IX REUNIÓN DE DIABETES Y OBESIDAD

30-31 de Enero de 2015
FIBES - Palacio de Exposiciones y Congresos de Sevilla
“Facilitating the add-on moment for T2DM patients. What after metformin?”

ANDY COLLIER,
SCOTLAND
University Hospital Ayr
Scotland 3
Spain 1
Diabetes in Scotland
Diabetes in Ayrshire and Arran

Population

- 2004: 10641
- 2005: 13717
- 2006: 15603
- 2007: 16017
- 2008: 17055
- 2009: 18067
- 2010: 19075
- 2011: 20175
- 2012: 21073
- 2013: 21630

Population
Obesity and deprivation in A&A
Mean BMI in A&A (2013)

<table>
<thead>
<tr>
<th></th>
<th>Non-diabetes</th>
<th>Type 2 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>26.1 kg/m²</td>
<td>31.4 kg/m²</td>
</tr>
<tr>
<td>Females</td>
<td>26.9 kg/m²</td>
<td>32.4 kg/m²</td>
</tr>
</tbody>
</table>
Type 2 diabetes in A&A

Collier et al, 2014
There was no association between glycaemic control and socioeconomic status (p = 0.12).

Collier et al, 2014
We know:

Type 2 diabetes

• Linked to obesity
• Obesity is becoming more prevalent
• Diabetes is becoming more prevalent
• Obesity and type 2 diabetes are linked to socioeconomic status.
Type 2 Diabetes: A Complex Metabolic Disorder


- Impaired insulin secretion
- Insulin resistance
- Macrovascular complications
- Central obesity
- Dyslipidaemia
- Hypertension
- Microvascular complications

“INSULIN RESISTANCE SYNDROME”
• diet & exercise/lifestyle change
• metformin
• combination of metformin + secretagogue
• more and more
  – triple oral therapy in patients
  – bedtime insulin + OHA
• multiple insulin injections + metformin (+pio/SGLT2i)

progressive β-cell failure
Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) June 2012

• “recommendations should be considered within the context of the needs, preferences, and tolerances of each patient; individualization of treatment is the cornerstone of success. Our recommendations are less prescriptive than and not as algorithmic as prior guidelines”.
“recommendations should be considered within the context of the needs, preferences, and tolerances of each patient; individualization of treatment is the cornerstone of success. Our recommendations are less prescriptive than and not as algorithmic as prior guidelines”.
ANTI-HYPERGLYCEMIC THERAPY

Glycemic targets

- HbA1c < 7.0% (8.3-8.9 mmol/l)
- Pre-prandial PG < 7.2 mmol/l
- Post-prandial PG < 10.0 mmol/l

- Individualization is key:
  - Tighter targets (6.0 - 6.5%) - younger, healthier
  - Looser targets (7.5 - 8.0%+) - older, comorbidities, hypoglycemia prone, etc.

- Avoidance of hypoglycemia
IX REUNIÓN DE DIABETES Y OBESIDAD
30-31 de Enero de 2015 • FIBES - Palacio de Exposiciones y Congresos de Sevilla

1984
Assuming

• Lifestyle advice
• Metformin as first line
• “start low, go slow”
• Better tolerance

• → sulphonylurea (cost)
Why do we continue to use a class of drugs?

Sulfonylureas

• Lead to further weight gain
• Efficacy falls away
Over time, glycaemic control deteriorates.
Empagliflozin versus glimepiride change in HbA1c

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Glimepiride</th>
<th>Empagliflozin 25 mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>8.0</td>
<td>7.9</td>
</tr>
<tr>
<td>4</td>
<td>7.8</td>
<td>7.7</td>
</tr>
<tr>
<td>12</td>
<td>7.6</td>
<td>7.6</td>
</tr>
<tr>
<td>28</td>
<td>7.4</td>
<td>7.4</td>
</tr>
<tr>
<td>40</td>
<td>7.2</td>
<td>7.2</td>
</tr>
<tr>
<td>52</td>
<td>7.1</td>
<td>7.1</td>
</tr>
<tr>
<td>65</td>
<td>7.0</td>
<td>6.9</td>
</tr>
<tr>
<td>78</td>
<td>6.9</td>
<td>6.8</td>
</tr>
<tr>
<td>91</td>
<td>6.8</td>
<td>6.7</td>
</tr>
<tr>
<td>104</td>
<td>6.7</td>
<td>6.6</td>
</tr>
</tbody>
</table>

