A Propensity-Matched Study of Obesity and Diabetes risk: A COVID-19 Perspective

Claire Nurse[1], Janet Rosenbaum[2]
[1]Department of Epidemiology and Biostatistics, SUNY Downstate School of Public Health, Brooklyn, NY, USA
[2]Department of Epidemiology and Biostatistics, SUNY Downstate School of Public Health, Brooklyn, NY, USA

Abstract
The COVID-19 pandemic spurred widespread weight gain, suggesting that type-2 diabetes may also increase. However, past research finding an association between obesity and type 2 diabetes is subject to potential confounding on socioeconomic and other variables. Using data from the nationally representative longitudinal Midlife in the US study, we evaluated the association between obesity and diabetes 18 years later using robust regression methods. To reduce potential confounding, we used nearest-neighbor propensity score matching on demographics (age, race, gender), socioeconomic status (educational attainment, household income), and health risks (physical activity, smoking status) to match adults with obesity (n=450) and without obesity (n=617), which resulted in covariate balance assessed by standardized differences. In Poisson regression in the matched sample, individuals with obesity had 2.3 times the risk of diabetes in 18 years than those without obesity (ARR , 95% confidence interval (1.62, 3.50)). COVID-19 pandemic recovery must include population-based obesity interventions (e.g., optimizing agricultural subsidies to target obesity) and type-2 diabetes screening.

Key Words: Obesity, Type-2 Diabetes, Propensity-Matched, COVID-19

1. Introduction

Diabetes is a global epidemic of major public health significance, associated with a significant reduction in functional status and increased risk of mortality[1]. Obesity, an established risk factor for Type II diabetes, has been described in the literature as the most important factor in the worldwide increase in Type 2 diabetes.[2,3]
Among adults hospitalized for severe COVID-19, one of the most common underlying conditions was obesity, accounting for nearly 50% of admissions.[4] Diabetes has been identified in the literature as a complication of obesity which predisposes patients to hospitalization and invasive ventilation.[4]

Observational studies are often unable to show a strong causal link between obesity and incident diabetes, due to inability to adequately control for confounding factors such as race, income and education. Cross-sectional studies which show a significant association between obesity and Type 2 diabetes, are unable to establish causality due to lack of temporal sequence. This study therefore aims to estimate a causal effect of obesity on diabetes in a propensity-score matched, longitudinal cohort study.

2. Materials and Methods

2.1 Data

The data was obtained from the National Survey of Midlife Development in the Unites States (MIDUS), a nationally representative sample of 7,444 Americans ages 25-74 surveyed in three waves: Wave 1 (1995-1996), Wave 2 (2004-2006) and Wave 3 (2013-2014).

The sample was predominantly White (89%), with approximately 24% of the participants classified as obese and 48% female. About 40% had at least some college education, and 84% reported having 'just enough' or 'less than enough' money to meet their needs. Less than half (40%) participated in regular physical activity and 23% smoked regularly.

2.2 Measures

The main predictor variable in this study was baseline obesity, measured by BMI, computed from self-reported height and weight at Wave 1. Obesity was coded as 1 for BMI ≥ 30 kg/m^2. Implausible values were identified using Tukey's method of outlier detection, such that BMI values below [Q1- 1.5*IQR] or above [Q3 + 1.5*IQR] were excluded.[5] The outcome measure was self-reported diabetes at Wave 3, defined as response "Yes" to the following question: In the past 12 months have you experienced or been treated for diabetes or high blood sugar?

Based on previous studies, control variables were selected which were likely to act as confounders in the association between obesity and diabetes. These included age, race, gender, physical activity, socioeconomic status, smoking status and educational attainment.[7,8] All variables were binary (coded 1 or 0), with the exception of age, which was coded 1, 2 and 3 corresponding to age groups of 20-34, 35-44 and 45 or older. For this analysis lower socioeconomic status was defined as having just enough or less money to meet needs, and physically active was defined as participating in exercise several times a week or more.

2.3 Statistical Methods

Pre-existing differences in the characteristics of the obese and non-obese groups have the potential to bias the results. Propensity score matching was used to match obese and non-obese (i.e., 'treatment' and 'control') via the nearest neighbor algorithm. A logistic regression model estimates the propensity for being in high BMI group, as a function of the covariates. These covariates included age, physical activity, race, gender, socioeconomic status, smoking status. 617 controls were matched with all 450 individuals in the treatment group using a nearest neighbor propensity -matching algorithm.

