longitudinal study of women's health and aging. We hypothesized that more depressive symptoms at baseline would be associated with greater increases in insulin resistance and increased risk of incident diabetes over 3 years of follow-up. We further hypothesized that the effects would most likely be observed in African Americans and Hispanics, in whom risk of diabetes is known to be higher than in Caucasians (14).

RESEARCH DESIGN AND METHODS

— Participants were from the Study of Women's Health Across the Nation (SWAN), an ongoing longitudinal study of the menopausal transition. De-

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Abbreviations: CES-D, Center for Epidemiological Studies Depression Scale; HOMA-IR, homeostasis model assessment of insulin resistance; SWAN, Study of Women's Health Across the Nation.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

tails of the study design, recruitment, and protocol have been published previously (15). SWAN is conducted at seven sites: Boston, Massachusetts; Chicago, Illinois; Oakland, California; Detroit, Michigan; Los Angeles, California; Newark, New Jersey; and Pittsburgh, Pennsylvania. Using community-based sampling techniques (random selection from established population lists, random-digit dialing), each site recruited Caucasians and women from one other race/ethnicity for a total of 3,302 women (46.9% Caucasian, 28.3% African American, 8.7% Hispanic [Puerto Ricans, Dominicans, Central Americans, Cubans, South Americans], 8.5% Japanese American, and 7.6% Chinese American). At two sites (Newark and Los Angeles), the primary sampling frame was supplemented using a "snowball" technique in which eligible women were asked for names and contact information of women they knew who also might qualify; these women were screened and, in turn, asked for names of other potentially eligible women. This process was repeated until recruitment targets were met. At baseline, all women were aged 42–52 years, with at least one ovary and an intact uterus, not currently pregnant or breast-feeding, reported menstrual bleeding, and did not use reproductive hormones affecting ovarian or pituitary function in the past 3 months. The SWAN protocol was approved by the Institutional Review Board at each site; all women provided written informed consent.

Participants with baseline fasting glucose levels of ≥126 mg/dl and/or a history of diabetes ($n = 245$) and those without data on depressive symptoms at baseline ($n = 7$) were not eligible and thus were excluded from all analyses. For the analyses of incident diabetes, 240 women were excluded because of unknown diabetes status at any follow-up examination and 148 were excluded because of missing covariate data, leaving a sample size of 2,662 (87.3% of eligible) for these analyses. For the analyses of insulin resistance, 206 women were excluded because of missing baseline data on insulin resistance (data were missing in 176 women, and 30 women had extreme baseline glucose or insulin values, thus insulin resistance could not be calculated). In 402 women, follow-up insulin resistance data were missing and, in 126 women, covariate data were missing, leaving a sample size of 2,316 (75.9% of eligible) for the these analyses. Women excluded from analyses because of missing data on covariates reported more depressive symptoms at baseline and were more likely to be Hispanic or African American, have less education, and have greater central adiposity (all $P < 0.001$).

At study entry (1996–1997) and annually thereafter, all participants underwent a standard assessment, including interviewer- and self-administered questionnaires assessing social, economic, behavioral, psychological, and lifestyle characteristics and analysis of fasting blood and urine specimens. Data for the present analyses come from the standard protocol completed at the baseline visit and at the first, second, and/or third annual follow-up. All questionnaires and interview forms were available in English, Cantonese, Japanese, and Spanish; women could participate in the language of their choosing, and bilingual staff members were available at all examinations.

Measurement of depressive symptoms

The 20-item Center for Epidemiological Studies Depression Scale (CES-D) (16) was used to measure depressive symptomatology at each SWAN visit. The CES-D is well validated, has been used extensively in prior research (17,18), and has good test-retest reliability in ethnically diverse populations (19–21). A score of ≥16 on the CES-D is considered indicative of clinically significant symptomatology (18). We conducted separate analyses with CES-D scores modeled continuously and categorically (CES-D score ≥16 vs. <16). Results were similar in these analyses; therefore, we report only the categorical models. For ease of presentation, we refer to the CES-D categories as "depressed" and "nondepressed."

