DIABETIC
Microvascular Complications
NEWS
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Life Expectancy Declines in 21st Century

In a special report from *The New England Journal of Medicine*, investigators said the steady increase of life expectancy over the past 1,000 years may decline this century.

"We anticipate that as a result of the substantial rise in the prevalence of obesity and its life-shortening complications such as diabetes, life expectancy at birth and at older ages could level off or even decline within the first half of this century," lead author S. Jay Olshansky, PhD, and colleagues wrote. "This is in contrast to both the recent decision by the SSA [Social Security Administration] to raise its forecast of life expectancy and what we consider to be the simple but unrealistic extrapolation of past trends in life expectancy into the future."

Dr. Olshansky and colleagues suggest that because the technology to extend one's life does not yet exist, the SSA should not increase life expectancy rates, nor should it use history to determine future life expectancy rates. "An informed approach to forecasting life expectancy should rely on trends in health and mortality that may be observed in the current population," they wrote.

This observation included an increased prevalence of obesity, as investigators wrote that obesity among US adults increased >50% per decade over two decades (1980s and 1990s). They also noted that overweight or obesity is present in two-thirds of all adults in this country, and children and minorities are the two largest groups being affected by the diseases. Also an issue, obese people are at an increased risk for fatal and nonfatal conditions related to the disease. These include diabetes and cardiovascular disease.

If obesity rates continue to rise, investigators wrote, it will have a negative effect on life expectancy as early as the first half of the 21st century. Using a calculation of the reduced rates of death from a population of people with "optimal" body mass indexes (BMIs), investigators estimated that life expectancy in the United States would be: 0.33 to 0.93 years higher for white males; 0.30 to 0.81 for white females; 0.30 to 1.08 for black males; and 0.21 to 0.73 for black females (Figure 1). If obesity is still prevalent across the 21st century, life expectancy may fall by one-third to three-fourths of a year.

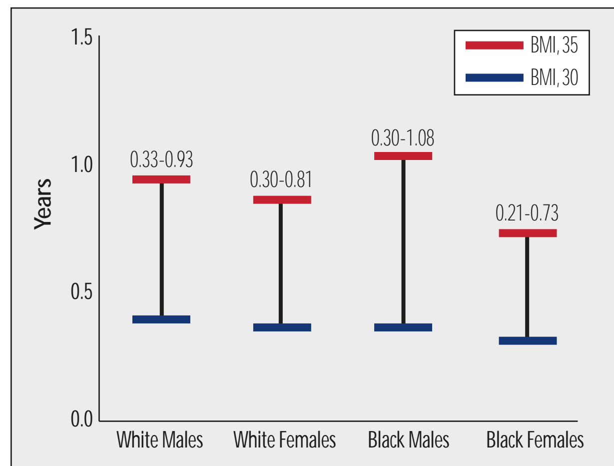

Figure 1. The life-shortening effect of obesity according to race and sex. The potential gain in life expectancy at birth for the US populaton in 2000 is illustrated, if obesity were eliminated. The range of estimates is shown between the bars, based on the assumption that all those who are obese have a BMI of 30 to 35.

Life expectancy forecasts are used by the government for programs such as Social Security and Medicare. Obese individuals have a 5- to 20-year shorter life expectancy than average Americans. "Its negative affect on the future life expectancy of the population is also critically important to public policy," investigators wrote.

Stay Active to Live Longer

Two studies in *Diabetes Care* add to a growing body of evidence that keeping physically active is important to reduce the risk of heart disease – even if high blood pressure, obesity or high cholesterol are a concern.

The first study, by researchers at the National Public Health Institute in Finland, found that people with type 2 diabetes who engaged in moderate or high levels of physical activity were far less likely to die from heart disease than those who engaged in low levels of physical activity. The benefits of physical activity were consistent regardless of BMI, blood pressure or cholesterol levels or whether or not the person smoked. Benefits were the same in both men and women.

