Do existing risk equations fail to adequately account for the relationship between body mass index and mortality in subjects with type 2 diabetes?

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Objectives

- There is a substantial body of epidemiological evidence relating body-mass index (BMI) to increased risk of cardiovascular disease and all-cause mortality (ACM) in subjects with type-2 diabetes mellitus (T2DM) [1-2].
- Cardiovascular (CV) and mortality risk equations typically incorporate the effects of elevated BMI via the inter-relation between modifiable CV risk factors (such as cholesterol and systolic blood pressure) and BMI; this approach may underestimate the risk of mortality associated with BMI.

Methods

- This study used the IMS Core Diabetes Model (CDM) [3-4], a lifetime simulation model designed to assess the health outcomes and economic consequences of interventions in T2DM or T2DM, to evaluate the degree to which the association between all cause mortality and BMI is captured by the CV and mortality risk equations included within the model.
- The CDM was applied to project the lifetime history of 1858 individual patient level complications and mortality as assessed for each individual patient profile and results were stratified by age and level of BMI.
- The association between BMI and QALE was explored using two distinct approaches:
  1. The risk of CV incidence and related death was projected through the original and unmodified UKPDS equations; (referred to as ‘UKPDS’).
  2. The long-term risk of death following a history of relevant complications and non-diabetes specific death risk scores were subsequently adjusted for BMI. A hazard ratio of 1.29 per kg/m2 higher BMI was assumed, based on data from a published prospective analysis of 90,000 adults [2]. BMI correlated risk factors such as HDL, SBP and LDL ratio were set to have no effect in the applied CV risk equations such that mortality difference was predominantly determined by BMI change; (referred to as ‘BMI adjust’).

Results

- Results were obtained for 1,853 subjects with mean age 63.5 years, 53% male; 16% current smokers; duration of diabetes 9.5 years; HDL: 4.74 mmol/l; SBP: 135 mmol/l; total cholesterol: 7.53 mmol/l and BMI 30.4 kg/m2. Table 1 reports summary statistics by BMI category.
- The relationship between discounted LE (Figure 1), discounted quality adjusted life expectancy (Figure 2) and age stratified by obesity shows a considerable degree of discordance between the two scenarios modeled.

- Using UKPDS mortality risk the predicted mean discounted LE was 11.8 years with each unit increase in BMI associated with a 0.05 years less life expectancy. Using BMI specific mortality decreased mean discounted LE to 10.85 years; with each unit increase in BMI linearly associated with a 0.17 years reduction in LE.
- Using UKPDS mortality risk the predicted QALE was 7.50 years (95% CI: 7.38 to 7.64) while using the BMI adjusted mortality risk QALE was 7.34 years (95% CI: 7.20 to 7.47). Figure 3 reports change in discounted QALE as a function of units change in BMI stratified by BMI category.

Table 1: Summary statistics of NHANES population used in the present analysis.

<table>
<thead>
<tr>
<th>N (%)</th>
<th>All</th>
<th>Normal</th>
<th>Overweight</th>
<th>Obese I</th>
<th>Obese II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Yrs) (SD)</td>
<td>63.81 (12.10)</td>
<td>67.07 (13.49)</td>
<td>65.40 (11.73)</td>
<td>62.09 (10.82)</td>
<td>58.70 (10.38)</td>
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<tr>
<td>Male [Proportion] (%)</td>
<td>0.51 (198)</td>
<td>0.55 (262)</td>
<td>0.49 (290)</td>
<td>0.51 (292)</td>
<td>0.45 (145)</td>
</tr>
<tr>
<td>systolic blood pressure (SD)</td>
<td>134.02 (21.09)</td>
<td>137.50 (24.22)</td>
<td>135.09 (20.29)</td>
<td>132.00 (20.10)</td>
<td>128.01 (20.08)</td>
</tr>
<tr>
<td>HDL cholesterol (SD)</td>
<td>42.90 (18.85)</td>
<td>31.58 (15.77)</td>
<td>42.35 (12.87)</td>
<td>46.01 (12.87)</td>
<td>48.35 (12.69)</td>
</tr>
<tr>
<td>HbA1c (SD)</td>
<td>7.39 (1.79)</td>
<td>7.49 (2.01)</td>
<td>7.38 (1.81)</td>
<td>7.41 (1.67)</td>
<td>7.28 (1.66)</td>
</tr>
<tr>
<td>Body mass index (kg/m2) (SD)</td>
<td>23.67 (1.73)</td>
<td>23.67 (1.73)</td>
<td>23.67 (1.73)</td>
<td>23.67 (1.73)</td>
<td>23.67 (1.73)</td>
</tr>
</tbody>
</table>

Figure 1: Discounted life expectancy predicted by the CDM and stratified based on age and level of obesity.

Figure 2: Discounted quality adjusted life years per unit change in BMI for the ‘BMI adjust’ and UKPDS equations stratified by BMI category.

Figure 3: Change in discounted quality adjusted life years per unit change in BMI for the ‘BMI adjust’ and UKPDS equations stratified by BMI category.

Conclusion

- The management of weight, either by avoiding therapy related or natural obesity weight gain, and promotion of weight loss is essential for the management of diabetes management.
- In the presence of conventional modifiable CV risk factors, such as SBP and cholesterol, may not fully capture the association between weight change and CV and all-cause mortality risk.
- Failure to adequately incorporate the deleterious effect of increasing levels of BMI on risk of mortality may substantially distort the health economic assessment of type 2 diabetes specific therapies, particularly those associated with the avoidance of weight gain or weight loss.

References


Acknowledgments

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