The model for the weight course included the weight during treatment with diet alone and during the first antidiabetic pharmacological treatment, if any. Thus all weight measurements were used for persons treated with diet only and for persons receiving only one type of antidiabetic drug. For the rest of the persons only weight measurements done during treatment with diet and during the first type of antidiabetic drug treatment were used. That is, the individuals were censored at the time when the first treatment stopped, if ever.

Let \( y_i = (y_{i1}, y_{i2}, \ldots, y_{in_i})^T \) denote the \( n_i \) measurements of weight for the \( i \)'th individual taken at the time points \( t_i = (t_{i1}, t_{i2}, \ldots, t_{ni})^T \), where time is measured in years since diabetes diagnosis. The linear mixed model can then be written as

\[
y_i = X_i \beta + Z_i b_i + e_i
\]

where the design matrix \( X_i \) contains explanatory variables for the mean (fixed effect) \( \beta \), the design matrix \( Z_i \) contains explanatory variables for the random effects \( b_i \) and \( e_i \) are errors. We assume that \( b_i \) and \( e_i \) are independent and both are normally distributed with zero mean and variance \( B \) resp. \( \sigma^2 I \), where \( I \) is the identity matrix. Then \( \text{var}(y_i) = Z_i B Z_i^T + \sigma^2 I \). In this model weight measurements for different persons are assumed to be independent, whereas weight measurements from the same person are correlated.

A piecewise linear curve can be modelled by an intercept, a slope and changes in the slope. This was included in the design matrix \( Z_i \) which for the \( i \)'th individual was obtained as

\[
Z_i = [1 \ t_i \ (t_i - 0.4) \ (t_i - s_i)]
\]

where \( t_i \) is time from diagnosis, \( s_i \) is time of initiation of first antidiabetic drug treatment and \((x)_+ = x \) when \( x \geq 0 \) and 0 otherwise. The time for the first change in the slope, at 0.4 years after diagnosis, was determined from preliminary analyses based on plots of the data as well as on the fit of various models with changes at different points in time. Only in 17 patients was the antidiabetic pharmacological treatment already started at 0.4 years after diagnosis.

For the individuals who start on the first antidiabetic drug treatment in the period between
diagnosis and 0.4 years after diagnosis there is only one change in the slope, namely at the initiation of first treatment, i.e. there is no change at 0.4 years. For those who do not start on antidiabetic drug treatment during follow-up, there will only be one change of the slope (at 0.4 years after diagnosis).

The design matrix $X_i$ for the mean was written for the $i$'th individual as

$$X_i = \begin{bmatrix}
1 & a_i & r_i & h_i & t_i & a_i & r_i & h_i & (t_i-0.4) & (t_i-0.4) & r_i & (t_i-s_i) & (t_i-s_i) & a_i & (t_i-s_i) & r_i
\end{bmatrix}$$

where $a$ denotes age at diabetes diagnosis (40–64 years, 65 years or over), $r$ denotes first antidiabetic treatment (sulphonylureas, metformin, combination of sulphonylureas and metformin, insulin, diet alone [i.e. no antidiabetic pharmacological treatment during the observation period]), $h$ denotes HbA$_1c$ measured at diabetes diagnosis (continuous variable), $t$ denotes time from diabetes diagnosis, $s$ denotes time of initiation of first antidiabetic drug treatment and $(x)_+ = x$ when $x \geq 0$ and 0 otherwise.

The result of estimation in this model is shown in ESM Tables 1 and 2. The main result is the non-significant effects of the change in slope at time of initiation of antidiabetic drug treatment (ESM Table 1). Thus the average change in the slope at initiation of treatment is 0. However, the model still includes a change in the slope at initiation of treatment as a random effect. Thus the piecewise linear curves for each individual are still allowed to change slope at initiation of drug treatment, but the changes have a mean of 0. The intercept and the slope are negatively correlated (ESM Table 2), which implies that a person with a higher intercept than the mean intercept tends to have a slope that is lower than the mean slope. The large negative correlation between slope and change in slope at 0.4 years after diagnosis indicates that a lower slope than on average from diabetes diagnosis to 0.4 years after is followed by a larger change in slope that on average.

The magnitude of the correlation between two weight measurements for the same person depends on the covariance matrix for the random effects ($b_i$) as well as on the time points for the measurements.
In the model restricted maximum likelihood (REML) was used for estimation. Wald tests were used to test for fixed effects (mean effects) in a backward reduction. The analyses were made using PROC MIXED in SAS version 6.12 on a UNIX computer.