In the study, those who were moderately active

reduced their risk of dying from heart disease by 39%, while those who were highly active reduced it by 48%. Moderate physical activities included any one of three types: 1) physical activity during the work day such as standing and walking, lifting or other heavy manual labor; 2) physical activity obtained as part of the daily commute such as walking or cycling for ≥30 minutes; 3) physical activity obtained through leisure activity such as walking, cycling or light gardening for >4 hours/week, not including time spent commuting to or from work; or engaging in vigorous physical activity such running, jogging, skiing or swimming for >3 hours/week during leisure time. High physical activity included two or more of the three types of physical activities during work, commuting and leisure time.

A separate study analyzed results from the US National Institute of Health's Diabetes Prevention Program, and found that intensive lifestyle changes including moderate levels of physical exercise (150 min/week) also lowered cardiovascular disease risk factors more than a diabetes medication.

The study found that high blood pressure, triglyceride and cholesterol levels all decreased significantly more through intensive lifestyle change including moderate exercise than through taking the diabetes drug metformin. Patients in the study were at high risk for diabetes and heart disease and also saw a greater increase in HDL as a result of increased physical activity.

A third study in *Diabetes Care*, conducted by researchers at the Centers for Disease Control and Prevention, found high concentrations of C-reactive protein in a large percentage of adolescents who had been diagnosed with the metabolic syndrome. Those with the metabolic syndrome tend to be physically inactive.

"All of these studies point, once more, to the importance of maintaining a physically active lifestyle and of developing a commitment to physical activity as young as possible," said Alan Cherrington, PhD, president of the American Diabetes Association. "What we have been seeing in recent decades, unfortunately, is a trend in the opposite direction. Children are becoming more sedentary instead of more active. Parents need to make a commitment to lifestyle changes that includes the entire family – or the entire family may suffer."

Improving Lipid Profiles Also Reduced Albumin Excretion

When taking fenofibrate, patients with type 2 diabetes improved their lipid profiles and reduced their progression of normal albumin excretion (NAE) to microalbuminuria.

Using data from the Diabetes Atherosclerosis Intervention Study (DAIS), investigators reporting in the *American Journal of Kidney Disease* measured overnight microalbuminuria samples from 314 patients at baseline and once a year for 3 years. Over 38 months, the patients were either treated with micronized fenofibrate or placebo. Those taking the fenofibrate reduced their progression of coronary artery disease while their abnormal lipoprotein levels improved.

Investigators found that with the exception of 3 patients, all albuminuria levels were within NAE (<20 μg/min) or microalbuminuria (albumin, 20 to 200 μg/min). They used either the chi-square or Fisher's exact test to compare patients who received the treatment to those who received placebo.

A total of 20 patients who received placebo progressed from NEA to microalbuminuria. There were 113 patients treated with placebo. When fenofibrate was used, three of 101 patients progressed to microalbuminuria ($P<.001$). Investigators noted that patients on the treatment had a significant reduction in the decline of albumin excretion compared to patients who received placebo (8% vs 18%, $P<.05$). This was not related to changes in lipid profiles or creatinine levels, weight, blood pressure or patient age, investigators wrote.

Retinal Screening May be Conducted Every 2 Years

Despite current recommendations suggesting that adolescents should have annual retinopathy screenings, it may be permissible to have a screening every 2 years.

Diabetic patients who have especially poor metabolic control, have had diabetes for >10 years or who already have retinopathy, however, should be screened more frequent, investigators reported in *Diabetes Care*. They enrolled and screened over 1,000 children and adolescents for retinopathy. Follow-up was conducted on 668 of the patients. All retinopathy screenings were done using the seven-field stereoscopic fundus photography through dilated pupils.

Retinopathy risk was compared to baseline in relation to yearly intervals, age group, higher risk groups

(those who had diabetes >10 years and those who had a HbA1c >10% at any of the retinopathy screenings) and stratification that constituted durations of ≤10 years and >10 years.

Of the 618 patients that were in the older group, the median HbA1c was 8.7% (range 8.0 to 9.5%). This group did not see an increase in retinopathy after 1 year. The younger group, which consisted of 50 patients with a median HbA1c 8.5% (range 8.0 to 9.2%), and those who were at high-risk for retinopathy also did not have an increased risk for retinopathy after 1 year.

