

DIABETES CLOSE UP

Diabetes Close Up, V2, #19
October 7, 2003

Greetings and warm wishes from Boston, where it is a stunning fall evening. I'm away for two weeks and am eagerly anticipating some work on the road; particularly the annual obesity meeting in Ft. Lauderdale early next week and the Canadian Diabetes Association meeting in Ottawa following shortly thereafter. **I want to alert you to a couple of recent publications pertinent to topics at hand:**

- **Today's Wall Street Journal has a fascinating front-page story entitled: *For Obese Teens, A Radical Solution: Stomach Surgery*.** (Story below.) www.wsj.com Star health beat reporters, Ron Winslow and Rhonda Rundle, have written a thorough piece detailing the trend toward bariatric surgery for teens. Despite arguments from numerous skeptics¹, this trend seems on at least a small roll. Indeed, at the AACE earlier this year, the session on bariatric surgery was packed; improving reimbursement for the most serious cases represented a big positive theme. Just take a look at the Inamed chart ~
- **Last week's JAMA has another sobering story: *Prevalence of Diabetes and Impaired Fasting Glucose in Adults - United States, 1999-2000*.** Usually Mokdad's obesity data comes out in January; this was a different but related piece reporting that **an estimated 29 million (14.4%) persons aged 20 years or older had either diagnosed diabetes, undiagnosed diabetes, or impaired fasting glucose!** Whew. 5.9% of those over 20 had diabetes; and as the percentage often increases with age, the study suggested that fully 15% of those over 60 have the disease and nearly 34% have either diabetes or impaired fasting glucose. Stats like these elucidate the scope of the problem as people are living longer. The most surprising statistic, however, was that the overall prevalence of diagnosed diabetes, undiagnosed diabetes, total diabetes, and the overall proportion of total of undiagnosed diabetes did not appear to change significantly from 1988-1994 to 1999-2000. This is curious. <http://jama.ama-assn.org/current.dtl>
- **Upcoming earnings reports with implications for diabetes/obesity markets**
 - a. **ABT – Thursday, October 9, 9:50 am EST - 3Q03 results** www.abott.com
 - b. **JNJ – Tuesday, October 14, 8:30 am EST – 3Q03 results** www.jnj.com
 - c. **Roche – Thursday, October 16, 1:00 am EST – 3Q03 results** www.roche.com
 - d. **BDX – TBD; likely week of October 13 – F2Q03 results** www.bdx.com
 - e. **LLY - Wednesday, October 22, 8:30 am EST**
 - f. **THER – Wednesday, October 22, 5 pm EST.** www.therasense.com
 - g. **AVE – Details TBD, likely week of Oct 27.** www.aventis.com
 - h. **Novo – Wednesday, October 29, 9:00 am EST**
 - i. **IMDC – Details TBD;** www.inamed.com
 - j. **AMLN – Details TBD;** www.amylin.com.
- **Upcoming diabetes/obesity-related conferences**
 - a. **October 11-15, NAASO Annual Scientific Meeting:** Ft Lauderdale www.naaso.org
 - b. **October 15 – 18, Canadian Diabetes Association:** Ottawa, Canada. www.diabetes.ca
 - c. **October 25, Diabetes Research Institute, 4th Annual Conference,** New York http://www.drinet.org/html/4th_annual_research_conference.htm
 - d. **November 4-8, Rachmiel Levine Symposium: Advances in Diabetes Research:** From Cell Biology to Cell Therapy. Universal City <http://levinesymposium.coh.org>
 - e. **November 6-8, Diabetes Technology:** San Francisco www.diabetestechology.org

¹ One example named is obesity expert David Ludwig, the renowned inventor of the glycemic index – let me know if you'd like a copy of his fascinating JAMA paper on this topic from mid 2002.