For inverse propensity-score weighting, subjects with baseline obesity (N= 1544), were assigned weights of the inverse propensity of having obesity (1/ps.est), while those without baseline obesity (N= 4781), were assigned weights of 1/(1-ps.est).

3. Results

3.1 Baseline characteristics and bivariate analysis before matching

Among individuals with baseline obesity, about 32% developed diabetes, compared to only 10% of those who were not obese. Pearson chi-square test found a significant association between the predictor and outcome with $p<0.0001$.

There were significant differences in confounding variables across treatment and control groups prior to matching. Among those classified as obese, 85% were White and 15% non-white; 56% female versus 44% male; 58% were age 20-35, 31% age 35-45 and 11%

age 45-56. Those with more money than they need accounted for 12% of the obese group, while 88% reported just enough or less money than they need. About 29% engaged in regular physical activity while 71% did not; 18% were regular smokers while 82% did not smoke regularly; 55% reported having at least some college education, while 45 % were high school graduates or less. Prior to matching, all covariates were significantly associated with the predictor at alpha of 0.05. Obesity was associated with female gender, non-white race, the 35-45 age group, smoking regularly, lower socioeconomic status, lack of regular physical activity and having less than a college education.

3.2 Covariate balance after propensity-matching

After propensity score matching, covariate balance was achieved as seen in Figure 1. The final matched dataset consisted of all 450 individuals from the obese group and 617 from the control group. Table 1 demonstrates the relative distribution of demographic and lifestyle factors between the two groups after matching.

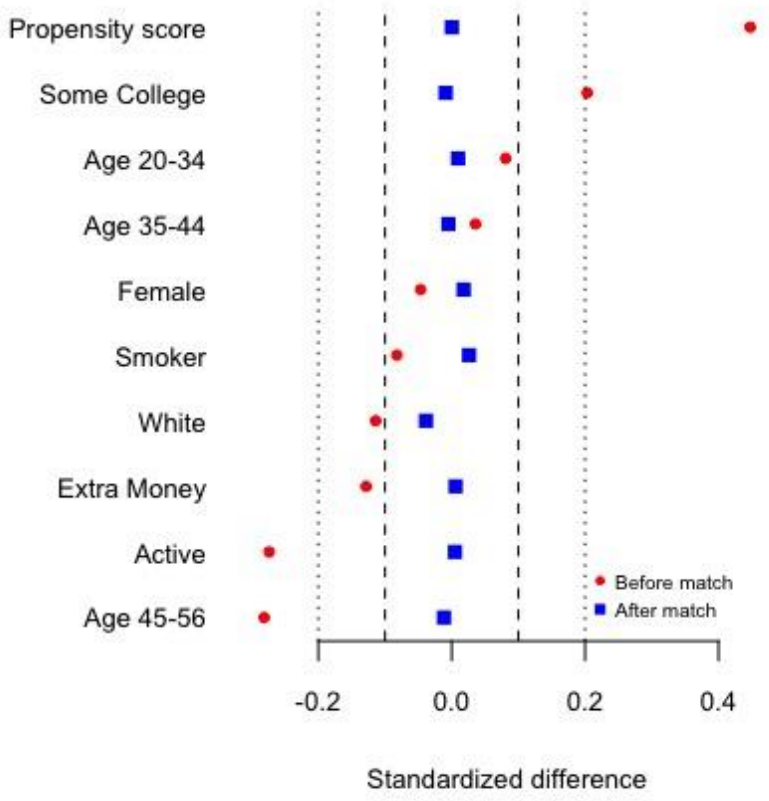

Figure 1: Covariate balance in standardized mean difference pre- and post-matching

Table1: Distribution of covariates in obese and non-obese groups post-matching and association with predictor

	BMI≥ 30	BMI <30	P-value
Age Category			0.4
Age (20-34)[1]	68.4	66.3	
Age (35-44)	27.8	28.1	
Age (45-56)	3.8	5.6	
Physical activity			0.4
Active (several times/week)	30	33.3	
Not active (≤ once per week)	70	67	
Race			0.2
White	90.9	93.6	
Non-white	9.1	6.4	
Gender			0.8
Female	56.2	57.3	
Male	43.8	42.7	
Household Income			0.9
More money than you need	18.0	18.6	
Less money than you need	82.0	81.4	
Smoking Status			1.0
Smokes regularly	13.6	14.0	
Does not smoke regularly	86.4	86.0	
Educational Attainment			0.3
Some College	59.1	65.0	
No college education	40.9	35.0	

[1] Referent group

3.3 Regression model for obesity in the fully matched sample

Poisson regression was used to model the outcome diabetes based on obesity status. The exponentiated regression coefficients provide an estimated incidence rate ratio (IRR), or risk for each covariate included in the model (Table 2).

