NEWS BRIEFING
Prevention of Type 2 Diabetes

Moderated by:
Edward W. Gregg, PhD
Embargo Policy

• All recordings are for personal use only and not for rebroadcast online or in any format.
• Information presented today in this briefing is under embargo.
• Please consult the top of each press release for embargo dates and times.
• Please respect the scientist. Only take photos if the presenter allows it and not with a flash.
PREVIEW Study Results
PREvention of Diabetes through Lifestyle Intervention and Population Studies Around the World

The PREVIEW diet / exercise / behavioural intervention

Ian Macdonald, University of Nottingham
Edith Feskens, Wageningen University on behalf of the PREVIEW consortium
Disclosures

**Funding sources**
- EU FP7 (FP7/2007-2013) grant agreement # 312057
- National Health and Medical Research Council - EU Collaborative Grant, AUS
- The Glycemic Index Foundation Australia through royalties to the University of Sydney
- The NZ Health Research Council (14/191) and Univ of Auckland Faculty Research Development Fund
- The Cambridge Weight Plan – donation of all products for the 8-weeks LED
- Several national funds in each participating country

**Ian Macdonald**
- Industry Advisory Boards: Nestle Research, European Juice Manufacturers, Novozymes, Mars (Inc, Europe, and Petfood),
- ILSI Europe – Dietary Carbohydrates Task Force
- Research Funding: EU, BBSRC, Innovate UK.
- Government: Public Health England – Scientific Advisory Committee on Nutrition
- Editorship: International Journal of Obesity
US Diabetes Prevention Program

Diet & Exercise target was >7% weight loss and > 150 min exercise per week (moderate intensity - e.g. brisk walking)

New cases of Type 2 DM

Almost 50% reduction over 4 years
Main Objective

To investigate if a high-protein, low-GI (glycemic index) diet in combination with moderate or high intensity physical activity can reduce the incidence of type-2 diabetes in people with overweight and prediabetes compared with the currently recommended diet (i.e. less protein and a medium GI)

Was a 3-yr randomized, controlled, multi-centre trial in over 2,200 participants
A total of 2223 subjects started
A total of 1857 achieved 8% weight loss
A total of 962 subjects completed 3 y

Attrition rates were similar in the 4 groups

543: withdrew consent for personal reasons
296: lost to follow-up
122: did not reach 8% weight loss
103: significant non-compliance with the study protocol or lack of cooperation
51: general condition contraindicated continuing the study, as judged by the Investigator
15: serious adverse event
79: other

CID: Clinical Investigation Day. LCD: Low Calorie Diet
Results: T2D – all four intervention groups

- T2D cases = 62
- Probability of not getting T2D ≈ 96%
- Cumulative incidence rate ≈ 4%
- Cases among drop-outs not known (yet)
- T2D cases much lower than estimated based on previous DP studies and our estimated incidence after 3 years:
  - 15.8% in MP;
  - 10.5% in HP
The Vitamin D and Type 2 Diabetes (D2d) Study—A Multicenter Randomized Controlled Trial for Diabetes Prevention

Anastassios G. Pittas, MD, MS
The why

• More than 84 million Americans are at high risk for type 2 diabetes based on have prediabetes. Lifestyle changes lower risk but are difficult to implement and maintain. Easier approaches that can be applied at the public health level may be needed.

• Observational studies have consistently reported an association between low blood vitamin D level and development of diabetes. However, whether vitamin D supplementation lowers risk of developing diabetes is not known.

• We did the vitamin D and diabetes (D2d) study to answer this question.
The how

Goal: detect a difference between vitamin D and placebo of 25% or more, i.e., the study would be less likely to detect a benefit smaller than that.
The where
Results: Mean blood vitamin D level
Safety: Pre-specified adverse events of interest

Mean follow-up: 2.5 years
New-onset diabetes

- Vitamin D (N=1211 randomized): 9.4% per year (N=293)
- Placebo (n=1212 randomized): 10.7% per year (N=323)
Rates free of diabetes between vitamin D and placebo

Hazard ratio for new-onset diabetes
0.88 (95%CI 0.75 to 1.04); p = 0.12
Comparison with other similar trials

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Intervention</th>
<th>Hazard ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tromso (Norway)</td>
<td>511</td>
<td>Vitamin D₃ ~2,900 IU/day</td>
<td>0.90 (0.69 to 1.18)</td>
</tr>
<tr>
<td>DPVD (Japan)</td>
<td>1,256</td>
<td>Eldecalcitol (active vitamin D analog) daily</td>
<td>0.87 (0.68 to 1.09)</td>
</tr>
<tr>
<td>D2d (US)</td>
<td>2,423</td>
<td>Vitamin D₃ 4,000 IU/day</td>
<td>0.88 (0.75 to 1.04)</td>
</tr>
</tbody>
</table>

Jorde et al JCEM 2016; Kawahara et al Diabetes 2017 (abstract; manuscript in preparation)
RESPONSE TO NUTRIENTS

The way the body responds to taking a vitamin, like vitamin D, likely depends on how much of the vitamin is already found in the body.

