# Obesity negatively affects disease progression, cognitive functioning, and quality of life in people with multiple sclerosis

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# Background.

**Several observational studies have shown that obesity is an important risk factor to develop multiple sclerosis (MS), which is also supported by Mendelian randomization studies, but studies investigating the potential influence of obesity on MS disease progression have been inconclusive.**

# Aim

**We aimed to study the influence of body mass index (BMI) on disease progression, cognitive performance, and health-related quality of life among patients with multiple sclerosis (MS).**

# Methods

- **MS cases from an incident population-based nation-wide Swedish case-control study (included between 2005-2019)**
- **Patients had answered an extensive questionnaire at study inclusion with information on lifestyle and environmental factors**
- **Another questionnaire was sent out 2021 to capture changes in exposures**

# Methods

- **Patients were followed up to 15 years post-diagnosis through the Swedish MS registry regarding changes in:**

- **Expanded Disability Status Scale (EDSS),**
- **Multiple Sclerosis Impact Scale 29, and (MSIS29)**
- **Symbol Digit Modalities Test (SDMT)**

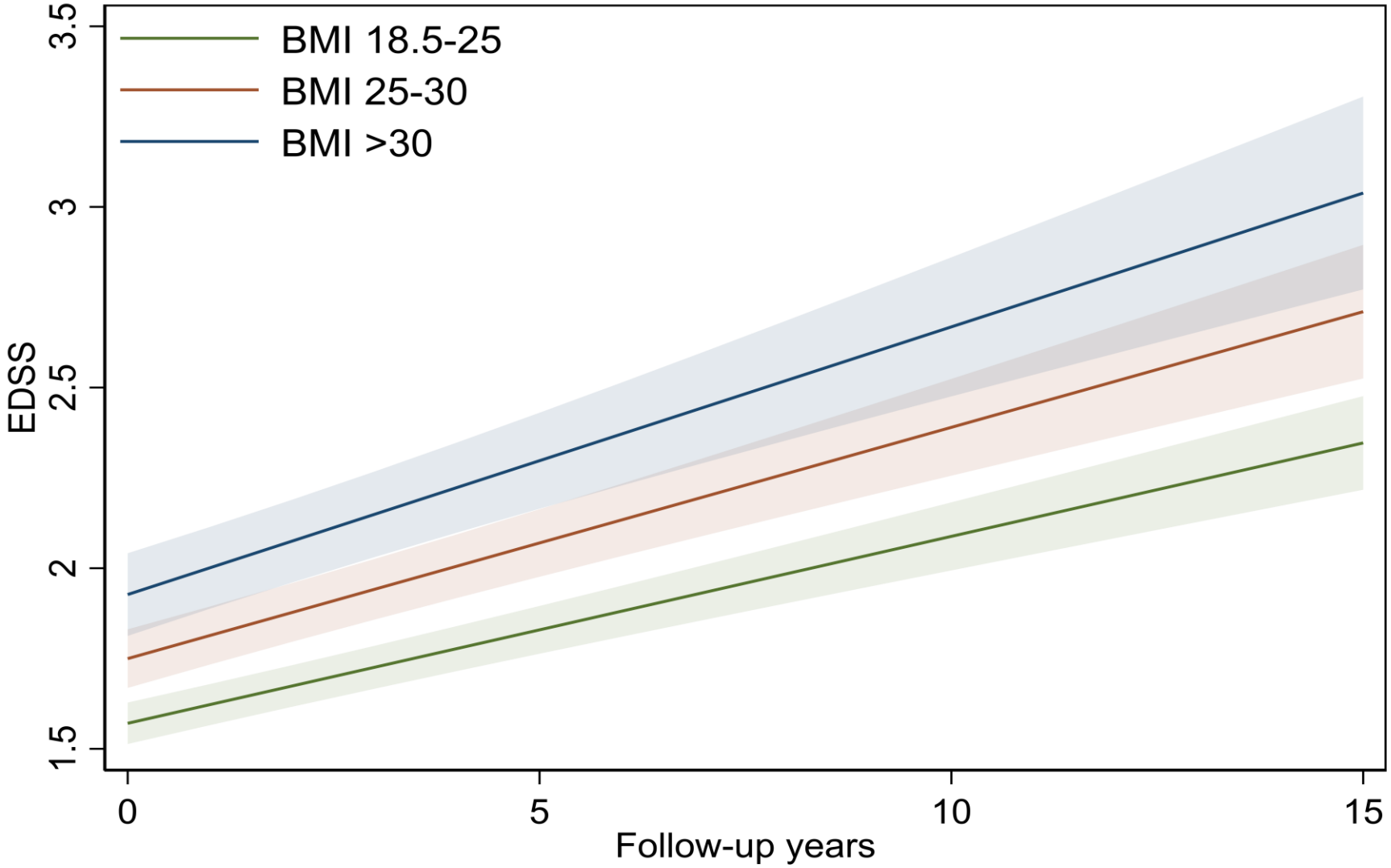
# Statistical Methods

- **Linear mixed models were used to analyse long-term changes**
- **Cox regression models were used to analyse**
  - **risk of 24-week confirmed disability worsening,**
  - **time to EDSS 3 and EDSS 4,**
  - **new lesions on magnetic resonance tomography (MRI)**
  - **patient-reported physical and psychological worsening** (≥ 7.5 p),
  - **processing speed worsening** (≥8 p)