Assessment of insulin resistance

Insulin resistance was calculated by the revised homeostasis model assessment of insulin resistance (HOMA-IR) model (22). HOMA-IR is considered a surrogate index of insulin resistance (23), suitable for use in epidemiologic studies in which more invasive measures of insulin resistance are prohibitive. The revised HOMA is derived from a computer algorithm, accounts for variations in hepatic and peripheral glucose resistance, and is calibrated to insulin assays that are currently available. Greater HOMA-IR values indicate reduced insulin sensitivity or insulin resistance. HOMA-IR values were log-transformed to normalize the distribution, and these values were used in all analyses of HOMA-IR. Glucose and insulin were measured from blood specimens obtained after a 12-h fast and drawn during days 2–5 of the follicular phase of the menstrual cycle at the baseline examination and the first and third annual follow-up (glucose and insulin assays were not conducted at the second annual follow-up). All blood specimens were kept at 40°F until separated and then frozen at −20°C and shipped on dry ice to the central laboratory (Medical Research Laboratories, Lexington, KY) for analysis. Plasma glucose was measured using a hexokinase-coupled reaction (Boehringer Mannheim, Indianapolis, IN), and plasma insulin was measured using a solid-phase radioimmunoassay procedure (DPC Coat-A-Count, Los Angeles, CA).

Ascertainment of incident diabetes

Presence of diabetes was ascertained in two ways. First, information on diabetes was obtained by self-report at each annual examination in response to the question: "Since your last study visit, has a doctor, nurse practitioner, or other health care provider told you that you had or treated you for diabetes?" Second, diabetes status was determined by fasting glucose level at the first or third annual follow-up. Women who reported that they had been or were being treated for diabetes at any annual follow-up visit or who had a fasting glucose level of ≥126 mg/dl at the first and/or third follow-up were designated as having diabetes.

Measurement of covariates

Age was assessed via self-report. Race was self-identified as African American, Hispanic, Japanese American, Chinese American, or Caucasian (referent). Education was reported as highest grade completed: high school degree or less, some college, college degree, or postgraduate education (referent). Medication use for depression or nervous conditions (yes/no) was assessed via self-report in response to a single question at each examination. Physical activity was measured at baseline via an adapted questionnaire (24) assessing frequency of sports activities, nonsports leisure time, and household/childcare ac-