- f. **November 8, American Heart Association:** Diabetes symposium led by the esteemed Dr. Steve Marso in Orlando www.scientificsessions.org.
 - g. **November 14, Designing an Accelerated Cure for Type 1 Diabetes: Integrating Biology with Bioengineering.** Symposium at Sunsun, Santa Barbara.
 - h. **February 6-8, 2004, ADA 51st Annual Postgraduate Course.** San Francisco, CA <http://www.diabetes.org/main/professional/conferences/default.jsp>
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APPENDIX: Articles of Note

For Obese Teens, A Radical Solution: Stomach Surgery

**Stapling Can Slash Weight, but Its Use
In Young People Is Being Questioned**

**By RON WINSLOW and RHONDA L. RUNDLE
Staff Reporters of THE WALL STREET JOURNAL**

CINCINNATI -- Heather Grill was four years old when she was first teased about her weight. Other kids told her fat people can't go to heaven because they are too heavy to fly with angel wings. In middle school, she remembers being pushed down a flight of stairs by "guys who thought it was fun to watch me roll."

Now 16, and after countless diets, Ms. Grill weighs 472 pounds. She has high blood pressure and an enlarged heart, and is borderline diabetic. She fears going to sleep because her body fat can crush her airways. She has chronic joint pain and takes an antidepressant. "Every day you're in front of the mirror looking for someone else because you don't want to believe it's you standing there," she says.

So Ms. Grill is ready for an extreme measure. She is talking to doctors at Cincinnati Children's Hospital about having a procedure called bariatric surgery that would permanently shrink her stomach by more than 90%.

In the past two years, as many as 150 teenagers around the U.S. have had the surgery, by some estimates, and the numbers are likely to grow. A dozen children's hospitals either offer the procedure or plan programs to meet surging demand. One pediatric surgeon estimates that 250,000 adolescents in the U.S. could be candidates.

The emerging teen-age market for this drastic operation illustrates how serious America's obesity epidemic has become. The National Center for Health Statistics says 15% of children between ages 6 and 18 were obese in 2000, compared with 6% in 1980, and experts believe the numbers are still increasing. The reasons aren't fully understood, though the likely causes include high-calorie diets and insufficient exercise.

Although surgery candidates constitute a tiny percentage of overweight adolescents, health-care experts believe they represent the leading edge of a troubling phenomenon: a generation of children poised to enter adulthood already burdened with maladies such as diabetes and heart disease that will shorten their lives and result in huge medical bills for society. Some worry that obese children pose such a severe problem that their generation could be the first in American history with a shorter life expectancy than their parents'.

Such concerns are helping to erode professional resistance to the procedure, which is not reversible. Two years ago, colleagues urged Mary L. Brandt, a professor of surgery and pediatrics at Baylor College of Medicine in Houston, to begin a program in bariatric, or obesity, surgery. "Absolutely not," she replied. Now, she has changed her mind because "it has become clear that there are children who need this operation," she says.

Skeptics remain. David Ludwig, a pediatrician who runs an obesity-prevention program for children at Children's Hospital Boston, advocates other remedies, including better insurance coverage for rigorous obesity prevention programs and new regulations, similar to antitobacco laws, on how fast-food and soft-drink companies market their products to children. Bariatric surgery for teens may be appropriate in "extreme cases," he says. "It is a sad comment on our society if we have to resort to this procedure frequently" for adolescents, he adds.

Most insurers are refusing to cover the surgery, which can cost as much as \$40,000. They say there aren't any conclusive data demonstrating that it works for adolescents and health-care costs are already soaring. Some insurers privately voice concerns that hospitals and surgeons are pushing weight-loss surgery to replace lucrative but waning procedures, including heart surgery.

Bariatric surgery is already big business with adults -- more than 100,000 patients will have it done this year. Results are generally good and insurance coverage varies.

In performing the procedure, doctors use a surgical stapler to seal off a tiny pouch that reduces the stomach from "the size of a bucket to the size of an egg," says Victor Garcia, a pediatric surgeon and head of the bariatric program at Cincinnati Children's Hospital. They also shorten a patient's small intestine by up to four feet, or 20%, and reroute the rest to shunt food quickly from the pouch to the bottom of the digestive tract. This sharply cuts the amount of food a person can eat and absorb.

The Cincinnati hospital, which has done 23 of the procedures on teenagers in the past two years, has seen some complications. One patient had a potentially life-threatening blood clot in her leg and spent a month in the hospital. Another had a leak in the portion of the stomach cut off from the digestive tract, a potentially serious problem that in this case quickly healed on its own. One patient failed to comply with a post-surgery diet and developed a serious vitamin deficiency and months later is still affected by leg weakness.