Investigators noted that the increased prevalence of retinopathy was significant in older diabetic patients after 2 years ($P = .003$) versus 6 years in younger patients ($P = .01$). If patients had a recorded HbA1c >10%, prevalence also increased after 2 years. With a lower HbA1c, patients had an extra year until retinopathy increased.

In the follow-up evaluation, investigators wrote that significant increases in retinopathy were noted at 3 years in older diabetic patients and 6 years in younger patients ($P = .028$ and .014, respectively).

Persistent CSME Found in Patients with High HbA1c

In an attempt to examine the association between persistent clinically significant macular edema (CSME) and HbA1c, investigators determined that type 2 diabetic patients with this complication have a higher HbA1c level.

This elevation was found when patients had CSME, not after CSME was resolved, investigators wrote. They reported their findings in the *American Journal of Ophthalmology.*

A total of 124 patients – 92 with persistent CSME and 32 with resolved CSME – were treated for CSME between January 2002 and January 2004, and their records were used to calculate HbA1c levels at between the two groups. Investigators also calculated HbA1c levels of patients with bilateral and unilateral diseases. All measurements were taken at Johns Hopkins Hospitals and were from 5.3% to 15.6% for all patients.

When just patients with persistent and resolved CSME were included, the highest HbA1c level was 9.7%, and the median level was 6.6% ($P = .0005$). The median HbA1c was 8.5% in patients with persistent unilateral CSME, and 8.9% in patients with persistent bilateral CSME.

LJM a Clinical Marker for Microvascular Disease

Although it seems that limited joint mobility (LJM) in diabetic patients has declined in the past 20 years, investigators reporting in *Diabetes Care* suggest that as a strong association with diabetes duration, it is a clinical marker for microvascular disease.

LJM may also be used as a way to identify patients who are at an increased risk for the disease, investigators wrote. A total of 204 patients with type 1 diabetes were surveyed to determine if the improved standards of glycemic control affected the prevalence of LJM. Patients were aged 27 ±1 years and had an HbA1c 8.3 ±0.1%. Patients took 63 ±2 units/day of insulin and had diabetes for 14.5 ±0.8 years.

Investigators found that LJM is not as common, as it has fallen from 43% in the 1980s to 23% in 2002 ($P < .0001$). This may be due to improvements in the standards of care for diabetes patients and the standards for glycemic control, they wrote.

The longer a patient had diabetes, the higher the prevalence of LJM (<10 years, 13%; 10-20 years, 19%; 20-29 years, 30%; >30 years, 65%; $P = .001$).

"The presence of LJM remains a common and important clinical marker for subsequent microvascular disease and can be a useful clinical tool for identification of patients at increased risk," they wrote.

Combining Pulse Oximetry, ABI Increased Diagnosis

To get an accurate diagnosis for lower extremity arterial disease (LEAD), the accuracy of pulse oximetry and ankle-brachial index (ABI) are similar.

Using both tests to determine the presence of LEAD increased the sensitivity of the diagnosis, concluded investigators reporting in the *Archives of Internal Medicine.*

Type 2 diabetic patients who had no signs of LEAD were enrolled in the outpatient study. Of the 57 patients, all aged ≥40 years, 31% were found to have LEAD. Investigators measured for LEAD using ABI, pulse oximetry and Doppler waveform analysis of the lower extremities. Pulse oximetry measured SaO_2 of the index fingers and big toes while elevated 12 inches and in supine position.

Investigators considered any ABI reading <0.9 and any finger or toe pulse oximetry reading >2% to be abnormal. When the methods of diagnosis were combined, two negative LEAD readings implied the patient was clear of the disease. If one of the readings came out posi-

tive, LEAD was present.