Table 1—*Participant characteristics: SWAN*

	All	CES-D <16	CES-D ≥16	*P**	Caucasians	African Americans	Hispanics	Japanese Americans	Chinese Americans	*P*†
n‡	2,662	2,056	606	—	1,318	696	182	256	210	—
CES-D score	10.2 ± 9.4	6.0 ± 4.3	24.5 ± 7.8	<0.0001	9.9 ± 9.0	11.0 ± 10.1	15.5 ± 11.1	8.3 ± 8.0	7.7 ± 7.5	<0.0001
Percent CES-D ≥16	22.8	—	—	—	21.6	26.4	40.7	14.8	12.4	<0.0001
Age (years)	46.4 ± 2.7	46.5 ± 2.7	45.9 ± 2.6	<0.0001	46.3 ± 2.7	46.3 ± 2.7	46.3 ± 2.8	46.8 ± 2.7	46.5 ± 2.6	0.095
Height (cm)	162.4 ± 6.7	162.5 ± 6.7	162.3 ± 6.9	0.52	164.2 ± 6.2	163.9 ± 6.3	156.6 ± 6.1	156.9 ± 4.9	158.1 ± 5.6	<0.0001
Weight (kg)	72.9 ± 19.0	72.0 ± 18.4	75.9 ± 20.6	<0.0001	73.8 ± 18.0	82.5 ± 19.5	69.7 ± 13.9	56.0 ± 8.9	58.1 ± 10.3	<0.0001
BMI (kg/m^2)	27.5 ± 6.6	27.1 ± 6.4	28.7 ± 7.3	<0.0001	27.3 ± 6.4	30.7 ± 7.0	28.4 ± 5.6	22.8 ± 3.7	23.2 ± 3.8	<0.0001
Waist (cm)	84.7 ± 14.8	83.8 ± 14.3	87.6 ± 16.1	<0.0001	84.6 ± 14.8	91.2 ± 15.0	85.5 ± 11.8	73.4 ± 8.7	76.8 ± 9.4	<0.0001
Education (%)				<0.0001						<0.0001
High school or less	22.3	19.5	31.9		14.3	25.3	70.3	18.0	26.7	
Some college	32.2	31.5	34.5		31.2	40.1	19.2	34.0	21.0	
College degree	21.3	22.2	18.3		22.5	16.4	7.7	30.8	30.4	
Postgraduate	24.2	26.8	15.3		32.1	18.2	2.8	17.2	21.9	
Physical activity§	7.7 ± 1.8	7.8 ± 1.7	7.4 ± 1.8	<0.0001	8.1 ± 1.8	7.3 ± 1.7	6.8 ± 1.5	7.9 ± 1.6	7.2 ± 1.7	<0.0001
Use of medication for depression or nervous conditions (%)	9.2	6.6	18.1	<0.0001	12.5	6.6	8.8	4.7	3.3	<0.0001
Baseline HOMA-IR	1.31 ± 0.86	1.27 ± 0.81	1.46 ± 1.00	<0.0001	1.24 ± 0.82	1.57 ± 0.98	1.64 ± 1.05	0.96 ± 0.43	1.06 ± 0.56	<0.0001
Percent change in HOMA-IR	24.1 ± 61.6	23.4 ± 56.7	26.3 ± 76.5	0.43	22.5 ± 58.3	24.2 ± 64.7	34.9 ± 100.0	18.8 ± 47.6	32.6 ± 51.7	0.04
Incident diabetes	3.6	3.0	5.8	0.001	2.7	5.9	5.5	1.6	2.9	0.001

Data are unadjusted means ± SD or percent. HOMA-IR values were log transformed for analyses, although the nontransformed values are shown. *P values in this column are from comparisons between depressed and nondepressed women. †P values in this column are from comparisons across race/ethnicity groups and represent the overall effect of race. ‡Because of missing data on height, weight, BMI, and baseline HOMA-IR, the number of participants in analyses of these variables varies somewhat. §Higher physical activity scores represent more activity (scores range from 3 to 14).

tivities. An activity score was created by summing across domains; a higher score indicated greater activity. Waist circumference was measured over nonrestrictive undergarments at the narrowest part of the torso at all examinations. All covariates were obtained at the baseline SWAN examination. A dummy-coded variable for study site also was included as a covariate.

Data analyses

We used descriptive statistics, linear regression, and χ^2 analyses to characterize the study sample on baseline age, height, weight, BMI, waist circumference, education, medication usage, physical activity, depressive symptoms, HOMA-IR, and incident diabetes (Table 1). Analyses were conducted on the sample as a whole, followed by separate comparisons by baseline depression status and race.

We used mixed-effects regression models (25) to model change in insulin resistance across the annual examinations as a function of baseline depressive symptoms. The first model included covariates for time, age, race, site, education, and medication use and tested the extent to which depression was associated with absolute levels of insulin resistance, averaged across baseline and the annual follow-up examinations. The second model included a depression-by-time interaction term to test whether change in HOMA-IR during the follow-up period was greater among depressed compared with nondepressed women. Subsequently, we examined whether associations varied by race by adding appropriate two- and three-way interaction terms to the model. A third model included terms for physical activity and waist circumference, both of which are related to depression and diabetes risk (26–28) and could mediate any observed associations. A set of time-dependent models was then calculated, in which the values for depressive symptoms and covariates were allowed to vary according to available data on these variables from the follow-up examinations.