# Results

- **We followed up 3249 individuals with MS, of which 74% were females.**
- **Mean age at baseline was 37.8 years.**
- **Compared to normal weight, obesity was associated with a 0.022-point faster annual increase in EDSS score (β for EDSS x time  0.022, 95% CI 0.003-0.041).**

# BMI och MS progression



# Results overall regarding confirmend disease worsening

| First clinical disease worsening (CDW) | | | | | |
|---|---|---|---|---|---|
| **BMI status** | **N** | **Years (SD)** | **Outcome (%)** | **HR (95% CI)[1]** | **HR (95% CI)[2]** |
| **Normal weight** | **1842** | **6.2 (4.4)** | **836 (45)** | **1.0 (reference)** | **1.0 (reference)** |
| **Overweight** | **933** | **5.7 (4.2)** | **438 (47)** | **1.10 (0.98-1.23)** | **1.02 (0.90-1.14)** |
| **Obesity** | **474** | **5.3 (3.8)** | **213 (45)** | **1.13 (0.98-1.32)** | **1.15 (0.99-1.34)** |

[1]crude; [2]adjusted for age at diagnosis, sex, disease phenotype, disease duration, baseline EDSS, disease-modifying therapy, and smoking

# BMI and risk of reaching EDSS 3.

HR with 95% CI of reaching EDSS 3, by BMI at diagnosis.

| BMI status (at diagnosis) | N | Years (SD) | Outcome (%) | HR (95% CI)[1] | aHR (95% CI)[2] |
|---|---|---|---|---|---|
| **Normal (18.5-24.99 kg/m$^2$)** | **1475** | **7.4 (4.6)** | **414 (28)** | **1.0 (reference)** | **1.0 (reference)** |
| **Over weight (25-30 kg/m$^2$)** | **713** | **6.9 (4.6)** | **206 (29)** | **1.08 (0.91-1.28)** | **1.05 (0.88-1.25)** |
| **Obesity (>30 kg/m$^2$)** | **355** | **5.9 (4,2)** | **124 (35)** | **1.51 (1.23-1.84)** | **1.43 (1.17-1.75)** |

[1]crude; [2]adjusted for age at diagnosis, sex, disease phenotype, disease duration, baseline EDSS, disease-modifying therapy, and smoking

# Results overall regarding EDSS 3 or 4 and Quality of Life

- **Obesity was associated with an increased risk of reaching EDSS 3 (HR 1.43 (1.17-1.75)) and EDSS 4 (HR 1.40 (1.07 - 1.73))**
- **Obesity was associated with increased risk of physical (HR 1.42 (1.19-1.69)) and psychological worsening (HR 1.23 (1.05-1.46))** (increased score of ≥ 7.5 p for each component, respectively)

# Results among those who had not changed BMI group

- **Among participants who did not change BMI group during follow-up, the differences were even greater**

  **HR to reach EDSS 3 was 1.53 (1.11-2.10)**

  **HR physical worsening was 1.70 (1.32-2.20)**

  **HR psychological worsening was 1.36 (1.05-1.75)**

- **Among participants who had not changed BMI group during follow-up, the HR of cognitive disability worsening was 1.51 (1.09-2.09) among obese participants, compared to those without obesity** (increased score of 8-point or more)

# BMI and risk of new leisons on MRI

**Overall sample**

| BMI status (at diagnosis) | N | Years (SD) | Outcome (%) | HR (95% CI)[1] | aHR (95% CI)[2] |
|---|---|---|---|---|---|
| Normal (18.5-24.99 kg/m$^2$) | 899 | 4.9 (3.2) | 397 (41) | 1.0 (reference) | 1.0 (reference) |
| Over weight (25-30 kg/m$^2$) | 459 | 4.7 (3.2) | 212 (46) | 1.18 (1.00-1.40) | 1.21 (1.02-1.44) |
| Obesity (>30 kg/m$^2$) | 235 | 4.1 (3.1) | 100 (43) | 1.22 (0.99-1.51) | 1.29 (1.03-1.62) |

**No change of BMI status during follow-up**

| BMI status (at diagnosis) | N | Years (SD) | Outcome (%) | HR (95% CI)[1] | aHR (95% CI)[2] |
|---|---|---|---|---|---|
| Normal (18.5-24.99 kg/m$^2$) | 473 | 5.3 (3.3) | 207 (44) | 1.0 (reference) | 1.0 (reference) |
| Overweight/obesity | 359 | 5.0 (3.3) | 182 (51) | 1.30 (1.06-1.60) | 1.35 (1.08-1.67) |

# Strenghts and weaknesses

- A large prospective cohort study
- Participation rate 93% at study inclusion
- All patients fulfill the McDonald criteria
- 94% of the patients could be followed in the Swedish MS register
- Possible to take a large number of potential confounding factors into account

# Weaknesses

- Self-reported information on BMI
- Potential residual confounding

# Conclusion

**Obesity appears to negatively influence both disease progression, health-related quality of life, and cognitive functioning in persons with MS.**

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Thank you for your attention! ☺

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