De reelle årsager til type 2 diabetes

Diabetes Update
København, 21. november 2016

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Standardised mortality rates for patients with diabetes 1997-2012 in Denmark

<table>
<thead>
<tr>
<th>Year</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>1.91</td>
</tr>
<tr>
<td>1998</td>
<td>1.86</td>
</tr>
<tr>
<td>1999</td>
<td>1.88</td>
</tr>
<tr>
<td>2000</td>
<td>1.86</td>
</tr>
<tr>
<td>2001</td>
<td>1.77</td>
</tr>
<tr>
<td>2002</td>
<td>1.77</td>
</tr>
<tr>
<td>2003</td>
<td>1.78</td>
</tr>
<tr>
<td>2004</td>
<td>1.73</td>
</tr>
<tr>
<td>2005</td>
<td>1.72</td>
</tr>
<tr>
<td>2006</td>
<td>1.68</td>
</tr>
<tr>
<td>2007</td>
<td>1.64</td>
</tr>
<tr>
<td>2010</td>
<td>1.59</td>
</tr>
<tr>
<td>2012</td>
<td>1.49</td>
</tr>
</tbody>
</table>
Cumulative mortality and cumulative incidence of the composite cardiovascular or death endpoint

Steno 2 study: Intensive intervention in type 2 diabetes patients with microalbuminuria

P Gæde et al, Diabetologia 2016; 59: 2298
Years of life lost due to diabetes in Denmark

Diabetologia 2012;55:294

OUH
Odense Universitetshospital
Pathophysiologically based phenotyping in type 2 diabetes
Type 2 diabetes heterogeneity

• Patients with clinically diagnosed type 2 diabetes does not constitute a homogeneous entity!

• Even though subphenotyping does not form the basis for individualised treatment
WHO classification of diabetes mellitus

- Type 1 diabetes
- Type 2 diabetes
- Other specific types
  - Genetic defects
  - Disease of the exocrine pancreas
  - Drug-induced diabetes
- Gestationel diabetes mellitus
Classification in clinical practice – and in clinical trials

- Non-obese and young ketosis prone patients are classified as type 1 diabetes

- Obese and elderly patients are classified as type 2 diabetes
Investigated phenotypes

- GAD positivity (latent autoimmune diabetes in adults (LADA))
- Secondary diabetes (pancreatitis)
- Steroid-induced diabetes
- Rare subtypes of diabetes
- “WHO-defined” type 2 diabetes
Prevalence of the phenotypes

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare subtypes of diabetes</td>
<td>6</td>
<td>0.6%</td>
</tr>
<tr>
<td>GAD positives</td>
<td>31</td>
<td>3.0%</td>
</tr>
<tr>
<td>Secondary diabetes (pancreatitis)</td>
<td>41</td>
<td>3.9%</td>
</tr>
<tr>
<td>Steroid-induced diabetes</td>
<td>61</td>
<td>5.8%</td>
</tr>
<tr>
<td>“WHO-defined” T2D</td>
<td>918</td>
<td>86.7%</td>
</tr>
</tbody>
</table>
• So, ~10% are misclassified

• However, can “WHO-defined” type 2 diabetes be further subdivided into pathophysiological subphenotypes?
Arterial hypertension

The pathophysiology of the dysmetabolic syndrome

Overeating and reduced physical activity

Visceral obesity

Polycystic ovary syndrome (PCOS)

Cancer

Insulin resistance and hyperinsulinism

Non-alcoholic fatty liver disease (NAFLD) → Non-alcoholic steatohepatitis (NASH)

Arterial hypertension

Dyslipidaemia

Glucose intolerance/Type 2 diabetes (T2D)

Atherosclerosis/Hypercoagulability

Cardiovascular disease (acute myocardial infarction (AMI), stroke, amputation)
Visceral fat distribution
Normal vs. type 2 diabetes
Obesity-induced metabolic syndrome

Overeating + leisure lifestyle + genetic predisposition

- Abdominal obesity
- Big insulin resistant fat cells (hypertrophia)
- BMI around 30 kg/m²
- Increased plasma free fatty acids
- Decreased plasma adiponectin

Metabolic syndrome

- Subcutaneous obesity
- Small relative insulin sensitive fat cells (hyperplasia)
- BMI >40 kg/m²
- Unchanged plasma free fatty acids
- Unchanged plasma adiponectin