Logistic regression models were used to investigate whether baseline depressive symptoms predicted incident diabetes. The first model tested the effects of baseline depression, adjusted for age, race, site, education, and medication use. Outcome was diabetes status assessed at each annual follow-up, with a summary variable that calculated the total number of

Table 2—*Participant characteristics: SWAN*

	Model statistics			Baseline HOMA-IR	Follow-up 01 HOMA-IR	Follow-up 03 HOMA-IR
	Estimate ± SE	*t*	*P*			
Model 1						
CES-D <16	referent			1.291 ± 0.02	1.352 ± 0.02	1.413 ± 0.02
CES-D ≥16	0.0453 ± 0.022	2.07	0.038	1.372 ± 0.04	1.432 ± 0.04	1.493 ± 0.04
Time	0.0494 ± 0.003	15.5	<0.0001			
Model 2						
CES-D <16	referent			1.353 ± 0.02	1.414 ± 0.02	1.475 ± 0.02
CES-D ≥16	0.0032 ± 0.017	0.19	0.85	1.365 ± 0.03	1.426 ± 0.03	1.487 ± 0.03
Time	0.0495 ± 0.003	15.6	<0.0001			
Physical activity	−0.015 ± 0.004	−3.72	0.0002			
Waist circumference	0.0199 ± 0.0005	39.2	<0.0001			

Data are adjusted means ± SE for HOMA-IR from the baseline examination and two follow-up visits, unless otherwise indicated. Nontransformed HOMA-IR values are shown. Because of skewness, log-transformed HOMA-IR values were used in the random effects regression analyses (n = 2,316). Statistics from these models are shown. Models 1 and 2 are adjusted for age, site, race, education, and use of medications for depression or nervous conditions; model 2 is also adjusted for physical activity and waist circumference.

diabetes cases occurring during follow-up (each case was counted once). A second model included total physical activity and waist circumference as covariates. These analyses then were repeated as time-dependent models. To examine whether the association between depressive symptoms and diabetes risk varied by race, we reestimated the risk factor–adjusted model, including a depression-by-race interaction term. Too few cases of incident diabetes occurred among Japanese Americans, Chinese Americans, and Hispanics to reliably estimate this interaction for these groups; therefore, only African Americans and Caucasians were included in this model.

All analyses were performed with PC-SAS, version 8.0 (SAS Institute, Cary, NC) using univariate, frequency, GLM, mixed, and/or logistic procedures.

RESULTS — Table 1 shows unadjusted means or prevalence of baseline characteristics, HOMA-IR, and percent change in HOMA-IR and incident diabetes for all participants (n = 2,662) as well as by depression status and race. Depressed and nondepressed women differed significantly on all characteristics except height and percent change in HOMA-IR over 3 years. Similarly, significant differences between races were noted for all characteristics except age.

Depression and insulin resistance

Depressed women had significantly greater absolute levels of HOMA-IR (P = 0.038) than nondepressed women, with adjustment for age, race, site, education, and medication use (Table 2, model 1). HOMA-IR increased over time for all women ($P < 0.0001$). All covariates were significant ($P < 0.05$) in this model.

Contrary to our primary hypothesis, we did not observe a significant depression-by-time interaction (P = 0.39), indicating that rate of increase in HOMA-IR per year did not differ between depressed and nondepressed women. The main effect of depression remained significant (P = 0.03). We also did not observe a depression-by-race interaction (P = 0.20) or a depression-by-time-by-race interaction ($P < 0.12$). Therefore, the risk factor–adjusted model did not include the interaction terms. With adjustment for physical activity (P = 0.0002) and waist circumference ($P < 0.0001$), the effect of depression on absolute levels of HOMA-IR was effectively eliminated (Table 2, model 2). Race and site were significant covariates ($P < 0.0001$), but age, education, and medication use were not ($P > 0.10$). Analyses examining the separate effects of physical activity and waist circumference (not shown) revealed that the association between depression and HOMA-IR became weaker and nonsignificant (P = 0.13) with physical activity in the model but was greatly diminished (P = 0.71) with waist circumference in the model.