Difference in change from baseline at Week 104:
-0.11% (95% CI: -0.21, -0.01) p = 0.026

Analysed patients

<table>
<thead>
<tr>
<th>Glimepiride</th>
<th>Empagliflozin</th>
</tr>
</thead>
<tbody>
<tr>
<td>761 758 738</td>
<td>699 660 609</td>
</tr>
<tr>
<td>562 524 494</td>
<td>494 461</td>
</tr>
</tbody>
</table>

Empagliflozin versus glimepiride change in HbA1c

CI, confidence interval; H2H, head-to-head; HbA1c, glycosylated haemoglobin; QD, once daily.
MMRM. FAS (OC).
Why do we use a drug?

• Leads to further weight gain
• Efficacy falls away
• Gliclazide – too large a dose!
• Contentious cardiovascular data (UGDP-1971)
• Increases the risk of hypoglycaemia
• Downstream costs are high
• Increases patients risk of needing to go onto insulin.
Diabetes Prescribing Strategy 2014 to 2016 (Scotland)

Sulfonylureas:

• “recognised as second-line agents in patients who are not overweight “
• “first-line agent for those who are intolerant of, or have contra-indications to, metformin”
• “reduce clinically important microvascular complications”
• “they remain the least expensive second line agent”
• >70% of type 2 patients on MF + SU
Diabetes Prescribing Strategy 2014 to 2016

- “Self Blood Glucose Monitoring (SBGM) is not suitable or recommended for all those with type 2 diabetes”
- “there are clear recommendations for specific groups of patients. SBGM is essential for people with type 2 diabetes.............
- who are at risk of hypoglycaemia due to sulfonylurea”.


Diabetes Prescribing Strategy 2014 to 2016

• Cheap drug
• Self Blood Glucose Monitoring
  a. Expensive
  b. Quality of life
  c. Patient satisfaction
  d. Anxiety scores
# ANTI-HYPERGLYCEMIC THERAPY

## Therapeutic options:

**Oral agents & non-insulin injectables**

<table>
<thead>
<tr>
<th>Oral Agents &amp; Non-insulin Injectables</th>
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<tbody>
<tr>
<td>Metformin</td>
</tr>
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<td>Sulfonylureas</td>
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<tr>
<td>Thiazolidinediones</td>
</tr>
<tr>
<td>DPP-4 inhibitors</td>
</tr>
<tr>
<td>SGLT-2 inhibitors</td>
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ANTI-HYPERGLYCEMIC THERAPY

Therapeutic options:

Oral agents & non-insulin injectables

Metformin

Sulfonylureas

Thiazolidinediones

DPP-4 inhibitors

SGLT-2 inhibitors
Healthy eating, weight control, increased physical activity & diabetes education

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Efficacy</th>
<th>Hypo Risk</th>
<th>Weight</th>
<th>Side Effects</th>
<th>Costs</th>
</tr>
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<tbody>
<tr>
<td>Metformin + Sulfonlurea</td>
<td>high</td>
<td>low</td>
<td>neutral/loss</td>
<td>GI / lactic acidosis</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Thiazolidinedione</td>
<td>high</td>
<td>low</td>
<td>intermediate</td>
<td>low risk</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + DPP-4 inhibitor</td>
<td>intermediate</td>
<td>low risk</td>
<td>neutral</td>
<td>rare</td>
<td>low</td>
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<tr>
<td>Metformin + SGLT2 inhibitor</td>
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<td>low risk</td>
<td>low</td>
<td>rare</td>
<td>high</td>
</tr>
<tr>
<td>Metformin + GLP-1 receptor agonist</td>
<td>high</td>
<td>low risk</td>
<td>high</td>
<td>rare</td>
<td>variable</td>
</tr>
<tr>
<td>Metformin + Insulin (basal)</td>
<td>highest</td>
<td>high risk</td>
<td>high</td>
<td>gain</td>
<td>hypoglycemia</td>
</tr>
</tbody>
</table>

If HbA1c target not achieved after ~3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):

