Insulin v GLP-1 RA: Old vs New

R A Malik
Professor of Medicine
Weill Cornell Medicine-Qatar
Does Improving HbA1c Improve Outcomes?

No
## Intensive Glucose Lowering

<table>
<thead>
<tr>
<th></th>
<th>ACCORD(^1)</th>
<th>ADVANCE(^2)</th>
<th>VADT(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>10,251</td>
<td>11,140</td>
<td>1,791</td>
</tr>
<tr>
<td>Primary CVD endpoint</td>
<td>↓ 10% (p=0.16)</td>
<td>↓ 6% (p=0.37)*</td>
<td>↓ 13% (p=0.12)</td>
</tr>
<tr>
<td>Mortality (overall)</td>
<td>↑ 22% (p=0.04)</td>
<td>↓ 7% (p=NS)</td>
<td>↑ 6.5% (p=NS)</td>
</tr>
<tr>
<td>CV mortality</td>
<td>↑ 39% (p=0.02)</td>
<td>↓ 12% (p=NS)</td>
<td>↑ 25% (p=NS)</td>
</tr>
</tbody>
</table>

Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials


Lancet 2009; 373: 1765-72
“The remedy is worse than the disease”
Francis Bacon (1561-1626)

Elephant in the room” is an English idiom for an obvious truth that is being ignored or goes unaddressed. It also applies to an obvious problem or risk no one wants to discuss.
What Happened?
## Weight Gain??

<table>
<thead>
<tr>
<th></th>
<th>ACCORD¹</th>
<th>ADVANCE²</th>
<th>VADT³</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number</strong></td>
<td>10,251</td>
<td>11,140</td>
<td>1,791</td>
</tr>
<tr>
<td><strong>Weight gain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive</td>
<td>&gt;10kg</td>
<td>+0.7kg</td>
<td>+8kg</td>
</tr>
<tr>
<td></td>
<td>1399/5036</td>
<td>105kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>27.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>&gt;10kg</td>
<td></td>
<td>+4kg</td>
</tr>
<tr>
<td></td>
<td>713/5042</td>
<td>101kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CV mortality</strong></td>
<td>↑ 39% (p=0.02)</td>
<td>↓ 12% (p=NS)</td>
<td>↑ 25% (p=NS)</td>
</tr>
</tbody>
</table>

What if you could lower the glucose without the weight gain?
52 yr old Type 2 on oral & Insulin treatment:
Metformin 850mg tds, Pioglitazone 45mg, Lantus 40U
Weight-142.7kg, HbA1c-8.1%

Diet
Exenatide 10ug bd
Liraglutide 1.8mg

Weight loss 16.7kg
HbA1c reduction 5.9%
Stopped Pioglitazone & Insulin
Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes

Marso et al NEJM 2016; 345: 312-22

LEADER

N=9340
HbA1c: -0.4%
Weight: -2.3 kg
SBP: -1.2mm Hg

Nephropathy/Retinopathy
HR 0.84; 95% CI, 0.73 to 0.97; P=0.02)
Retinopathy: 1.15; 95% CI, 0.87 to 1.52; P=0.33).
Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Nephropathy: HR 0.64; 95% CI, 0.46 to 0.88; P=0.005
Retinopathy: HR 1.76; 95% CI, 1.11 to 2.78; P=0.02

N=3297
HbA1c: -1.1-1.4%
Weight: -2.9-4.3 kg
SBP: -1.3-2.6 mm Hg
Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

N=7027
HbA1c: -0.5-0.6%
Weight: -2.0 kg
SBP: -4.0 mm Hg

Zinman et al NEJM 2015; 373: 2117-28
THANK YOU