Time-dependent models showed the same pattern of associations. Depressed women had significantly higher absolute levels of HOMA-IR (estimate [±SE] = 0.032 ± 0.01, $P < 0.02$) before adjusting for physical activity and waist circumference, but this association was not significant (0.012 ± 0.01, P = 0.35) after adjustment for risk factors.

Depression and risk of diabetes

Diabetes was 66% more likely to develop during follow-up in depressed women than nondepressed women (odds ratio [OR] 1.66, 95% CI 1.05–2.61; $P < 0.03$), adjusting for age, race, site, education, and medication use. Risk of diabetes was 10.6% greater with each increasing year of age ($P < 0.008$). No other covariates were significant in this model. After further adjustment for physical activity and waist circumference, the association between depression and risk of diabetes became nonsignificant (1.46, 0.90–2.36; P = 0.12). Waist circumference was a highly significant covariate (1.07, 1.05–1.08; $P < 0.0001$) but physical activity was not (P = 0.70). Age remained a significant covariate ($P < 0.02$).

Time-dependent models showed similar results. Depression was associated with diabetes risk (χ^2 = 3.63, P = 0.057) in the model that included age, race, education, site, and medication use. Adjusting for physical activity and waist circumference diminished the association (χ^2 = 1.77, P = 0.18).

In the risk factor–adjusted analysis limited to African Americans and Caucasians, we observed a significant depression-by-race interaction (estimate [±SE] = 1.08 ± 0.54, χ^2 = 3.9, $P < 0.05$). To demonstrate this interaction, we conducted race-stratified models. Depression

predicted a >2.5-fold risk of diabetes in African Americans (OR 2.56, 95% CI 1.27–5.15; $P = 0.008$) in a fully adjusted model. Age and waist circumference were the only significant covariates in this model. Depression was unrelated to diabetes risk in Caucasians (0.65, 0.27–1.59; $P = 0.34$).

Secondary analyses

We examined a number of additional covariates in secondary analyses of HOMA-IR and diabetes. Including self-reported income in models that adjusted for age, race, site, education, and medication use did not alter results for either outcome. Because education and income were highly correlated ($r = 0.5$, $P < 0.0001$) and a number of women refused to provide information on income, we included only education as a socioeconomic indicator in our models. Further adjustment for marital status, social support, total caloric intake, percent calories from fat, and chronic cardiovascular conditions also did not change the findings for HOMA-IR or risk of diabetes. Only presence of chronic cardiovascular conditions was a significant covariate in these models, but this did not alter the effect of waist circumference on the observed associations.

CONCLUSIONS — We found that depressive symptoms were significantly related to excess risk of diabetes and overall levels of insulin resistance, as indexed by HOMA-IR, in a multi-ethnic sample of women in midlife. However, we did not find evidence for our hypothesis that greater depressive symptoms would predict increases in HOMA-IR over time. In the full sample, these associations were largely mediated through central adiposity. These findings are consistent with previous studies that have shown associations between depression and diabetes (5–7) and obesity (26) and with prior research showing that central adiposity exacerbates insulin resistance (28,29).

Our failure to find a significant prospective association between depression and changes in insulin resistance may be due to the variability in HOMA-IR change that we observed among all women (Table 1). Depressed women showed a larger percent change over time than nondepressed women but also greater variability; therefore, this difference was not significant. Logarithmically transformed values were used to normalize the distribution of HOMA-IR for analyses but variability remained high. Nonetheless, HOMA-IR values are valid. Correlations among HOMA-IR values across study visits were 0.60–0.65 ($P < 0.0001$), and baseline HOMA-IR values were strong predictors of subsequent diabetes ($P = 0.0001$) in adjusted analyses (data not shown).

