# Supplemental Information
# Severe Obesity in Adolescence Predicts Greater Health Risk in Adults Undergoing Bariatric Surgery

## METHODOLOGY

### Demographics, BMI, and Health Status at Time of LABS-2 Enrollment

Data collection for the LABS-2 observational, longitudinally followed cohort has been previously described.[1,2] Briefly, LABS-2 used standard instruments or established standard definitions of data elements. When feasible, objective measures of patient status and comorbidities were used. Standardized data collection protocols were codified in Manuals of Operations. For example, detailed instructions for obtaining physical measures (eg, height, weight, neck and waist circumference, blood pressure) were developed. LABS-2-provided equipment was used to reduce the chances that cross-site differences were due to differences in instrumentation. Certification on data collection protocols was required for all data collectors, including dedicated project coordinators and clinicians, to enhance consistent data collection across sites. Gender, race, ethnicity, marital status, education, employment status, household income, and smoking status were assessed by questionnaire. Age on day of surgery was determined based on date of birth. Height and weight were measured according to standard protocol, and BMI was calculated.

Comorbidities: the data used to describe the presence or absence of comorbid conditions was collected in a rigorously defined fashion. A LABS-2-certified clinical researcher used the best available information (medical records, physical examination, patient interview) to determine presence or absence of a history of ischemic heart disease (defined as history of percutaneous coronary intervention, coronary artery bypass surgery, angina, or myocardial infarction) and lower extremity venous edema with skin manifestation (defined as leg swelling and ≥1 other symptom such as blistering, infection, discoloration, or alteration). The diagnosis of obstructive sleep apnea was based on an Apnea-Hypopnea Index of ≥5 from a diagnostic polysomnogram in the 12 months before the LABS-2 baseline visit. If results from a past-year diagnostic polysomnogram were unavailable, then a LABS-2-certified researcher used the best available information to determine presence or absence of sleep apnea, for example, participant-reported use of continuous positive airway pressure, previous diagnostic Apnea-Hypopnea Index result. Hypertension was defined as having systolic blood pressure of ≤140 mm Hg or a diastolic blood pressure of at least 90 mm Hg during the baseline visit as measured using the standard LABS-2 protocol or if the participant self-reported currently taking antihypertensive medication. Hyperlipidemia was defined as taking a lipid-lowering medication or having LDL cholesterol of ≥160 mg/dL. Dyslipidemia is more inclusive term and further took into consideration high-risk high-density lipoprotein levels. Thus, dyslipidemia was defined as having either hyperlipidemia or a low level of high density lipoprotein (<40 mg/dL) or high triglycerides (≥200 mg/dL). Diabetes was defined as taking diabetes medication or having glycosylated hemoglobin (HbA1c) of ≥6.5% or, if HbA1c was unavailable, an 8-hour fasting glucose of ≥126 mg/dL.[3] An exception was made for participants who reported a diagnosis of polycystic ovary syndrome (PCOS), did not meet either the HbA1c or fasting glucose requirements, and were taking metformin but no other diabetes medication; these participants were considered to not have diabetes.

Participants self-reported asthma ("have you ever been told by a doctor or other health care professional that you have asthma?"), urinary incontinence (responded "weekly [once or more each week]" or "daily [once or more each day]" to the question, "Many people complain that they leak urine accidentally. In the past 3 months, how often have you typically leaked urine, even a small amount? [Please record urine loss for any reason and check one box only]") and a severe walking limitation (defined as self-reporting the inability to walk 200 feet without assistance).

Abnormal kidney function was based on having a GFR $<60$[4] where GFR $= 77.24 \times (\text{cystatin-C})^{-1.2623}$ according to Dade-Behring formula.[5] When cystatin-C was below the detection limit ($n = 1$), a uniform random number between 0 and the detection limit was used to impute the value.[6]

Microalbuminuria was based on having an albumin creatinine ratio ≥3%.[7] The detection limits for urine albumin depended on the batch; thus, there were different detection limits, namely, <0.21,

$<0.22$, and $<0.23$. When urine albumin levels were below the detection limit ($n = 89$), a uniform random number between 0 and the detection limit was used to impute the value.[6]