Although a few bariatric surgeons did the procedure on adolescents over the past two decades, until recently it was rare and essentially taboo. William J. Klish, a professor of pediatrics at Baylor, for years lectured medical students against the surgery for children. He opposed it after a 400-pound boy he had recommended for the operation more than a decade ago died from a post-surgical infection.

Today, though, he regularly sees obese children who have diabetes, high blood pressure and chronic joint problems. He's had patients who died of suffocation in their sleep. Now he has changed his mind and physicians at Texas Children's Hospital, affiliated with Baylor, are evaluating surgery candidates and expect to perform their first operation early next year.

Some doctors at children's hospitals figure that if they don't perform the procedure, surgeons already doing a brisk bariatric business on adults will add adolescents to their caseload. Pediatricians argue that if bariatric surgery is to be performed on children, it should be done within a comprehensive program involving specially trained doctors, psychologists and counselors in nutrition and exercise.

Alan Wittgrove, a bariatric surgeon in San Diego, says he and colleagues who have done the surgery on adolescents have been criticized by pediatricians for "mutilating our youth." He thinks new programs such as the one at Cincinnati Children's Hospital will help quiet critics by validating the procedure with clinical research. To speed that, some bariatric surgeons who specialize in adults are instructing pediatric surgeons on the procedure. That cooperation could eventually turn into a turf battle, though, as more children seek the operation -- especially if insurers start to pay for it.

The procedure comes with serious risks, including subsequent weight gain, poor nutrition and even death. It triggers biochemical responses in the body that aren't well understood. It requires strict compliance with a harsh diet that is crucial to the procedure's success. Without proper nutrition, the patients may lose

desirable lean body mass, suffer serious vitamin deficiency and not get enough minerals to ensure healthy bones.

But the consequences of untreated obesity are also severe. In addition to high blood pressure, diabetes and depression, super-obese children are likely to have abnormally large hearts, which risk failing later in life. They are prone to kidney problems and have a high incidence of liver disease, a precursor to hepatitis and, eventually, a liver transplant. Some girls don't menstruate or ovulate so they get hair growth on their faces. They also risk failed pregnancies and infertility.

The emotional toll includes taunting, the struggle to get a date or a job, the inability to fit in a seat at the movies.

Healthy diets and regular exercise, the recommended strategies for preventing obesity, typically don't do enough once children become very overweight, doctors say. For a child weighing 300 pounds or more, even a brisk walk around the block isn't possible because of serious joint pain and other problems. Once a person reaches a certain weight, their metabolism changes and the body fights aggressively to preserve its level of body fat. Many candidates for surgery report having lost 40 or 50 pounds at summer obesity camps, only to regain the weight -- and more -- once they get home.

Anecdotal reports from kids who have had the surgery are encouraging. Within the first six months, patients can lose more than 100 pounds. In some cases, diabetes goes away before patients leave the hospital. Sleep patterns return to normal. Doctors believe that abnormally large hearts gradually return to a healthier size.

While bariatric surgery is increasingly attractive to some teens, a big question is who pays. Ms. Grill has been cleared for the procedure by doctors at Cincinnati Children's Hospital but her family can't cover the bill. The hospital charges around \$40,000, which includes two years of follow-up treatments such as psychological and nutrition counseling.

The family's insurance company, Anthem Blue Cross & Blue Shield, has refused to pay, despite a letter from Dr. Garcia saying the procedure is a "medical necessity." The family has hired an attorney to appeal Anthem's denial.

Since Ms. Grill and other dangerously obese young people will probably run up big medical bills as they get older, doctors at Cincinnati Children's Hospital criticize the no-coverage policy. "We think this is a pay-me-now or pay-me-much-more-later scenario," says Stephen R. Daniels, a pediatrician and director of the hospital's lipid, hypertension and weight-management clinics.

Anthem says it doesn't cover obesity surgery in adolescents. The insurer reviewed its bariatric-surgery policy this spring "with the help of outside medical experts" and determined that there wasn't enough "conclusive medical and scientific evidence" to support coverage for members under age 18, says Deborah New, a spokesperson for the Indianapolis-based insurer.

Advocates of the procedure point to patients such as Natalie Moore. About three years ago, shortly before her 16th birthday, she weighed 325 pounds. Doctors said she'd be dead within a year. Searching the Internet, she entered her obesity-linked medical problems. Gastric bypass was listed as a remedy for nearly all of them. But every hospital she found that performed the operation said she had to be at least 18 years old.

