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Assessing the clinical impact of decreasing weight in young adults using the Metabo-Reno Cardiovascular Disease Model©

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Aim

- This study aimed to assess the clinical impact of reducing weight at different starting ages using the Metabo Reno Cardiovascular Disease Model (MRCDM©) before complications of obesity had occurred.

Introduction

- Health technology assessment bodies typically recommend weight-loss treatments for patients with obesity who already have comorbidities which tends to favour older patients.
- Preventing obesity-related complications, such as type 2 diabetes (T2D) and cardiovascular disease, in individuals that do not yet have comorbidities, such as younger patients is less common, although potentially more benefits can be achieved.

Methods

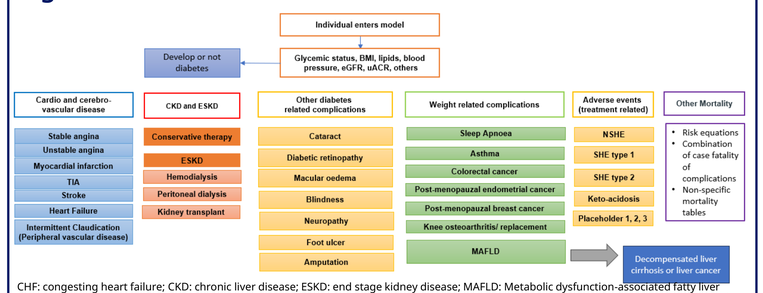
- The MRCDM© is a microsimulation model, with specific disease submodules and complications represented within a structure of Markov Health states (Figure 1).
- In the MRCDM©, different age cohorts were programmed: 20, 35 and 50 years of age.
- The starting BMI was 40 kg/m². BMI was reduced by 5, 10, 15, 20 and 25% (BMI values applied: 40-38-36-34-32-30 kg/m²). It was assumed that BMI stayed constant over time.
- Cholesterol and blood pressure were also kept constant over time and were both initiated at normal values.
- Baseline characteristics were taken from the STEP Teens and STEP 1 clinical trials (Table 1)[1,2]. Data from STEP Teens informed the 20-year age group, while STEP 1 provided data for the 35- and 50-year age groups.
- eGFR and uACR were following a natural progression over time [3,4].
- Development of T2D was predicted using the QDiabetes equation combined with Framingham offspring evolution of HbA1c in NGT individuals [5,6]. Once T2D developed UKPDS 90 progression was followed.
- To predict cardiovascular disease the Office based Framingham equation was used[8]. Framingham equations were also used to predict intermittent claudication, heart failure and recurrent events[9-11].
- Specific risk equations were used to predict metabolic dysfunction-associated steatotic liver disease (MASLD), weight-related cancer (WRC), total knee replacement (TKR), sleep apnoea, and end-stage kidney disease (ESKD).
- To predict mortality general US mortality and case fatality were applied.
- Evidence suggest that obesity and underweight have an impact on mortality independent of the incidence of complications that could be fatal. As a scenario an additional BMI related mortality factor was considered.
- The time horizon was 80 years. US costs and utilities were applied[12-15].
- The public healthcare payers' was considered using annual discounting rates of 3.0% on costs and outcomes.

Table 1: Baseline characteristics for the three age groups

Age (Y)	20	35	50
Proportion of males	38%	26%	26%
BMI (kg/m²)	40 to 30	40 to 30	40 to 30
SBP (mmHg)	120	126	126
DBP (mmHg)	73	80	80
Total cholesterol (mg/dL)	180	190	190
HDL-cholesterol (mg/dL)	43	49	49
LDL-cholesterol (mg/dL)	114	111	111
Triglycerides (mg/dL)	110	127	127
HbA1c	5.5%	5.7%	5.7%
eGFR (mL/min/1.73m²)	98	96	96
uACR (mg/g)	6	6	6
History of myocardial infarction	0	3%	3%
Hypertension	0	36%	36%
Asthma	0	12%	12%

Abbreviations: HbA1c: haemoglobin A1c, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, BMI: Body mass index, eGFR: Estimated glomerular filtration rate; uACR: urine albumin-creatinine ratio

Figure 1: MRCDM© model structure



CHF: congesting heart failure; CKD: chronic liver disease; ESKD: end stage kidney disease; MAFLD: Metabolic dysfunction-associated fatty liver disease; MI: myocardial infarction; Mort: mortality; NSHE: non-severe hypoglycaemic event; PVD: peripheral vascular disease; UA: unstable angina; SHE: severe hypoglycaemic event (type 1: requiring non-medical assistance, type 2: requiring medical assistance); TIA: transient ischaemic attack

Results

- At the age of 20 years, with a BMI of 30 versus 40 kg/m² the MRCDM predicts a LE of 76.34 versus 74.18 years (losing 10 points of BMI extends LE by 2.16 years).
- In the older age groups (35 and 50 years), the same BMI reduction results in less 1.98 and 1.41 years LE respectively (see Table 2).
- Predictions are aligned with the US life expectancy (LE) of 77.43 years for an average US citizen with BMI 29.27 kg/m² [16].
- Survival curves are shown in Figure 2.