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<th>Drug Combination</th>
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<td>GI / lactic acidosis</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Sulfonlurea</td>
<td>high</td>
<td>moderate risk</td>
<td>gain</td>
<td>hypoglycemia</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Thiazolidinedione</td>
<td>high</td>
<td>low risk</td>
<td>legal</td>
<td>edema, HF, fx</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + DPP-4 inhibitor</td>
<td>intermediate</td>
<td>low risk</td>
<td>neutral</td>
<td>rare</td>
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<td>Metformin + SGLT2 inhibitor</td>
<td>intermediate</td>
<td>low risk</td>
<td>low</td>
<td>rare</td>
<td>high</td>
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<td>high</td>
<td>rare</td>
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<td>Metformin + Insulin (basal)</td>
<td>highest</td>
<td>high risk</td>
<td>high</td>
<td>rare</td>
<td>variable</td>
</tr>
</tbody>
</table>

If HbA1c target not achieved after ~3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference – choice dependent on a variety of patient- & disease-specific factors):

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Efficacy</th>
<th>Hypo Risk</th>
<th>Weight</th>
<th>Side Effects</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin + Metformin + Sulfonlurea</td>
<td>high</td>
<td>low</td>
<td>neutral/loss</td>
<td>GI / lactic acidosis</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Metformin + Thiazolidinedione</td>
<td>high</td>
<td>low risk</td>
<td>intermediate</td>
<td>low risk</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Metformin + DPP-4 inhibitor</td>
<td>intermediate</td>
<td>low risk</td>
<td>neutral</td>
<td>rare</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Metformin + SGLT2 inhibitor</td>
<td>intermediate</td>
<td>low risk</td>
<td>low</td>
<td>rare</td>
<td>high</td>
</tr>
<tr>
<td>Metformin + Metformin + GLP-1 receptor agonist</td>
<td>high</td>
<td>low risk</td>
<td>high</td>
<td>rare</td>
<td>variable</td>
</tr>
<tr>
<td>Metformin + Metformin + Insulin (basal)</td>
<td>highest</td>
<td>high risk</td>
<td>high</td>
<td>gain</td>
<td>hypoglycemia</td>
</tr>
</tbody>
</table>

If HbA1c target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGL T2-i:

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Efficacy</th>
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<tr>
<td>Metformin + Metformin + Metformin</td>
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<td>low</td>
</tr>
<tr>
<td>Metformin + Metformin + Metformin + Sulfonlurea</td>
<td>high</td>
<td>moderate risk</td>
<td>gain</td>
<td>hypoglycemia</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Metformin + Metformin + Thiazolidinedione</td>
<td>high</td>
<td>low risk</td>
<td>legal</td>
<td>edema, HF, fx</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Metformin + Metformin + DPP-4 inhibitor</td>
<td>intermediate</td>
<td>low risk</td>
<td>neutral</td>
<td>rare</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Metformin + Metformin + SGLT2 inhibitor</td>
<td>intermediate</td>
<td>low risk</td>
<td>low</td>
<td>rare</td>
<td>high</td>
</tr>
<tr>
<td>Metformin + Metformin + Metformin + GLP-1 receptor agonist</td>
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<td>low risk</td>
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<td>rare</td>
<td>variable</td>
</tr>
<tr>
<td>Metformin + Metformin + Metformin + Insulin (basal)</td>
<td>highest</td>
<td>high risk</td>
<td>high</td>
<td>gain</td>
<td>hypoglycemia</td>
</tr>
</tbody>
</table>

If HbA1c target not achieved after ~3 months of combination injectable therapy, move to injectables, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i:

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Efficacy</th>
<th>Hypo Risk</th>
<th>Weight</th>
<th>Side Effects</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin + Basal Insulin + Mealtime Insulin</td>
<td>high</td>
<td>low</td>
<td>neutral/loss</td>
<td>GI / lactic acidosis</td>
<td>low</td>
</tr>
<tr>
<td>Metformin + Basal Insulin + GLP-1-RA</td>
<td>high</td>
<td>low</td>
<td>neutral/loss</td>
<td>GI / lactic acidosis</td>
<td>low</td>
</tr>
</tbody>
</table>