Finally she found a doctor in Spain who agreed to do it. After she and a friend bought plane tickets, Ms. Moore went back to her own physician. "I told her to get me help or get out of my way," she says. The doctor got her an appointment with Dr. Garcia.

As chief of surgery at Walter Reed Army Medical Center in the 1980s, Dr. Garcia had performed gastric bypasses on adults. A few years ago, he did the procedure on a 19-year-old patient at Cincinnati Children's who was so obese she needed a tube to breathe. Her success helped convince Dr. Garcia the procedure could benefit teens. He and his colleagues spent two years developing a program to offer it.

Before Ms. Moore was cleared for surgery, a team including a colleague of Dr. Garcia's, a pediatric psychologist and expert in nutrition and exercise, interviewed her parents and her brother "to see if my family could handle the changes" necessary for success, she says. She watched videos of the surgery and went on a supervised diet for a few months to see if she would lose any weight.

On the morning she went to the operating room, Ms. Moore weighed 298 pounds. She remembers thinking: "This is going to change the rest of my life."

It changed immediately. Before surgery, she was a cupcake junkie and often drank a 12-pack of Mountain Dew a day. Now, protein and vitamins dominate her diet. She concentrates on chewing her food. "The opening to my stomach is the size of a dime," she says. When one patient didn't chew thoroughly, doctors had to thread an instrument down her throat to fish out the food.

Ms. Moore also discovered that her senses of taste and smell had changed. Food such as tuna fish that she liked before the operation now nauseate her. She no longer likes the smell of perfume or food cooking.

Other patients report similar reactions. For reasons that aren't clear, the surgery seems to trigger biochemical changes that suppress appetite, providing an unexpected ally. The long term consequences, though, aren't known.

Maintaining nutrition is a huge challenge, doctors say. Getting sufficient calories and protein is difficult on a small stomach, says Dr. Garcia, as is drinking the recommended two quarts of water a day. If the teenagers drink any liquid within an hour of a meal, they'll be too full to eat and risk not getting needed vitamins.

During a recent "support group" meeting, attended by both young people who had had the surgery and ones who were considering it, Ms. Moore reported that almost two years after her operation she weighs 150 pounds -- half her size when she had the surgery. She raised her blouse to show a large zig-zag scar circling her body like a belt, from a second operation to remove excess layers of skin. "You're losing so much weight you don't have time to put the skin anywhere," she explained later. The scar, she added, is "something I earned."

Prevalence of Diabetes and Impaired Fasting Glucose in Adults—United States, 1999-2000

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Diabetes and its complications are major causes of morbidity and mortality in the United States and contribute substantially to health-care costs. Data from the National Health Interview Survey (NHIS) and the Behavioral Risk Factor Surveillance System (BRFSS) have documented steady increases in the prevalence of diabetes.^{1,2} However, these surveys rely only on self-reports of previously diagnosed diabetes and cannot measure the prevalence of undiagnosed diabetes. The change in prevalence demonstrated by these data might reflect other factors such as enhanced detection rather than true increases. The National Health and Nutrition Examination surveys (NHANES) are the only nationally representative surveys that examine both diagnosed and undiagnosed diabetes. During 1976-1980 (NHANES II) and 1988-1994 (NHANES III), the overall combined prevalence of diabetes (diagnosed and undiagnosed on the basis of fasting glucose) increased.³ This report presents data on prevalence of diagnosed and undiagnosed diabetes and impaired fasting glucose from NHANES 1999-2000 and NHANES III (1988-1994). The findings indicate that diabetes and impaired fasting glucose continue to affect a major proportion of the U.S. population. An estimated 29 million (14.4%) persons aged 20 years had either diagnosed diabetes,

undiagnosed diabetes, or impaired fasting glucose; 29% of diabetes cases were undiagnosed. Persons can reduce their risk for diabetes through weight management and physical activity.