PROPORTION OF PARTICIPANTS WITH SUFFICIENT VITAMIN D LEVEL TO BEGIN WITH

- <20 ng/mL
- ≥20 ng/mL

- 22%
- 78%
Post-hoc subgroup analysis by very low vitamin D level

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Vitamin D n/N</th>
<th>Placebo n/N</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum 25-hydroxyvitamin D</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 12 ng/mL</td>
<td>15/60</td>
<td>18/43</td>
<td>0.38 (0.18, 0.80)</td>
</tr>
<tr>
<td>&gt;= 12 ng/mL</td>
<td>278/1151</td>
<td>304/1168</td>
<td>0.92 (0.78, 1.08)</td>
</tr>
</tbody>
</table>

Important caveats: small numbers; study was not designed for this effect
Summary / Recommendations / Future plans

- Among people at high risk for type 2 diabetes and with sufficient vitamin D levels, vitamin D at 4000 units/day did not have any adverse effects but did not significantly lower risk of diabetes.

- Based on results from D2d and other trials, the potential benefit of vitamin D for prevention of type 2 diabetes, if present, is modest and it is probably more relevant for those at risk for the disease who also have very low vitamin D levels to begin with.
The future of vitamin D and diabetes prevention

• Answers to clinical questions are rarely clear-cut and D2d was one (large) piece of the puzzle in the vitamin D and diabetes prevention field.

• We plan to continue to learn about vitamin D and diabetes from additional data analyses within D2d and by synthesizing data from other similar trials.
Early Progression To Diabetes Or Regression To Normal Glucose Tolerance Among People With Impaired Glucose Tolerance Affects Long-term Outcomes: 30-year follow-up of Da Qing Diabetes Prevention Study

Guangwei Li, MD
Background and rationale

• People with impaired glucose tolerance (IGT), one of the several types of ‘prediabetes,’ have a much higher likelihood of developing diabetes, and a higher risk of developing cardiovascular disease (CVD) and other complications compared with people with normal glucose.

• However, the extent to which the increased risk of complications is directly attributable to the development of diabetes, or other factors associated with IGT is uncertain.
Aims of the study

• The present analysis was designed to document the extent that development of CVD and other diabetes-related complications differed among people with IGT who within a six-year period progressed to diabetes compared with those who remained with IGT, or reverted to normal glucose tolerance.
Sample selection

1986-1992

- 576 participants with IGT enrolled into intervention trial

138 assigned to control group

438 assigned to intervention group

1992

- 67% of participants in control group developed DM
- 44% of participants in intervention group developed DM

DM n=252
IGT n=114
NGT n=174

540 participants

Status at end of six year intervention period

DM= Diabetes
IGT= Impaired Glucose Tolerance
NGT= Normal Glucose Tolerance
• In 2016, 30 years after the start of the trial we conducted a follow-up study to assess the number and proportion who had developed CVD and microvascular disease among these three groups.

• CVD was defined as the first occurrence of non-fatal or fatal stroke, myocardial infarction, or hospitalized heart failure, and the microvascular disease as the first occurrence of severe retinopathy, nephropathy or neuropathy.
Incidence of CVD events and micro-complications over 30 years among IGT people who progressed to diabetes, remained IGT or reverted to normal glucose at the end of six year trial.
IGT reverted to **normal glucose** during 6-year trial had lower risk of CVD and microvascular disease than those developed **diabetes** (After adjustment for multiple baseline risk factors)
IGT reverted to normal glucose or remained IGT during 6-year trial had lower risk of CVD and microvascular disease than those developed diabetes (After adjustment for multiple baseline risk factors)
Conclusion

• People with IGT have a high risk of progressing to diabetes. The magnitude of serious long-term complications associated with IGT is much greater in people whose glucose tolerance worsens rapidly to ‘diabetes’ than in those who retain non-diabetic levels in earlier years.

• But if that progression can be reversed or delayed for six years or more, the likelihood of developing long-term serious CVD and microvascular disease is much reduced.

• The findings further reinforce and are consistent with the thesis that the longer the progression to diabetes can be delayed, the fewer the complications.
Embargo Reminder

• Any reporters in violation of the embargo policy will be barred from this and future Scientific Sessions.

• For interviews with any of the presenters, please contact Michelle Kirkwood or a member of the Press Office team.
Media Contact

On-site Press Office – Room 314

SciSessionsPress@diabetes.org