Results indicated that the sensitivity from pulse oximetry readings was higher than the sensitivity of ABI readings (77%; 95% CI, 61-88% vs 63%; 95% CI 46-77%). Both methods had a specificity of 97% (95% CI, 91-99%), however. When used in combination, they had a sensitivity of 86% (95% CI, 71-94%) and a specificity of 92% (95% CI, 84-96%).

"Pulse oximetry of the toes seems as accurate as ABI to screen for LEAD in patients with type 2 diabetes," investigators wrote.

Pulse oximetry produced a ratio of 30 for the positive likelihood of LEAD (95% CI, 7.6-121) and a ratio of 0.23 (95% CI, 0.12-0.43) for the negative likelihood ratio. Ratios for ABI were 24.8 (95% CI, 6.2-99.8) and 0.38 (95% CI, 0.25-0.59), respectively.

GD Prevalent Among Other Ethnicities

First found to be prevalent in Pima Indians, investigators have now reported that gestational diabetes (GD) may also be prevalent in other ethnicities.

A study in *Diabetes Care* has shown that GD is on the rise across multiethnic populations and has increased in prevalence for all ethnic groups. Investigators used a database of 36,403 patients from a Kaiser Permanente of Colorado (KPCO) protocol that screens for diabetes to test the trends of GD in the United States. Investigators were interested in patients with diverse ethnic backgrounds, and they used data collected from KPCO between 1994 and 2002.

Investigators found that the number of women who had GD during this time doubled (2.1-4.1%, P <.001). This increase was seen across all of the patients, despite ethnicity. They listed the following as having a significant tie to GD: year of diagnosis, age of the mother and ethnicity (not including mothers who were non-Hispanic white).

Waist Circumference Better Type 2 Diabetes Predictor

The circumference of a man's waist may indicate the likelihood of type 2 diabetes more accurately than waist-to-hip-ratio (WHR) or BMI, according to researchers at Johns Hopkins University.

Reviewing 13 years worth of data from 27,270 men – 884 with diabetes – investigators reporting in *The American Journal of Clinical Nutrition* divided them in to groups based on waist size to compare the "predictive power" of BMI, waist circumference (WC) and WHR. Cutoffs for WC and WHR may need to be updated, and their uses as measures for abdominal adiposity are weary. At baseline, all men were measured for WC, WHR and BMI.

Investigators found that WC better predicted the incidence of type 2 diabetes versus WHR – the WC age adjusted relative risk (RR) were 1.0, 2.0, 2.7, 5.0 and 12.0 versus 1.0, 2.1, 2.7, 3.6 and 6.9 for WHR. When investigators looked at the RR in relation to BMI (1.0, 1.1, 1.8, 2.9, and 7.9), they found that it was similar to WC and still predicted type 2 diabetes better than WHR.

According to a news release from the American Diabetes Association, men with larger WC were at twice the risk for type 2 diabetes versus men whose WC was 29 to 34 inches. If a man's waist size rose above 40 inches, type 2 diabetes was 12 times more prevalent.

Type 3 Diabetes May be a New Buzzword

According to investigators reporting in the *Journal of Alzheimer's Disease*, the possible link between Alzheimer's disease and diabetes may warrant a distinction of type 3 diabetes.

Although sporadic Alzheimer's disease may be a neuroendocrine disorder that closely resembles diabetes, investigators from Rhode Island Hospital and Brown Medical School in Providence have concluded that its form is distinct.

Alzheimer's disease has been found to have abnormalities that are histopathological, molecular and biochemical in nature, however, a solid link between these has not been established.

Investigators have hypothesized that these abnormalities, occurring in the brain of Alzheimer's patients, may be linked to those in insulin and insulin-like growth factors I and II. Levels of these growth factors are lower in these patients.

"The strikingly reduced central nervous system expression of genes encoding insulin, IGF-1 and IGF-II, as well as the insulin and IGF-I receptors, suggests that AD [Alzheimer's disease] may represent a neuroendocrine disorder that resembles, yet is distinct from diabetes mellitus," investigators wrote. "Therefore, we propose the term, 'type 3 diabetes' to reflect this newly identified pathogenic mechanism of neurodegeneration." ■