Table 2: Undiscounted life expectancy per BMI and age group

	BMI 40	BMI 38	BMI 36	BMI 34	BMI 32	BMI 30
Age 20						
Without BMI adj	74.18	74.48	75.03	75.48	75.98	76.34
With BMI adj	68.55	69.87	71.15	72.58	73.79	74.95
Age 35						
Without BMI adj	75.02	75.82	75.39	76.69	76.23	77.14
With BMI adj	70.45	72.80	71.59	72.80	71.59	75.99
Age 50						
Without BMI adj	78.95	79.25	79.48	79.79	80.15	80.45
With BMI adj	75.23	76.13	76.98	77.94	78.82	79.65

Figure 2: Survival curves of cohorts of patients at starting ages of 20, 35, 50 years and with BMI ranging from 30-40. Mortality approach without BMI adjustment.

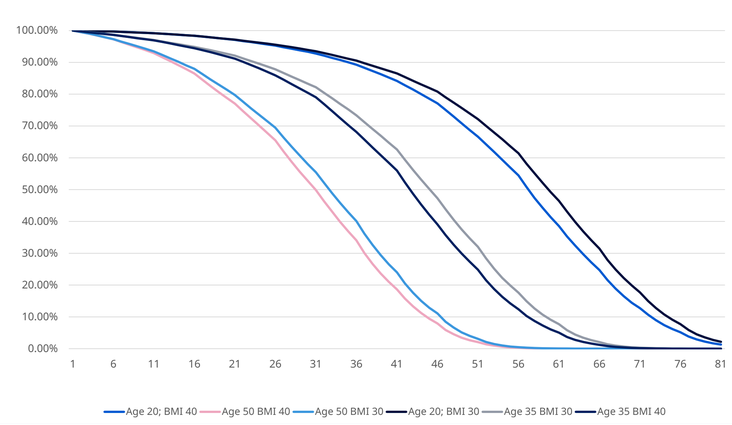
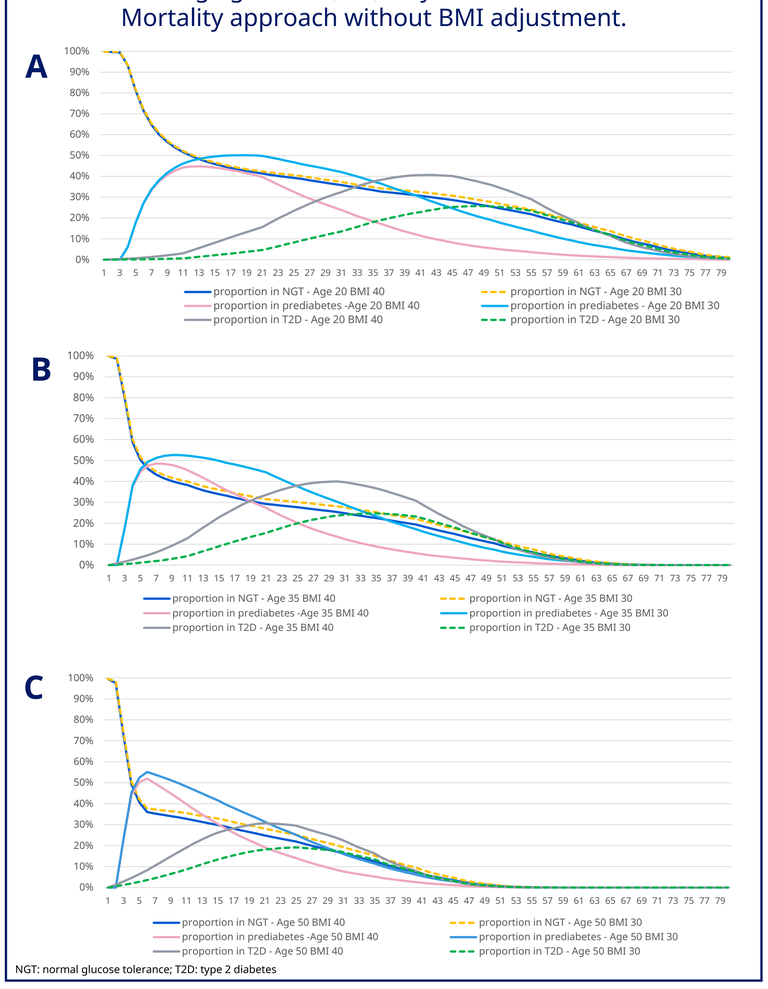


Figure 3: Evolution of glycaemic status over time in patients at starting ages of 20, 35, 50 years and BMI of 30 to 40. Mortality approach without BMI adjustment.



