Prediabetes, T2D and Weight Management
The Nexus between Obesity and Dysglycaemia
Estimated prevalence of T2DM in Australia

Obesity and diabetes rates in Australia

Travelling companions

Data from AusDiab 2000

- The AusDiab 2000 findings, Australians ≥ 25 years old:
  - 7.4% had diabetes (doubled since 1981)
  - 16.3% had pre-diabetes (IFG/IGT*)
  - 59.6% were mildly overweight or obese

Obesity as a risk factor for T2D

Incidence of diabetes Ausdiab 2005 according to baseline glucose tolerance status
### Prevention of T2D: Selected Lifestyle Modification Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>N</th>
<th>Baseline BMI (kg/m²)</th>
<th>Intervention Follow-up Period (years)</th>
<th>RRR (%)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Prevention Program</td>
<td>Finland</td>
<td>523</td>
<td>31</td>
<td>4</td>
<td>39%</td>
<td>22</td>
</tr>
<tr>
<td>Da Qing Diabetes Prevention Program</td>
<td>China</td>
<td>577</td>
<td>25.8</td>
<td>6</td>
<td>51%</td>
<td>30</td>
</tr>
<tr>
<td>Diabetes Prevention Program</td>
<td>USA</td>
<td>3234</td>
<td>34.0</td>
<td>2.8</td>
<td>58%</td>
<td>21</td>
</tr>
</tbody>
</table>

NNT, number needed to treat; RRR, relative risk reduction; T2D, type 2 diabetes.


### Lifestyle Intervention More Effectively Prevents Diabetes as Populations Age

![Graph showing diabetes prevention program](image)

**Graph legend:**
- Diabetes Prevention Program (N=3234)
- Placebo
- Metformin
- Lifestyle

**Note:** The Diabetes Prevention Program showed that lifestyle interventions were superior to placebo in reducing diabetes risk, especially in older populations.

### Treatment of prediabetes to prevent new onset T2D diabetes

**Weight loss interventions shown to delay or prevent T2D**

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Follow-up Period (years)</th>
<th>Reduction in Risk of T2D (%) (P-value vs placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Prevention Program</td>
<td>Baseline</td>
<td>3.8 years</td>
</tr>
<tr>
<td>SENOS study</td>
<td>4 years</td>
<td>87% (P=0.003)</td>
</tr>
<tr>
<td>DBC/2006/NO-300 CONCORD/2006</td>
<td>2 years</td>
<td>79% (P=0.016)</td>
</tr>
<tr>
<td>SOD Obesity and Prediabetes</td>
<td>1 year</td>
<td>84% (P=0.01)</td>
</tr>
<tr>
<td>S.O.S</td>
<td>10 years</td>
<td>79% (P=0.001)</td>
</tr>
</tbody>
</table>

**SEQUEL Prediabetes/Metabolic Syndrome Cohort (Phentermine/Topiramate)**

**Graph:**
- ITT/LOCF Analysis

**Graph legend:**
- 10–20% weight loss
- Magnitude of weight loss (%)

**Note:** The ITT/LOCF analysis demonstrated a significant reduction in diabetes risk with weight loss interventions, especially in the 10–20% weight loss category.

### Relationship Between Weight Loss and Prevention of Type 2 Diabetes

**Graph:**
- ITT/LOCF Analysis

**Graph legend:**
- Annualized incidence rate of T2D
- ITT, intent to treat; LOCF, last observation carried forward.


### 5–10% weight loss is clinically meaningful

**Graph:**
- Weight loss required for therapeutic benefit (%)

**Graph legend:**
- Obesity complication
- Maximum benefit at 10%
- Triglycerides still decreasing at >15%
- HbA1C still decreasing at >15%
- Improves steatosis, inflammation, and mild fibrosis
- Improves symptoms and joint stress mechanics
- Continues to improve with weight loss
- Blood pressure still decreasing at >15%

![Graph showing weight loss benefits](image)

**Graph legend:**
- Maximum benefit at 10%
- Triglycerides still decreasing at >15%
- HbA1C still decreasing at >15%
- Improves steatosis, inflammation, and mild fibrosis
- Improves symptoms and joint stress mechanics
- Continues to improve with weight loss

**Note:** A 5–10% weight loss is clinically meaningful for a range of health outcomes, including improved health-related quality of life. **Cefalu WT et al. Diabetes care 2015;38(8):1567-82. Wright F et al. J Health Psychol. 2013;18:574-86.**

### Diabetes and weight loss

**Graph:**
- Weight loss interventions shown to delay or prevent T2D

**Graph legend:**
- Minimum benefit at 10%
- Triglycerides still decreasing at >15%
- HbA1C still decreasing at >15%
- Improves steatosis, inflammation, and mild fibrosis
- Improves symptoms and joint stress mechanics
- Continues to improve with weight loss

**Note:** Weight loss interventions are effective in improving health outcomes, especially in patients with type 2 diabetes. **Garvey WT, et al. Diabetes Care. 2014;37:912-921.**
Glycaemic control deteriorates over time

Lifestyle Modification
- UKPDS pre-trial “nutrition run-in” (3 months)
  - NHMRC type diet
  - Reduced intake of high fat food, high CHO
  - 500 kcal deficit daily
  - 0.5-1 kg/week
- After 3 months:
  - Lost 3.5 kg
  - HbA1c dropped by 1.9%

Effect of Weight Reduction on Haemoglobin A1c in weight loss trials of Type 2 Diabetes Patients (Apr 18th 2017)

Aims: To quantify the effect of weight loss on HbA1c at group level based on data from published weight loss trials in overweight and obese type 2 diabetes patients.
- January 1990 through December 2012
- 58 eligible articles
- 124 treatment groups.
- 17,204 subjects

Our Ability to Achieve Tight Glycemic Control With Several Therapies is Limited By:
- Hypoglycemia
- Weight Gain

Diabetes blood glucose treatment with a view to mitigating weight gain and assisting weight loss
An example of the implementation of a ‘Weight sensitive algorithm’

1st Line  Metformin
2nd Line  SGLT2i OR GLP1a
3rd Line  Basal Insulin

But what if that is insufficient?
2016 Addition to the T2D guidelines

Metabolic surgery in the treatment algorithm of T2D

Summary of surgical treatment algorithm:

- Obese class 1 - 3 not achieving control with optimal therapy: Consider metabolic surgery
- Class 2 obese not achieving glycaemic targets: Recommend metabolic surgery
- Class 3 obese, irrespective of glycaemic control: Recommend metabolic surgery

Systematic Review & Meta-Analysis (2009)
T2DM response to bariatric surgery


Conclusion - Diabesity

- These two epidemics are inseparable
- They share the same environmental determinants
- They are both conditions of dysregulation
- The need to be addressed simultaneously
- Primary prevention will involve a whole of society approach
- We work in the area of secondary prevention and management of these conditions
- We have clear clinical pathways, therapies and responsibilities in managing diabesity