



Summary

Early-onset obesity is a severe disease, with the need of early diagnosis and treatment, without waiting for the development of comorbidities, to minimize long-term negative outcomes



Study Design

We examined the far-reaching effects of early-onset obesity on life expectancy and selected comorbidities. We searched the literature for studies assessing the prevalence and mortality risk of comorbidities in relation to BMI, BMI z-score and age, and studies assessing the duration of obesity in relation to obesity severity. We then selected studies with sufficient and reliable quantification of the effects of obesity. A total of 226 studies were assessed, of which 50 were included in the EObesity model. No extrapolation was used to fit the selected study results to the model, but in some cases interpolation was used to fill in the "gaps" in available data. These adjustments were used to produce risk tables and resulting graphs, which form the basis of all calculations in the EObesity model



Model Development

- 1 $R_{Mortality} = ((P_{T2DM} * R_{MortalityT2DM}) + (P_{CV} * R_{MortalityCV}) + \dots + (P_{Asthma} * R_{MortalityAsthma})) * RI_{DurationMortality}$
- 2 $R_{MorbidityT2DM} = P_{T2DM} * RI_{DurationT2DM}$
- 3a $DALY_{LY} = (R_{MorbidityT2DM} * DW_{T2DM}) + (R_{MorbidityCV} * DW_{CV}) + \dots + (R_{MorbidityAsthma} * DW_{Asthma})$
- 3b $DALY_{Total} = DALY_{LY1} + DALY_{LY2} + \dots + DALY_{LYX}$

To assess the consequences of early-onset obesity, obesity-related factors studied best and shown to influence mortality and co-morbidities were identified and included in the model, those factors are:

- age of onset (of obesity)
- severity (of obesity)
- duration (of obesity)
- age in combination with weight



Life expectancy and comorbidity risk factors were assessed separately to avoid inaccuracy by double counting.

1. Life expectancy was estimated by combining mortality risks with prevalence figures. This yielded into to an all-comorbidity risk, which was subsequently modified with a specific mortality-related duration factor
2. Comorbidity risk was estimated by combining prevalence factors with specific comorbidity duration factors
- 3a/b. Comorbidity risks as well as the life expectancy were further utilized to calculate the total burden of disease related to obesity (DALYs)

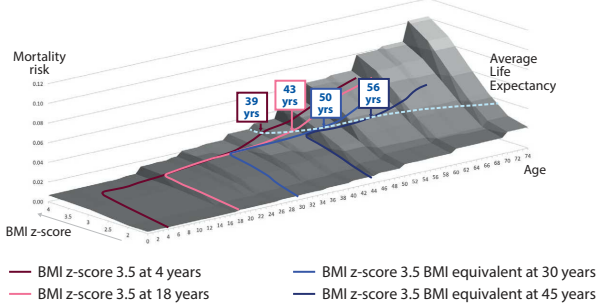
CV, cardiovascular; DALY, disability-adjusted life year; DW, disability weight; LY, life year; P, prevalence; R, risk; RI, risk increase; T2DM, type 2 diabetes mellitus



Outcomes

This model enables scenario-based assessments, highlighting the severe effects of early-onset obesity on life expectancy and health risks, validating the importance of early intervention for long-term health

Impact of early-onset obesity on accumulation of mortality risk leading to significant reduction in life expectancy



Impact of age at onset and magnitude of obesity on DALYs

Age at obesity onset	BMI z-score 2	BMI z-score 2.5	BMI z-score 3	BMI z-score 3.5	BMI z-score 4
5	23.5	37.6	44.5	48.5	49.7
10	23.4	36.6	43.5	46.7	48.7
15	23.3	36.4	42.3	45.6	47.5
20	23.1	35.3	40.3	43.6	45.5
25	22.0	33.2	37.4	41.3	43.1
30	21.7	31.9	35.9	38.9	40.0
35	21.3	29.8	34.4	36.5	36.8
40	20.1	27.6	32.1	34.1	34.3
45	19.0	26.3	29.8	31.0	31.9

- The model allows estimating the impact of early-onset obesity on life expectancy, DALYs and comorbidities
- Both the magnitude and duration of obesity are critical determinants of outcomes
- The age at obesity start has profound effect on life expectancy, with earlier onset leading to more years of life lost



FOR THE ABSTRACT

BMI, body mass index

For more information, please contact: EU_Medinfo@Rhythmtx.com.

Summary

Early weight reduction in paediatric obesity can reduce the negative impact on long-term outcomes including life expectancy and development of comorbidities

Study Design

Please see the graphical abstract "Early-Onset of Obesity-Model: Impact of early-onset obesity on life expectancy and on risks of comorbidities" for a description of the study design

Model

Please see the graphical abstract "Early-Onset of Obesity-Model: Impact of early-onset obesity on life expectancy and on risks of comorbidities" for a description of the model

Outcomes

A hypothetical patient example describes severe early-onset obesity with rapid weight gain in infancy, reaching a BMI z-score of 2.5 by age 2 and BMI z-score of 4 by age 4, and the effect of different degrees of weight loss at different ages.

Intervention	Life expectancy (years)	T2DM likelihood at age 35 (%)	CV event likelihood at age 35 (%)
None	37	54.9	39.2
1-point BMI z-score decrease at age 6	42	38.6	33.6
1.5-point BMI z-score decrease at age 6	50	36.3	28.6
2-point BMI z-score decrease at age 6	64	28.9	26.0

These results illustrate:

- The benefits of early weight reduction among patients with severe, early-onset obesity
- Benefits are slightly reduced with delayed intervention
- The significant impact of reducing BMI z-scores on life expectancy, even if patients remain with obesity
- The value of achieving a body weight that is close to, or within, normal range

Delaying the onset of weight loss reduces the benefits of intervention: A weight loss of 1.5 points in BMI z-score at ages 12, 18 or 30 increases life expectancy by 12, 10 and 5 years, respectively, with, in parallel, smaller reductions in the risk of comorbidities.

BMI, body mass index; CV, cardiovascular; T2DM, type 2 diabetes mellitus.

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