## Laboratory Analyses

Fasting blood specimens were drawn at the research visit. Laboratory assays were performed by the Northwest Lipid Metabolism and Diabetes Research Laboratories (Seattle, WA). LDL cholesterol was calculated using the Friedewald equation except for participants whose triglycerides were $\geq$400 mg/dL, for whom LDL cholesterol was measured directly by $\beta$-quantification. Analysis of fasting glucose was performed enzymatically using Roche reagents on a Roche Module P Chemistry autoanalyzer (Roche Diagnostics, Inc, Indianapolis, IN). The Roche reagent is based on the glucose hexokinase method. Measurement of the relative proportion of hemoglobin subclasses and calculation of the HbA1c levels were performed by a dedicated analyzer (TOSOH, Biosciences, Inc, South San Francisco, CA) using nonporous ion exchange high-performance chromatography to achieve rapid and precise separation of stable HbA1c from other hemoglobin fractions. The immunochemical measurement of albumin in urine was performed by using Siemens reagent (Siemens Healthcare Diagnostics, Inc, Newark, DE) on a Siemens BN II Nephelometer. The immunochemical measurement of cystatin C levels was performed by the nephelometric method using Siemens reagents (Siemens Healthcare Diagnostics) to estimate kidney function.

## Cincinnati Weight History Questionnaire Elements

The following excerpt shows the item in the Cincinnati Weight History Questionnaire that was used for this analysis.

On your **18th birthday**, which happens when most people are seniors in high school, how tall were you and how much did you weigh or, if you were pregnant, how much did you weigh before you were pregnant?

| | | **Completely sure** | | | | | | | | | | **Not at all sure** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 100% | 90 | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 | 0% |
| a. Height at 18 years: ____feet ___inches | *How sure of answer:* | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| b. Weight at 18 years: pounds | *How sure of answer:* | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

## REFERENCES


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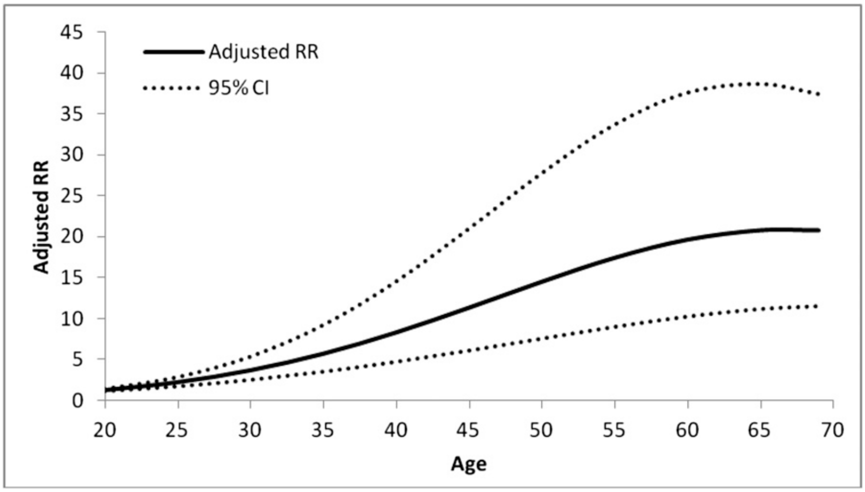
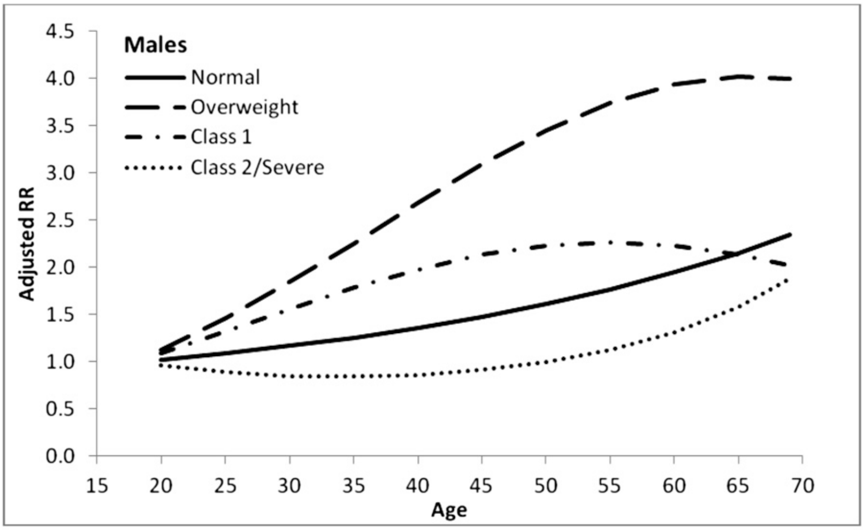
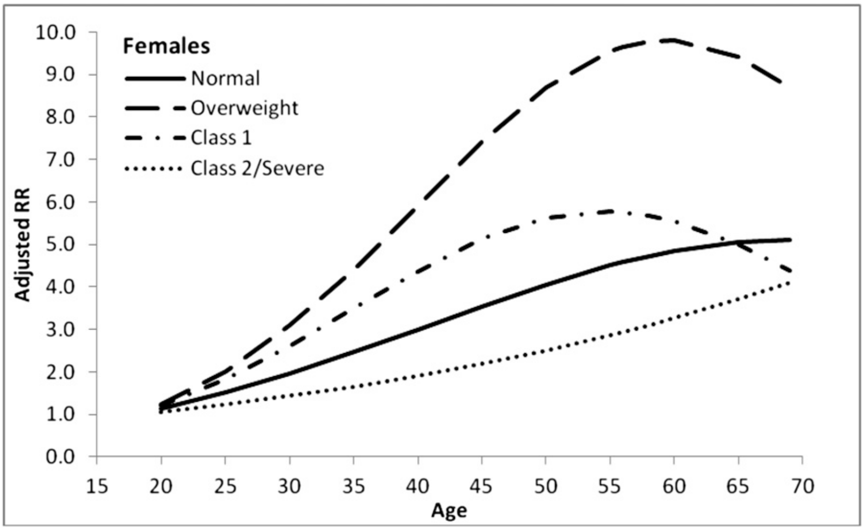