References: Diabetes Care 2015;38:140-149; Diabetologia 2015;10.1077/s00125-014-3460-0
<table>
<thead>
<tr>
<th>Class</th>
<th>Mechanism</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides</td>
<td>• Activates AMP-kinase</td>
<td>• Extensive experience</td>
<td>• Gastrointestinal</td>
</tr>
<tr>
<td>(Metformin)</td>
<td>• ↓ Hepatic glucose production</td>
<td>• No hypoglycemia</td>
<td>• Lactic acidosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weight neutral</td>
<td>• B-12 deficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ? ↓ CVD events</td>
<td>• Contraindications</td>
</tr>
<tr>
<td>SUs /</td>
<td>• Closes KATP channels</td>
<td>• Extensive experience</td>
<td>• Hypoglycemia</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>• ↑ Insulin secretion</td>
<td>• ↓ Microvascular risk</td>
<td>• Weight gain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Low durability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ? ↓ Ischemic preconditioning</td>
</tr>
<tr>
<td>TZDs</td>
<td>• Activates PPAR-γ</td>
<td>• No hypoglycemia</td>
<td>• Weight gain</td>
</tr>
<tr>
<td></td>
<td>• ↑ Insulin sensitivity</td>
<td>• Durability</td>
<td>• Edema / heart failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↓ TGs, ↑ HDL-C</td>
<td>• Bone fractures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ? ↓ CVD events (pio)</td>
<td>• MI (rosi)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ? Bladder ca (pio)</td>
</tr>
</tbody>
</table>

*Diabetes Care 2015*  
*Diabetologia 2015*
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</table>
| Biguanides (Metformin) | • Activates AMP-kinase  
• ↓ Hepatic glucose production | • Extensive experience  
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• Weight neutral  
• ? ↓ CVD events | • Gastrointestinal  
• Lactic acidosis  
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• Contraindications |
| SUs / Meglitinides | • Closes KATP channels  
• ↑ Insulin secretion | • Extensive experience  
• ↓ Microvascular risk | • Hypoglycemia  
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• Low durability  
• ? ↓ Ischemic preconditioning |
| TZDs              | • Activates PPAR-γ  
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• Durability  
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• Edema / heart failure  
• Bone fractures  
• Macular edema  
• ? ↑ MI (rosi)  
• ? Bladder ca (pio) |

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<tbody>
<tr>
<td>DPP-4 inhibitors</td>
<td>• Inhibits DPP-4&lt;br&gt;• Increases GLP-1, GIP</td>
<td>• No hypoglycemia&lt;br&gt;• Well tolerated</td>
<td>• Modest ↓ A1c&lt;br&gt;• ? Pancreatitis&lt;br&gt;• Urticaria</td>
</tr>
<tr>
<td>GLP-1 receptor agonists</td>
<td>• Activates GLP-1 receptor&lt;br&gt;↑ Insulin, ↓ glucagon&lt;br&gt;↓ gastric emptying&lt;br&gt;↑ satiety</td>
<td>• Weight loss&lt;br&gt;• No hypoglycemia&lt;br&gt;• ? ↑ Beta cell mass&lt;br&gt;• ? CV protection</td>
<td>• GI&lt;br&gt;• ? Pancreatitis&lt;br&gt;• Medullary ca&lt;br&gt;• Injectable</td>
</tr>
<tr>
<td>SGLT-2 inhibitors</td>
<td>• Inhibits SGLT2 in proximal tubule&lt;br&gt;• Increases glycosuria</td>
<td>• ↓ weight&lt;br&gt;• No hypoglycaemia&lt;br&gt;• ↓ blood pressure&lt;br&gt;• Effective at all stages</td>
<td>• GU infections&lt;br&gt;• Polyurria&lt;br&gt;• Volume depletion&lt;br&gt;• ↑ LDL-chol&lt;br&gt;• ↑ Creat (transient)</td>
</tr>
</tbody>
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| **DPP-4 inhibitors**        | • Inhibits DPP-4  
• Increases GLP-1, GIP                                      | • No hypoglycemia  
• Well tolerated                                   | • Modest ↓ A1c  
• ? Pancreatitis  
• Urticaria                                             |
| **GLP-1 receptor agonists** | • Activates GLP-1 receptor  
• ↑ Insulin, ↓ glucagon  
• ↓ gastric emptying  
• ↑ satiety                                              | • Weight loss  
• No hypoglycemia  
• ? ↑ Beta cell mass  
• ? CV protection                                    | • GI  
• ? Pancreatitis  
• Medullary ca  
• Injectable                                             |
| **SGLT-2 inhibitors**       | • Inhibits SGLT2 in proximal tubule  
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• ↑ Creat (transient)                                   |
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<tr>
<td>Insulin</td>
<td>• Activates insulin receptor</td>
<td>• Universally effective</td>
<td>• Hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>• ↑ Glucose disposal</td>
<td>• Unlimited efficacy</td>
<td>• Weight gain</td>
</tr>
<tr>
<td></td>
<td>• ↓ Hepatic glucose production</td>
<td>• ↓ Microvascular risk</td>
<td>• ? Mitogenicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Injectable</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Training requirements</td>
</tr>
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<td></td>
<td>• “Stigma”</td>
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</tbody>
</table>
Type 2 diabetes