NGT

Photo: Michael Krumphanzl, AP Politiken
Sunday 7 April 2002
How to reduce BMI

- Reduce calorie intake
- Behaviour modification by using
  - modern communication
  - continuous measurement of calorie intake and physical activity
  - group motivation and professional supervision
- Very-low calorie diet
- Anorectic drugs (i.e. liraglutide)
- Gastric bypass operation
Treatment with hypocalorie diet

Effects of 8 weeks of a very-low calorie diet

Knop and Taylor, Diabetes Care 2013; 36:S287
Effect of bariatric surgery

- Bariatric surgery induces an average **weight loss** of 30-40 kg
- Randomised trials show that bariatric surgery is clearly superior to pharmaceutical treatment with regard to **glycaemic control** in obese patients with type 2 diabetes
- The majority of patients will experience **remission of diabetes**, but some will experience recurrence of hyperglycaemia subsequently
- Observational studies have shown a positive effect on **micro- and macrovascular diabetes complications** and reduced **mortality** following bariatric surgery

Svane et al, Ugeskr Laeger 2016
Individual goals for treatment of weight

- In all patients, BMI <30kg/m² is preferable
- But, a 10% weight loss results in significant improvement of glucose metabolism
Effect of interval walk in 4 months in 32 patients with type 2 diabetes (3x30 min per week)

Adherence to training: 90%

Karstoft et al., Diabetes Care 2013
Treatment options

- Treat-to-target (failure)
  vs.
- Treatment based on pathophysiology
EASD/ADA treatment algorithm

Healthy eating, weight control, increased physical activity and diabetes education

Mono-therapy
- Metformin
  - High efficacy
  - Low risk hypoglycaemia
  - Neutral risk weight
  - Low risk side effects
  - Low cost

If HbA1c target not achieved after ~5 months of monotherapy, proceed to two-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

- Metformin + Sulfonylurea
  - High efficacy
  - Moderate risk hypoglycaemia
  - Low risk weight
  - Low risk side effects
  - Low cost

- Metformin + Thiazolidinedione
  - Intermediate efficacy
  - Low risk hypoglycaemia
  - Low risk weight
  - Rare side effects
  - Low cost

- Metformin + DPP-4 inhibitor
  - Intermediate efficacy
  - Intermediate risk hypoglycaemia
  - Intermediate risk weight
  - Rare side effects
  - Low cost

- Metformin + GLP-1 receptor agonist
  - High efficacy
  - Lowest risk hypoglycaemia
  - High risk weight
  - Low cost

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

- Metformin + Sulfonylurea + TZD
  - High efficacy
  - Moderate risk hypoglycaemia
  - High risk weight
  - High risk side effects
  - High cost

- Metformin + Thiazolidinedione + SU
  - Intermediate efficacy
  - Low risk hypoglycaemia
  - Low risk weight
  - Rare side effects
  - Low cost

- Metformin + DPP-4 inhibitor + TZD
  - Intermediate efficacy
  - Intermediate risk hypoglycaemia
  - Intermediate risk weight
  - Rare side effects
  - Low cost

- Metformin + GLP-1 receptor agonist + SU
  - High efficacy
  - Lowest risk hypoglycaemia
  - High risk weight
  - Low cost

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 medtline insulin. In resistant patients consider adding TZD or SGLT-2i:

- Metformin + Basal insulin + Medline insulin or GLP-1 RA
  - High efficacy
  - Lowest risk hypoglycaemia
  - Lowest risk weight
  - Low cost

Diabetologia 2015;58:429
Pharmacological profile for a patient with type 2 diabetes in 2015 treated with the "treat-to-target" algorithm

- Metformin
- Glucagon-like peptide 1 (GLP-1) analogue/dipeptidyl peptidase 4 (DPPIV) inhibitors
- Insulin
- Angiotensin converting enzyme (ACE) inhibitors
- Angiotensin II (ATII) inhibitors
- Diuretics
- Magnyl
- Simvastatin
- H2 blocker
- Bronchodilator/steroid inhalator
- Non-steroidal Anti-inflammatory Drug (NSAID)
ACCORD: Treatment effects on glucose control

ACCORD: Treatment effect on all-cause mortality


Patients with events (%)

Time (years)

0 1 2 3 4 5 6

Standard therapy

Intensive therapy

HR 1.22 (1.01-1.46)
P = 0.04
Treatment options

- Treat-to-target (failure) vs.
- Treatment based on pathophysiology
Future treatment of type 2 diabetes