In the matched regression model, the risk of developing diabetes was 2.3 times higher in obese individuals than in those who were not obese (95% CI 1.62, 3.50). Increased risk of developing the disease was also associated with regular smoking (IRR 1.46, 95% CI:1.20, 1.77). Decreased risk of diabetes was observed in Whites (IRR 0.72, 95% CI: 0.58, 0.92), individuals of higher socioeconomic status (IRR 0.72, 95% CI: 0.56, 0.92) and those with some college education (IRR 0.84, 95% CI: 0.71, 0.98).

Table 2: Poisson regression with outcome diabetes diagnosis 18 years later, among individuals without diabetes at baseline

	IRR	95% CI	*P*
Obese (BMI >=30)	2.33	(1.62, 3.50)	<0.0001
Regular smoker	1.46	(1.20, 1.77)	<0.001
White	0.72	(0.58, 0.92)	0.007
SES (more money than needed)	0.72	(0.56, 0.92)	0.009
Some college	0.84	(0.71, 0.98)	0.03
Female	1.17	(0.98, 1.38)	0.08
Physically active	0.88	(0.73, 1.06)	0.18
Age (35-45)	0.93	(0.77, 1.12)	0.47
Age (45-56)	1.17	(0.72, 1.80)	0.49

4. Discussion

This study found that obesity measured as BMI, is a significant predictor of developing diabetes in later life. These results were the same for both matched and unmatched samples. This finding mirrors that of previous studies which indicate that increased body fat and obesity in adults is associated with a higher risk for diabetes.[9,10] The proposed mechanism linking obesity and diabetes is based on genetically predetermined growth potential in adipose tissue, which leads to hypertrophy of adipocytes, chronic inflammation and eventually insulin resistance.[9,10] Insulin resistance, the decreased responsivity of cells to insulin is one of the primary precursors of Type 2 diabetes.[9,10] Whites, individuals with higher socioeconomic status and those with some college education, had a lower risk of developing diabetes. This result was expected as socioeconomic status is frequently cited in the literature as a key modifier of the association between BMI and diabetes.[11] In this sample, Whites accounted for 95% of individuals who reported having more money than they need, providing strong evidence of a racial divide in socioeconomic status. In Table 2, the incidence rates and confidence intervals for White and higher socioeconomic status are virtually identical, indicating a high degree of overlap between the two variables. Previous studies have shown an association between lower socioeconomic status and poor nutrition, lower autonomy, higher levels of the stress hormone cortisol and higher rates of preventable diseases including diabetes.[12]

While there is disagreement regarding the exact mechanism by which smoking increases diabetes risk, there is evidence to support a link between nicotine use, decreased insulin sensitivity and increased serum triglyceride levels.[13] This study's findings of increased risk of diabetes in regular smokers provides support for this link.

The lack of association between diabetes and physical activity was unexpected based on the literature. It is likely that the selected variable did not accurately capture differences in activity levels cross the comparison groups. Limitations in this and other control variables will be discussed in the following section.

5. Strengths and Limitations

This has several limitations. As with any observational study it is impossible to be certain that all confounders have been adequately controlled and therefore the possibility of bias exists.
Self-reported measures for height, weight and diabetes status, as opposed to clinician-confirmed measurements, were used in the analysis. Furthermore, since MIDUS does not distinguish between Type 1 and Type 2 diabetes on its survey, it is possible that some cases of Type 1 diabetes have been misclassified. However, because of the high prevalence of Type 2 diabetes (over 90%) relative to Type 1[11], it is reasonable to assume that the majority of self-reported cases are Type 2.
Since exercise guidelines in the U.S are 150 minutes of moderate to vigorous activity per week, the measurement variable for physical activity should be similarly defined. While some modifications have been made, these guidelines have remained virtually unchanged over the years, essentially an average of 30 minutes per day, most days of the week.[14]

Despite its limitations, the use of doubly robust regression methods and a longitudinal design, provide greater confidence in the estimate of diabetes risk based on exposure status. This design allowed for exclusion of pre-existing cases of diabetes at Wave 1, increasing the likelihood that diabetes reported at Wave 3 reflected incident cases.