• progressive disease
• ß-cell failure
• development of complications
• medications at diagnosis
• medications later in disease process
• co-morbidities.
Comorbidities

- Coronary Disease
- Heart Failure
- Renal disease
- Liver dysfunction
- Hypoglycemia

- Metformin: CVD benefit (UKPDS)
- Avoid hypoglycemia
- ▼ SUs & ischemic preconditioning
- ▼ Pioglitazone & ▼ CVD events
- ▼ Effects of incretin-based therapies
Comorbidities

- Coronary Disease
- Heart Failure
- Renal disease
- Liver dysfunction
- Hypoglycemia

- Metformin: May use unless condition is unstable or severe
- Avoid TZDs
- Effects of incretin-based therapies
Comorbidities

- Coronary Disease
- Heart Failure
- Renal disease
- Liver dysfunction
- Hypoglycemia

- Increased risk of hypoglycemia
- Metformin & lactic acidosis
  - US: stop @SCr ≥ 1.5 (1.4 women)
  - UK: half-dose @GFR < 45 & stop @GFR < 30
- Caution with SUs (esp. glibenclamide)
- DPP-4-i’s – dose adjust for most (not linagliptin)
- Avoid exenatide if GFR < 30
- SGLT2 inhibitors @GFR < 60
Comorbidities

- Coronary Disease
- Heart Failure
- Renal disease
- Liver dysfunction
- Hypoglycemia

- Most drugs not tested in advanced liver disease
- Pioglitazone may help steatosis
- Insulin best option if disease severe
Comorbidities

- Coronary Disease
- Heart Failure
- Renal disease
- Liver dysfunction
- Hypoglycemia

- Emerging concerns regarding association with increased morbidity / mortality
- Proper drug selection is key in the hypoglycemia prone
Add ≥2 rapid insulin* injections before meals ("basal-bolus")

**Basal Insulin**
(usually with metformin +/- other non-insulin agent)

- **Start:** 10U/day or 0.1-0.2 U/kg/day
- **Adjust:** 10-15% or 2-4 U once-twice weekly to reach FBG target.
- **For hypo:** Determine & address cause; ↓ dose by 4 units or 10-20%.

If not controlled after FBG target is reached (or if dose > 0.5 U/kg/day), treat PPG excursions with meal-time insulin. (Consider initial GLP-1-RA trial.)

**Add 1 rapid insulin* injections before largest meal**

- **Start:** 4U, 0.1 U/kg, or 10% basal dose. If A1c<8%, consider ↓ basal by same amount.
- **Adjust:** ↑ dose by 1-2 U or 10-15% once-twice weekly until SMBG target reached.
- **For hypo:** Determine and address cause; ↓ corresponding dose by 2-4 U or 10-20%.

**Change to premixed insulin* twice daily**

- **Start:** Divide current basal dose into 2-3 AM, 1/3 PM or 1/2 AM, 1/2 PM.
- **Adjust:** ↑ dose by 1-2 U or 10-15% once-twice weekly until SMBG target reached.
- **For hypo:** Determine and address cause; ↓ corresponding dose by 2-4 U or 10-20%.

**Add ≥2 rapid insulin* injections before meals ("basal-bolus")**

- **Start:** 4U, 0.1 U/kg, or 10% basal dose/meal.↑ If A1c<8%, consider ↓ basal by same amount.
- **Adjust:** ↑ dose by 1-2 U or 10-15% once-twice weekly to achieve SMBG target.
- **For hypo:** Determine and address cause; ↓ corresponding dose by 2-4 U or 10-20%.