NHANES 1999-2000⁴ was designed to be nationally representative of the U.S. civilian, noninstitutionalized population on the basis of a complex, multistage probability sample. Survey participants were interviewed in their homes and subprovide estimates that were representative of the U.S. population. Prevalence based on fasting glucose in the morning sample of persons without diagnosed diabetes was adjusted as described previously⁶ so estimates based on these data would represent the total U.S. population. Age- and sex-adjusted rates were computed by the direct method by using U.S. 2000 Census data, with age categories of 20-39, 40-59, and 60 years. Replicated variance estimation methods were used to calculate the standard errors, accounting for both the complex sample design and the use of both interview and morning examination sample data in combination. Two sample t-tests were used to test differences in proportions.

The estimated unadjusted prevalence of previously diagnosed diabetes in adults aged 20 years during 1999-2000 was 5.9% (95% confidence interval [CI] = 4.9-6.9), representing 11.8 million (95% CI = 9.8-13.8 million) U.S. adults. The prevalence increased by age, reaching 15.0% (95% CI = 12.6-17.5) among persons aged 60 years. Rates were similar by sex. The adjusted prevalence was significantly lower in non-Hispanic whites compared with Mexican Americans and non-Hispanic blacks. The unadjusted prevalence of undiagnosed diabetes based on fasting glucose in adults aged 20 years was 2.4% (95% CI = 1.5-3.4) during 1999-2000, representing 4.9 million (95% CI = 3.0-6.8 million) U.S. adults. Prevalence increased slightly with age and was similar in men and women. Rates were similar by race/ethnicity.

Combining diagnosed and undiagnosed diabetes, the unadjusted prevalence of total diabetes during 1999-2000 was 8.3% (95% CI = 6.9-9.8), affecting an estimated 16.7 million (95% CI = 13.8-19.6 million) persons aged 20 years. Differences in prevalence by age, sex, and race/ethnicity mirrored those for diagnosed diabetes. During 1999-2000, the proportion of total diabetes that was undiagnosed was 29% (95% CI = 21%-38%). The overall prevalence of diagnosed diabetes, undiagnosed diabetes, total diabetes, and the overall proportion of total diabetes that was undiagnosed did not change significantly from 1988-1994 to 1999-2000.

Overall prevalence of impaired fasting glucose during 1999-2000 was 6.1% (95% CI = 4.4-7.9), representing 12.3 million (95% CI = 8.8-15.8 million) persons aged 20 years. Rates increased with age, were higher in men (7.9%) (95% CI = 5.5-10.2) than in women (4.5%) (95% CI = 2.8-6.2), and were similar by race/ethnicity. The overall decrease in prevalence observed from 1988-1994 to 1999-2000 was not statistically significant.

During 1999-2000, the combined unadjusted prevalence of total diabetes and impaired fasting glucose in adults aged 20 years was 14.4% (95% CI = 12.3%-16.5%), representing 29.0 million (95% CI = 24.8-33.2 million) persons. Prevalence increased with age, reaching 33.6% (95% CI = 28.8%-38.4%) by age 60 years. Adjusted prevalence was significantly lower in women than in men, and in non-Hispanic whites compared with non-Hispanic blacks and Mexican Americans. Rates were similar in 1988-1994 and 1999-2000.

Reported by:

CC Cowie, PhD, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda; KF Rust, PhD, Westat, Inc., Rockville; D Byrd-Holt, Social & Scientific Systems, Inc., Silver Spring, Maryland. MS Eberhardt, PhD, S Saydah, PhD, National Center for Health Statistics; LS Geiss, MA, MM Engelgau, MD, ES Ford, MD, EW Gregg, PhD, National Center for Chronic Disease Prevention and Health Promotion, CDC.

CDC Editorial Note:

Diabetes continues to affect a substantial proportion of U.S. adults. On the basis of NHANES 1999-2000, a total of 8.3% of persons aged 20 years had either diagnosed or undiagnosed diabetes, and this percent increased to 19.2% for persons aged 60 years. Men and women were affected similarly by diabetes. However, non-Hispanic blacks and Mexican Americans had a disproportionately high prevalence compared with non-Hispanic whites. Impaired fasting glucose increases the risk for diabetes and is associated with other cardiovascular risk factors.⁷ In 1999-2000, an additional 6.1% of adults had impaired fasting glucose (a rate similar in magnitude to the prevalence of diagnosed diabetes), increasing to 14.4% for persons aged 60 years, with men affected more than women. Overall, an estimated 14.4% of the U.S. population aged 20 years and 33.6% of those aged 60 years had either diabetes or impaired fasting glucose.