5. Conclusion

This study found a significant association between obesity and risk of diabetes after 18 years follow up. Since obesity is typically due to overconsumption of calorie-dense foods such as refined grains, fast foods and sugary beverages, it follows that Type 2 diabetes may be largely preventable with dietary changes.[1,9] Diets high in whole grains, legumes, fruits and vegetables are associated with lower rates of obesity and are effective in preventing, treating and reversing Type 2 diabetes.[1] Data from the pandemic have shown a strong link between obesity, diabetes and poor COVID-19 outcomes. Therefore, public health interventions for COVID-19, need to prioritize obesity prevention to effectively reduce susceptibility to and consequences of COVID-19 infection.

6. References

1. McMacken M, Shah S. A plant-based diet for the prevention and treatment of type 2 diabetes. *J Geriatr Cardiol*. 2017;14(5):342-354. doi:10.11909/j.issn.1671-5411.2017.05.009

2. Toplak H, Leitner DR, Harreiter J, et al. „Diabesity“ – Adipositas und Typ-2-Diabete (Update 2019). *Wien Klin Wochenschr*. 2019;131(1):71-76. doi:10.1007/s00508-018-1418-9

3. Adeva-Andany MM, Rañal-Muíño E, Vila-Altesor M, Fernández-Fernández C, Funcasta-Calderón R, Castro-Quintela E. Dietary habits contribute to define the risk of type 2 diabetes in humans. *Clinical Nutrition ESPEN*. 2019;34:8-17. doi:10.1016/j.clnesp.2019.08.002

4. Finer, N., Garnett, S. P., & Bruun, J. M. (2020). COVID-19 and obesity. *Clinical Obesity*, *10*(3). https://doi.org/10.1111/cob.12365

5. Islam S, Rosenbaum JE, Cataletto M. Asthma at mid-life is associated with physical activity limits but not obesity after 10 years using matched sampling in a nationally representative sample. *Health Serv Outcomes Res Method*. 2019;19(1):8-22. doi:10.1007/s10742-019-00197-1

6. Linmans JJ, Spigt MG, Deneer L, et al. Effect of lifestyle intervention for people with diabetes or prediabetes in real-world primary care: propensity score analysis. *BMC Fam Pract*. 2011;12(1):95. doi:10.1186/1471-2296-12-95

7. Lionetti L, Mollica MP, Lombardi A, Cavaliere G, Gifuni G, Barletta A. From chronic overnutrition to insulin resistance: The role of fat-storing capacity and inflammation. *Nutrition, Metabolism and Cardiovascular Diseases*. 2009;19(2):146-152. doi:10.1016/j.numecd.2008.10.01

8. Petersen MC, Shulman GI. Mechanisms of Insulin Action and Insulin Resistance. *Physiol Rev*. 2018;98(4):2133-2223. doi:10.1152/physrev.00063.2017

9. Xu G, Liu B, Sun Y, et al. Prevalence of diagnosed type 1 and type 2 diabetes among US adults in 2016 and 2017: population based study. *BMJ*. 2018;362. doi:10.1136/bmj.k1497

10. Kautzky-Willer A, Harreiter J, Pacini G. Sex and Gender Differences in Risk, Pathophysiology and Complications of Type 2 Diabetes Mellitus. *Endocr Rev*. 2016;37(3):278-316. doi:10.1210/er.2015-1137

11. Volaco A, Cavalcanti AM, Filho RP, Précoma DB. Socioeconomic Status: The Missing Link Between Obesity and Diabetes Mellitus? *Curr Diabetes Rev*. 2018;14(4):321-326. doi:10.2174/1573399813666170621123

12. Maddatu J, Anderson-Baucum E, Evans-Molina C. Smoking and the Risk of Type 2 Diabetes. *Transl Res*. 2017;184:101-107. doi:10.1016/j.trsl.2017.02.004

13. Centers for Disease Control. Morbidity and Mortality Weekly Report https://www.cdc.gov/mmwr/preview/mmwrhtml/mm4925a2.htm

14. Fukuoka Y, Choi J, Bender MS, Gonzalez P, Arai S. Family history and body mass index predict perceived risks of diabetes and heart attack among community-dwelling Caucasian, Filipino, Korean, and Latino Americans—DiLH Survey. *Diabetes Res Clin Pract*. 2015;109(1):157-163. doi:10.1016/j.diabres.2015.04.015