NGT: normal glucose tolerance; T2D: type 2 diabetes

- The percentage of patients per glycaemic status is shown in Figure 3.
- The percentage of individuals with BMI 40 kg/m² that develop T2D goes up to 40% for the 20- and 35-year age groups. In the 50-year age group it is 30%. With a BMI of 30 kg/m² this percentage decreases to only 30% in the 20- and 35-year age groups and to 20% in the 50-year age group .
- Table 3 shows that an intervention with a higher impact on BMI provides more life years gained, more QALYs gained, and generates savings in the long-term.
- These gains (QALYs and total costs) are higher in the younger cohort compared to older cohorts.

Table 3: Health economic outcomes for the different age groups

Age 20 years	BMI 40	BMI 38	BMI 36	BMI 34	BMI 32	BMI 30
Without BMI adjustment to mortality						
LYs	26.63	26.7	26.81	26.9	27	27.06
QALYs	13.38	13.54	13.73	13.93	14.13	14.3
Direct costs (USD)	80,240	76,362	71,219	66,980	62,886	57,963
With BMI adjustment to mortality						
LYs	25.02	25.38	25.73	26.1	27.06	26.67
QALYs	12.98	13.21	13.47	13.73	14.3	14.19
Direct costs (USD)	69,013	67,829	65,475	62,270	57,963	56,419
Age 35 years	**BMI 40**	**BMI 38**	**BMI 36**	**BMI 34**	**BMI 32**	**BMI 30**
Without BMI adjustment to mortality						
LYs	22.87	23.11	22.98	23.36	23.24	23.5
QALYs	11.27	11.81	11.53	12.36	12.1	12.59
Direct costs (USD)	110,677	103,140	107,619	93,835	98,334	90,149
With BMI adjustment to mortality						
LYs	21.08	21.95	21.52	21.95	21.52	23.06
QALYs	10.74	11.43	11.08	11.44	11.08	12.45
Direct costs (USD)	98,685	94,929	96,647	94,929	96,647	89,002
Age 50 years	**BMI 40**	**BMI 38**	**BMI 36**	**BMI 34**	**BMI 32**	**BMI 30**
Without BMI adjustment to mortality						
LYs	18.81	18.94	19.03	19.17	19.31	19.42
QALYs	8.88	9.2	9.55	9.92	10.28	10.62
Direct costs (USD)	102,263	97,801	93,311	88,798	85,513	81,178
With BMI adjustment to mortality						
LYs	17.02	17.45	17.86	18.29	18.68	19.05
QALYs	8.29	8.71	9.15	9.64	10.09	10.43
Direct costs (USD)	90,748	88,825	86,838	83,.911	81,658	80,055

Abbreviations: BMI: body mass index; LY: life years; QALY: quality adjusted life years

Limitations/Discussion

- Hypothetical cohorts are used.
- Natural evolution of several risk factors (lipids and blood pressure) was not included to ensure only the impact of changes in BMI is studied.
- Clinical trials were used to define baseline characteristics, however real word data could have been collected and used for each cohort.
- Non-specific mortality was not corrected for the different case fatalities associated to the complications already included in the MRCDM© predictions (due to unavailable US disease specific mortality data).
- The BMI adjustment to mortality is key to assess the additional impact BMI may have on mortality that could otherwise be missed. The BMI impact on mortality linked to complications is already included, via the case fatality applied to cardio-, cerebrovascular and weight related complications dependent of BMI.

Conclusion

- The evidence provided in these analyses shows the value of managing obesity at any age group, but supports the hypothesis that treatment should start as early as possible to provide the following better benefits:
  - Increased life expectancy
  - Decrease and delay the incidence of T2D
  - Decrease incidence of CVD, microvascular and weight related complications
  - Increase total QALYs
  - Reduce healthcare costs to treat obesity related complications

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References:

(**1**) Weghuber et al. New England Journal of Medicine. 2022;387(24):2245-2257; (**2**) Wilding et al. Diabetes Obes Metab. 2022;24(8):1553-1564 (**3**) Grams et al. Nephrol Dial Transplant. 2021;36(9):1685-1693. (**4**) Coresh et al. Lancet Diabetes Endocrinol. 2019;7(2):115-127. (**5**) Hippisley-Cox J, Coupland C. BMJ. 2017;359:j5019. (6) Pani et al. Diabetes Care. 2008;31(10):1991-1996. (**7**) Leal et al. Diabet Med. 2021;38(10). (**8**) Framingham Heart Study https://www.framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk / (**9**) Kannel et al Arch Intern Med. 1999;159(11):1197-1204; (**10**) Murabito et al Circulation. 1997;96(1):44-49. (**11**) D'Agostino et al Circulation. 2008;117(6):743-753. (**12**) Kim et al. J Manag Care Spec Pharm. 2022;28(7):740-752; (**13**) McEwan et al. *J Med Econ. 2025;28(1):268-278.* ; (**14**) Hammer et al. *Med Decis Making. 2006;26(4):391-400..* ; (**15**) Laxy et al. *Int J Obes (Lond). 2018;42(3):318-326..* ; (**16**) World Bank Open Data. World Bank Open Data. Accessed June 18, 2025. https://data.worldbank.org.