• Treat the patients individually based on patophysiological investigations
• Set individual goals for HbA1c, LDL cholesterol, blood pressure and BMI
• Treat the primary cause (dysmetabolic syndrome) first i.e. improvement of lifestyle:
  – Reduce body weight significantly
  – Increase physical activity
• Reduce the number of pharmaceutical compounds
Individual goals for treatment of blood glucose

Chosen by the doctor

- Good control: HbA1c ≤ 6.5% ~ 48 mmol/L
- Acceptable control: HbA1c 7-8% ~ 58 mmol/L
- Well-being without an upper level for HbA1c
Individual goals for treatment of blood pressure

Chosen by the doctor

• <140/90 mmHg in general
• Kidney disease: <125/85 mmHg
• Systolic blood pressure should be >120 mmHg
Individual goals for treatment of serum LDL

- <2.5 mmol/L in general
- At atorvastatin treatment of 80 mg/day, serum LDL >2.5 mmol/L must be accepted
How to normalise blood glucose

- Increase insulin secretion (GLP1 analogues, DPPIV inhibitors, SU and insulin)
- Increase insulin action (metformin, glitazones, hypocalorie diet and exercise)
- Reduce glucose uptake in the gut (acorbase) or increase glucose secretion in the urine (SGLT2 inhibitors)
- Reduce glucose intake – low carbohydrate diet
How to treat hypertension individually

• Measure causes to hypertension:
  – Increase body fluid and/or
  – Increase peripheral resistance of vessels and/or
  – Increase chronotropy

• Treatment in accordance with:
  – Diuretics
  – ACE inhibitors/ARB
  – Beta-blockers
How to treat hypercholesterolaemia

• This cannot be done individually based on patophysiology, but side effects occur individually.

• Treatment to all without side effects:
  – Simvastatin 40 mg/day
  – With serum LDL >2.5 mmol/L despite simvastatin, atorvastatin 80mg/day

P.S. High triglycerides >5 mmol/L can be treated with gemfribrozil
## Risk for a primary CVD end-point – Odds Ratio

Adjusted for age, gender, prevalent IHD, stroke and cancer diagnosed before screening and lipid lowering drugs before screening

<table>
<thead>
<tr>
<th></th>
<th>Risk for a primary CVD end-point</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Both groups:</strong></td>
<td>1</td>
<td>1.7 (1.0-3.1)</td>
<td>3.1 (1.6-6.0)</td>
</tr>
<tr>
<td><strong>Intervention:</strong></td>
<td>1</td>
<td>2.5 (1.2-5.6)</td>
<td>2.9 (1.2-7.0)</td>
</tr>
<tr>
<td><strong>Control:</strong></td>
<td>1</td>
<td>0.5 (0.2-1.4)</td>
<td>3.9 (1.5-10.1)</td>
</tr>
</tbody>
</table>

### Graphical Representation

- **Proportion of people on lipid-lowering drugs within first 2 years**
- **Risk for a primary CVD end-point – Odds Ratio**
- **Adjusted for age, gender, prevalent IHD, stroke and cancer diagnosed before screening and lipid lowering drugs before screening**

#### Graph Details:
- **11 intensive practices**
- **15 routine practices**
- Practices did not prescribe any lipid lowering drugs.

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Unpublished data by RK Simmons, AH Carlsen, S Griffin, M Charles, JS Christiansen, A Sandbæk, T Lauritzen
Pharmacological treatment of hyperglycaemia in type 2 diabetes
Mean HbA$_{1c}$ (%) over time

**Background metformin**

- Sulfonylurea (n=1084)
- Rosiglitazone (n=1106)

**Background sulfonylurea**

- Metformin (n=1096)
- Rosiglitazone (n=1083)

Model-adjusted mean (%, SE)

HbA$_{1c}$ (%) over time:

- Time (years): 0, 1, 2, 3, 4, 5
- Model-adjusted mean (%, SE)
- P<0.0001
SGLT2 Inhibitors and Diabetic Ketoacidosis
"The European Experience"

Henning Beck-Nielsen
Professor, Consultant Physician, DMSc
Odense University Hospital
All patients (including those who discontinued study drug or initiated new therapies) were included in this mixed model repeated measures analysis (intent-to-treat) timepoints with reasonable amount of data available for pre-scheduled measurements.