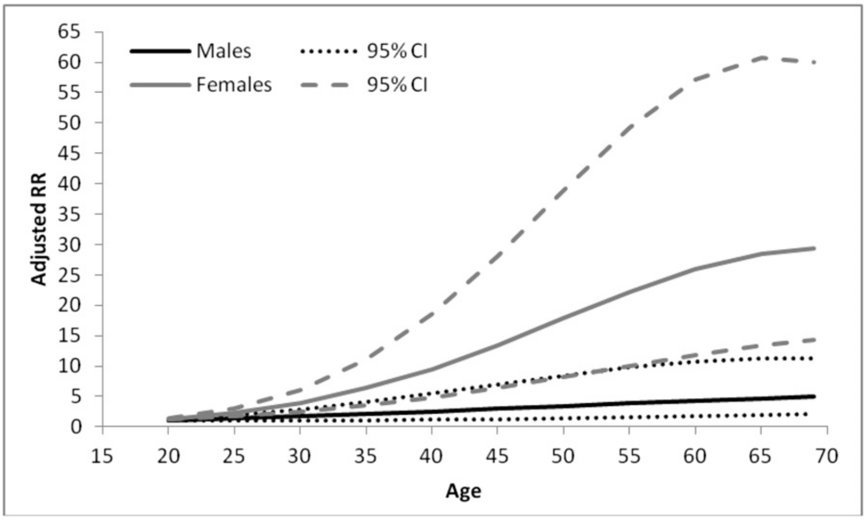

**SUPPLEMENTAL FIGURE 1**
Adjusted relative risk (RR) of diabetes at time of bariatric surgery attributed to age (age 18 = reference). Adjusted for gender, race, weight status at age 18, and change in BMI since age 18. Risk of diabetes increases until age 67. Thirteen participants ≥70 years were excluded from the figure.



