The twin cycle hypothesis

Substantial weight loss in people with type 2 diabetes will:

**Liver**
- Decrease fat – improve insulin action
- and
- normalise overnight blood sugar

**Pancreas**
- Decrease fat – normalise the insulin response to eating

*and*
The Counterpoint study – Type 2 diabetes, 800kcal diet

Liver

Pancreas
Reversibility of type 2 diabetes

The pathophysiological defects in the liver and pancreas are reversible – if diabetes duration <4yr

Can long duration type 2 diabetes also be reversed?
The Counterbalance Study –

Counteracting Beta cell failure by Long term Action to Normalize Calorie intake

Questions:
Can people with longer duration type 2 diabetes reverse to normal?
Is the reversal of type 2 diabetes durable if body weight remains stable?
Protocol for CounterBalance study

- **T2DM < 4 yr**
  - Very low calorie diet
  - 0 1 4 8 weeks
  - Stepped return to normal eating

- **T2DM > 8 yr**
  - Very low calorie diet
  - 0 1 4 8 weeks
  - Weight maintenance
  - 10 + 6 months

Weeks
## Counterbalance Subjects

<table>
<thead>
<tr>
<th></th>
<th>0-4y (n=15)</th>
<th>8-23y (n=14)</th>
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<tbody>
<tr>
<td><strong>Diabetes duration</strong></td>
<td></td>
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<tr>
<td><strong>Age (yr)</strong></td>
<td>52.1 ± 2.6</td>
<td>61.6 ± 2.0</td>
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<tr>
<td><strong>Weight (kg)</strong></td>
<td>99.0 ± 3.7</td>
<td>96.9 ± 3.8</td>
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<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>34.6 (27.6-38.0)</td>
<td>33.0 (29.4-45.7)</td>
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Results: weight loss during diet

Weight loss: 14.6 ± 0.8 % vs. 14.5 ± 0.7 %

p=0.662
Fasting plasma glucose during diet

Short duration

Long duration

Steven et al. Diabetic Med 2015
By diabetes duration

- <4 y: 5.8 mM
- 8-12 y: 6.2 mM
- >12 y: 10.6 mM

Spearman 0.501; p=0.006

Steven et al Diabetic Med 2015