- **Start:** 10U/day or 0.1-0.2 U/kg/day
- **Adjust:** 10-15% or 2-4 U once-twice weekly to reach FBG target.
- **For hypo:** Determine & address cause; ↓ dose by 4 units or 10-20%.
• Two clinical cases
Busy, active mother of three
Age: 45

- Office administrator
- Diagnosed with type 2 diabetes three years ago
- Drives to work and ‘ferries’ children every day
- Attended a structured education programme last year

- Joined a slimming club but still struggling to find time to plan healthier meals that the whole family will eat
- Hesitant to take add-on therapy - “I’m very young to be on all these medications”

- Weight gain over last 2 years - BMI: 29 kg/m²
- BP: 132/83 mmHg
- HbA₁c: 8.1%
- Normal renal function

- Currently on metformin: 1 g bd (the maximum dose tolerated, adherence confirmed)
Busy, active mother of three
Age: 45

Management review
• HbA$_{1c}$ 8.1% - requires additional control
• Attended structured education programme last year
• Struggling to improve diet
• Recent weight gain

Treatment options
• A sulphonylurea (e.g. gliclazide)
• A DPP-4 inhibitor (gliptin)
• A thiazolidinedione (glitazone)
• An SGLT2 inhibitor
• A GLP-1 agonist
• Basal insulin
45 years old

- Further lifestyle advice
- Gliclazide 80 160 mgs twice daily
48 years old – 3 years later

- 5kgs heavier
- BMI > 30kg/m²
- HbA₁c 8.6%

**Treatment options**
- A DPP-4 inhibitor (gliptin)
- A thiazolidinedione (glitazone)
- An SGLT2 inhibitor
- A GLP-1 agonist
- Basal insulin
48 years old – 3 years later

- Reduce or stop gliclazide
- Gliptin
- SGLT2 inhibitor
- Pioglitazone
- (GLP1 analogue)

- Reinforce lifestyle advice
- Cardiovascular risk factors
- Insulin therapy
A.S. 59 year old male

Travelling salesman – driving every day
Diet is poor and sporadic
Diagnosed with type 2 diabetes three years ago
Offered structured education programme and declined

Recently cut his work hours and general activity due to ill health, consequently gained weight
A smoker: concerned about further weight gain if he gives up smoking
Co-morbidity: COPD (managed with appropriate inhalers)
BMI: 36 kg/m²
BP: 136/78 mmHg
HbA₁c: 8.9%
eGFR: normal
“does not want injections”

Currently on metformin 1 g bd (the maximum dose tolerated)
A.S. 59 year old male

**Lifestyle advice**
- Smoking cessation programme enrolment
- Participation in structured education ‘refresher’
- Driving is part of his business

**Treatment options**
- A sulphonylurea (e.g. gliclazide)
- Gliptin
- Pioglitazone
- An SGLT2 inhibitor
- A GLP-1 agonist
- Basal insulin
A.S. 59 year old male

- Reinforce lifestyle advice
- Cardiovascular risk factors
- Insulin therapy

**Treatment options**
- A sulphonylurea (e.g. gliclazide)
- Gliptin
- Pioglitazone
- An SGLT2 inhibitor
- A GLP-1 agonist
- Basal insulin
KEY POINTS

- Glycemic targets & BG-lowering therapies must be individualized.

- **Diet, exercise, & education**: foundation of any T2DM therapy program

- Unless contraindicated, metformin = optimal 1st-line drug - “start low, go slow”.

- **Progressive disease:**
  - β-cell failure
  - increased weight → further insulin resistance
  - development of complications
  - impact on management
KEY POINTS

- After metformin, data are limited. Combination therapy with 1-2 other oral / injectable agents is reasonable; minimize side effects.

- Ultimately, many patients will require insulin therapy alone / in combination with other agents to maintain BG control.

- All treatment decisions should be made in conjunction with the patient (focus on preferences, needs & values.)

- Comprehensive CV risk reduction - a major focus of therapy.
• Thank you
• Any questions?
IX REUNIÓN DE DIABETES Y OBESIDAD

30-31 de Enero de 2015 • FIBES - Palacio de Exposiciones y Congresos de Sevilla
What I do

At diagnosis

• Tight control
• Metformin
• Gliclazide (80mg twice daily as maximum/stop after a few weeks)
What I do

At diagnosis

• Tight control
• Metformin
• [Gliclazide (80mg twice daily as maximum/stop after a few weeks)]
• DPP-4-i’s
• SGLT2 inhibitor
• Pioglitazone
• If BMI>35 kg/m² – GLP1 inhibitor
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• Tight control
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10-15 yrs into diagnosis

• Less tight control
• Metformin
• Reduce or stop gliclazide
• DPPIV I
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