There are several mechanisms by which depression may contribute to central adiposity and glucose metabolism. Major depressive disorder alters the hypothalamic-pituitary-adrenal axis and can lead to excess cortisol secretion (30), which may contribute to visceral fat deposition and increase insulin resistance (28). It is not clear whether depressive symptoms, without a diagnosis of depressive disorder, have similar glucocorticoid effects, although such effects are plausible. However, we did not have cortisol data with which to test this hypothesis. Depression also may influence central adiposity and glucose metabolism via behavioral or psychosocial mechanisms. Individuals who are depressed are less compliant with medical regimens (31) and generally report poorer lifestyle habits (32). A recent cross-sectional report from SWAN (33) found that health-related and psychosocial factors (social support, stress, life events) were important correlates of CES-D scores and mediated the observed associations between socioeconomic indicators and depression. In our risk factor–adjusted models, education was not a significant covariate, and physical activity was significant only in the HOMA-IR models. Income, marital status, dietary factors, social support, and chronic cardiovascular conditions also did not influence our results (data not shown). Nevertheless, further research is needed to fully understand the interrelationships among depressive symptoms, central adiposity, glucose metabolism, risk of diabetes, and these various mechanisms.

The effects of depression on absolute levels of HOMA-IR did not vary by race. In contrast, in our analyses of risk of diabetes limited to African Americans and Caucasians, depression predicted increased risk of diabetes among African-American women only, independent of known diabetes risk factors, including central adiposity. African Americans had the highest incidence of diabetes in 3 years of follow-up; the incidence rate was more than twice that in Caucasian, Chinese-American, or Japanese-American women. African Americans also had the greatest central adiposity and greatest overall obesity (Table 1). Our data suggest that mechanisms other than central adiposity may contribute to the excess risk of diabetes experienced by African-American women with significant depressive symptomatology. Depression may alter immune function and influence inflammatory processes (34), functions that may be altered in diabetes (35). Behavioral or psychosocial mechanisms also could be important, although our secondary analyses indicated that marital status, social support, and dietary factors were not significant covariates.

The findings from this study have clinical relevance. Patients and their providers should recognize that depressive symptoms can increase risk of diabetes and are related to higher levels of insulin resistance, which is a risk factor for diabetes. Patients should be encouraged to seek treatment for clinically significant depressive symptoms and to maintain or adopt active lifestyles, healthy diets, and weight loss if needed to reduce their risk of diabetes.

Limitations

Depressive symptoms were self-reported, which is common among large epidemiologic studies if clinical interviews are prohibitive. We used a well-validated and commonly used measure of depressive symptoms with demonstrated reliability in ethnically diverse populations. Examining clinically assessed depressive symptoms and risk of diabetes may allow us to further characterize this association and putative underlying mechanisms. More detailed information on use of antidepressants also would be useful, although self-reported use of medication for depression or nervous conditions was not an important covariate in our analyses. We were not fully able to assess whether the association between depression and incident diabetes varied by race because of the relatively small numbers of Hispanic, Japanese-American, and Chinese-American women in SWAN. Although accepted community-based sampling and recruitment procedures were used in SWAN, potential for selection bias exists at the sites that used the snowball technique to supplement the primary sampling frame.

Some loss to follow-up occurred; however, 75.9 and 87.3% of participants, were included in our analyses of HOMA-IR and risk of diabetes, respectively. Loss to follow-up was greatest among Hispanic women, most of whom were of low socioeconomic status and were non–Mexican-American Latinas. It may be difficult to generalize findings from this group to the larger population of Hispanic women in the U.S., 60% of whom are Mexican American. Finally, our 3-year follow-up was relatively short. With continued follow-up, we can further study the influence of depression on glucose metabolism and diabetes risk.

Summary

Symptoms of depression were related to greater absolute levels of insulin resistance and increased risk of diabetes in women at midlife, and these associations were largely mediated by central adiposity. However, African-American women with depression continued to be at increased risk for diabetes, independent of known risk factors for the disease. Depression and diabetes are important, expanding public health problems (36,37) that contribute greatly to disability and impaired quality of life. Further research is needed to develop appropriate treatments and prevention efforts to reduce the burden of diabetes, particularly in high-risk populations.

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