The findings in this report are subject to at least two limitations. First, the substantially smaller sample size of NHANES 1999-2000 limits the precision of estimated prevalences and the statistical power to detect changes in these estimates between the surveys. Second, because an oral glucose tolerance test (OGTT) was not performed in NHANES 1999-2000, this survey does not capture the additional proportion of persons with abnormal postload glucose tolerance and normal fasting glucose levels. NHANES III (1988-1994) indicated that total glucose intolerance was 36% higher based on OGTT data.³

The findings in this report indicate that the prevalence of diabetes, either diagnosed or undiagnosed, and impaired fasting glucose did not appear to increase substantially during the 1990s. Estimates of diagnosed diabetes in NHANES 1999-2000 are similar in magnitude to those from NHIS and BRFSS during the same years. The apparent lack of increase in prevalence is unexpected in light of the increasing prevalence of obesity and overweight in U.S. adults documented by the NHANES surveys.⁸ Although a potential change in the ratio of undiagnosed to total diabetes prevalence would be an important finding, the observed differences are not statistically significant. Further investigation with additional years of NHANES data will be necessary to provide more precise estimates. In addition, the potential impact on the prevalence estimates of the change in diagnosis of diabetes adopted by the ADA in 1997⁵ should be accounted for, along with changes in demographic characteristics and overweight.

Recent trials have documented that lifestyle modification (i.e., weight management and increased physical activity) reduces the risk for developing diabetes among persons with impaired glucose tolerance.⁹ Other clinical trials and studies have demonstrated that the risk for diabetic complications is reduced substantially by blood glucose, blood pressure, and blood lipid control.¹⁰ These messages should continue to be communicated through education and outreach activities such as the "Steps to a Healthier US" by the U.S. Department of Health and Human Services (<http://www.healthierus.gov/steps>), and the "Small Steps, Big Rewards" (<http://ndep.nih.gov/get-info/dpc.htm> and "Control the ABCs of Diabetes" (<http://ndep.nih.gov/control/control.htm>) campaigns of the National Diabetes Education Program.

Children Who Diet May Gain Weight

Report Warns That Youths Often Resort To Overeating After Trying to Lose Pounds

CHICAGO -- Children who diet may actually gain weight in the long run, perhaps because of metabolic changes but more likely because they resort to binge eating, doctors report.

"Although medically supervised weight control may be beneficial for overweight youths, our data suggest that for many adolescents, dieting to control weight is not only ineffective, it may actually promote weight gain," said the report from Brigham and Women's Hospital in Boston.

The study was based on a look at more than 16,000 boys and girls age 9 to 14 from 1996 to 1998. It was published in the October issue of "Pediatrics," the journal of the American Academy of Pediatrics.

The report found that about 30% of the girls and 16% of the boys were dieting to one degree or another when the study began.

On the basis of questionnaires sent to the children, the researchers found that although children who said they were dieters reported being more active and getting fewer calories than their peers, they gained more weight than nondieters.

For example, one girl in the study who was a frequent dieter gained about 2 pounds a year more than other girls her age who weren't dieting, the report said. In general, girls who dieted less often gained slightly less weight, but still more than nondieters, it added.

Similar differences were observed among the boys.

One theory: The dieters could have gained more weight because their metabolism became more efficient, requiring fewer calories to maintain weight or become overweight.

A more likely reason, the report said, was that restrictive diets are often not maintained for long periods and are often followed by binge eating.

"In that scenario it would be the repeated cycles of overeating between the restrictive diets that would be responsible for weight gain," the study said.

The researchers suggested that young people and adults who aren't severely overweight should be encouraged to adopt "a modest and therefore sustainable weight control strategy that includes physical activity and does not require severe restriction of total calories."

The number of overweight U.S. children is growing. In July, the National Center for Health Statistics said 15% of children age 6 to 18 were seriously overweight in 2000, up from 6% in 1980.

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Diabetes Close Up is a newsletter highlighting notable information and events related to selected companies with diabetes/obesity businesses. This newsletter is put forth as an unbiased commentary on the industry. If you have any suggestions or comments regarding content, please contact info@closeconcerns.com. Many thanks!

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