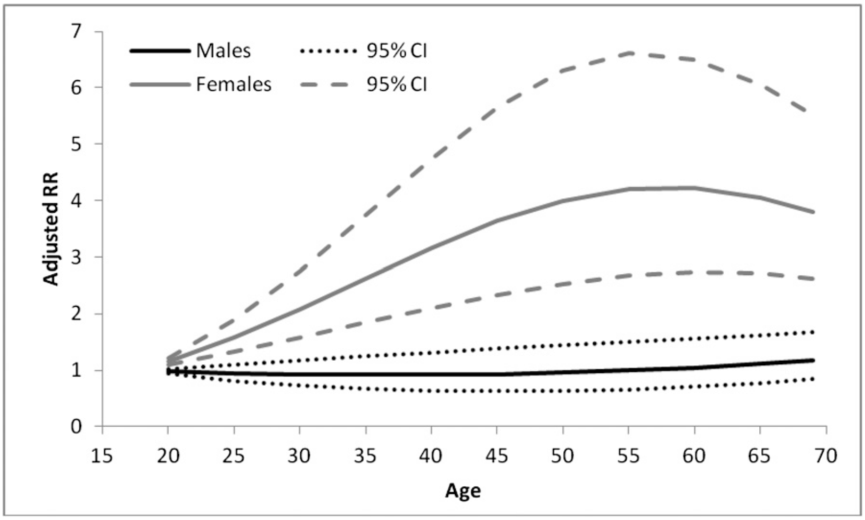

**SUPPLEMENTAL FIGURE 2**

Adjusted relative risk (RR) of hypertension at time of bariatric surgery attributed to age (age 18 = reference) by gender and weight status at age 18. Adjusted for change in BMI since age 18 and an interaction of weight status at age 18 and gender. Risk of hypertension increases until age 66 for men who were overweight at age 18 and until age 53 for men who were class 1 at age 18. Age was not significantly related to hypertension status in males who were normal weight or class 2/3 obese at age 18. Risk of hypertension increases until age 60 for women who were overweight at age 18 and until age 55 for women who were class 1 at age 18. Risk continues to increase with increasing age for women who were normal weight or class 2/3 obese at age 18. Twelve participants (5 men, 7 women) aged ≥70 years were excluded from the figure. To improve readability, CIs are not shown in this graph.




**SUPPLEMENTAL FIGURE 3**

Adjusted relative risk (RR) of hyperlipidemia at time of bariatric surgery attributed to age (age 18 = reference). Adjusted for weight status at age 18 and change in BMI since age 18. Risk of hyperlipidemia increases until age 70 for women and continues to increase for men. Eleven participants (4 men, 7 women) aged ≥70 years were excluded from the figure.




**SUPPLEMENTAL FIGURE 4**

Adjusted relative risk (RR) of obstructive sleep apnea at time of bariatric surgery attributed to age (age 18 = reference) by gender. Adjusted for weight status at age 18 and change in BMI since age 18. Risk of hyperlipidemia increases until age 66 for women. Age was not significantly related to obstructive sleep apnea status in men. Fourteen participants aged ≥70 years were excluded from the figure.

**SUPPLEMENTAL TABLE 4** Adjusted Relative Risk of Comorbidities at Time of Bariatric Surgery Attributed to Age, in Which the Relationship With Age Was Quadratic

| | Age, y | | | | | | |
|---|---|---|---|---|---|---|---|
| | 18 | 20 | 30 | 40 | 50 | 60 | 69 |
| Diabetes | 1.0 (Ref) | 1.28 | 3.69 | 8.30 | 14.49 | 19.61 | 20.74 |
| Hypertension | 1.0 (Ref) | | | | | | |
| Men | | | | | | | |
| Normal | 1.0 (Ref) | 1.02 | 1.17 | 1.36 | 1.61 | 1.95 | 2.34 |
| Overweight[a] | 1.0 (Ref) | 1.12 | 1.84 | 2.68 | 3.45 | 3.94 | 4.00 |
| Class 1 | 1.0 (Ref) | 1.09 | 1.56 | 1.98 | 2.23 | 2.23 | 2.01 |
| Class 2/severe[a] | 1.0 (Ref) | 0.96 | 0.85 | 0.86 | 0.996 | 1.31 | 1.88 |
| Women | | | | | | | |
| Normal | 1.0 (Ref) | 1.13 | 1.96 | 3.00 | 4.06 | 4.84 | 5.10 |
| Overweight | 1.0 (Ref) | 1.24 | 3.09 | 5.92 | 8.70 | 9.80 | 8.70 |
| Class 1 | 1.0 (Ref) | 1.21 | 2.62 | 4.37 | 5.62 | 5.55 | 4.39 |
| Class 2/severe | 1.0 (Ref) | 1.06 | 1.43 | 1.91 | 2.51 | 3.26 | 4.09 |
| Hyperlipidemia | | | | | | | |
| Men | 1.0 (Ref) | 1.11 | 1.75 | 2.56 | 3.46 | 4.32 | 4.94 |
| Women | 1.0 (Ref) | 1.29 | 3.97 | 9.53 | 17.82 | 25.94 | 29.39 |
| Obstructive sleep apnea | | | | | | | |
| Men[b] | 1.0 (Ref) | 0.98 | 0.93 | 0.92 | 0.96 | 1.05 | 1.18 |
| Women | 1.0 (Ref) | 1.15 | 2.09 | 3.16 | 4.00 | 4.22 | 3.80 |

All models were adjusted for gender, weight status at age 18, and change in BMI since age 18. Results are stratified by gender and/or weight status if interactions were significant. This table represents a synopsis of data contained in Supplemental Figures 1–4.

[a] Age was not significantly related to hypertension status in men who were overweight or class 2/3 obese at age 18.

[b] Age was not significantly related to obstructive sleep apnea status in men.