### CV death, MI and stroke

<table>
<thead>
<tr>
<th>Patients with event/analysed</th>
<th>Empagliflozin</th>
<th>Placebo</th>
<th>HR</th>
<th>(95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-point MACE</td>
<td>490/4687</td>
<td>282/2333</td>
<td>0.86</td>
<td>(0.74, 0.99)*</td>
<td>0.0382</td>
</tr>
<tr>
<td>CV death</td>
<td>172/4687</td>
<td>137/2333</td>
<td>0.62</td>
<td>(0.49, 0.77)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>213/4687</td>
<td>121/2333</td>
<td>0.87</td>
<td>(0.70, 1.09)</td>
<td>0.2189</td>
</tr>
<tr>
<td>Non-fatal stroke</td>
<td>150/4687</td>
<td>60/2333</td>
<td>1.24</td>
<td>(0.92, 1.67)</td>
<td>0.1638</td>
</tr>
</tbody>
</table>

This figure has been created by Boehringer Ingelheim based on data from reference
Cox regression analysis. MACE, Major Adverse Cardiovascular Event; HR, hazard ratio; CV, cardiovascular; MI, myocardial infarction
*95.02% CI
Supplementary Appendix to Zinman B et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. Published online September 17. http://www.nejm.org/doi/full/10.1056/NEJMoa1504720
Other adverse events (1)

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (n=2333)</th>
<th>Empagliflozin 10 mg (n=2345)</th>
<th>Empagliflozin 25 mg (n=2342)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>Rate</td>
<td>n (%)</td>
</tr>
<tr>
<td>Diabetic ketoacidosis*</td>
<td>1 (&lt;0.1%)</td>
<td>0.02</td>
<td>3 (0.1%)</td>
</tr>
<tr>
<td>Acute kidney injury†</td>
<td>155 (6.6%)</td>
<td>2.77</td>
<td>121 (5.2%)</td>
</tr>
<tr>
<td>Events consistent with volume depletion§</td>
<td>115 (4.9%)</td>
<td>2.04</td>
<td>115 (4.9%)</td>
</tr>
<tr>
<td>Serious events</td>
<td>24 (1.0%)</td>
<td>0.42</td>
<td>19 (0.8%)</td>
</tr>
<tr>
<td>Events leading to discontinuation</td>
<td>7 (0.3%)</td>
<td>0.12</td>
<td>1 (&lt;0.1%)</td>
</tr>
<tr>
<td>Venous thrombotic events**</td>
<td>20 (0.9%)</td>
<td>0.35</td>
<td>9 (0.4%)</td>
</tr>
</tbody>
</table>

Rate = per100 patient-years
This figure has been created by Boehringer Ingelheim based on data from reference
Patients treated with ≥1 dose of study drug
*Based on 4 MedDRA preferred terms. †Based on 1 standardised MedDRA query
§Based on 8 MedDRA preferred terms. **Based on 1 standardised MedDRA query
Conclusion

• The antidiabetic effect of SGLT2 inhibitors is modest

• The effect on heart failure in patients with type 2 diabetes with cardiovascular disease is dramatic

• This schism may influence the decision on licensing
Meta-analysis of the effect of metformin on cardiovascular events in type 2 diabetes:

No statistically significant proof of a protective effect of metformin
MALA and non-MALA in Denmark in the period 2004-2012

MALA rates vs. non-MALA rates = $p < 0.01$
## Primary and Secondary Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Liraglutide (N = 4668)</th>
<th>incidence rate</th>
<th>Placebo (N = 4672)</th>
<th>Incidence rate</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients (%)</td>
<td>no. of events/100 patient-yr</td>
<td>no. of patients (%)</td>
<td>no. of events/100 patient-yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary composite outcome†</td>
<td>608 (13.0)</td>
<td>3.4</td>
<td>694 (14.9)</td>
<td>3.9</td>
<td>0.87 (0.78–0.97)</td>
<td>0.01</td>
</tr>
<tr>
<td>Expanded composite outcome‡</td>
<td>948 (20.3)</td>
<td>5.3</td>
<td>1062 (22.7)</td>
<td>6.0</td>
<td>0.88 (0.81–0.96)</td>
<td>0.005</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>381 (8.2)</td>
<td>2.1</td>
<td>447 (9.6)</td>
<td>2.5</td>
<td>0.85 (0.74–0.97)</td>
<td>0.02</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>219 (4.7)</td>
<td>1.2</td>
<td>278 (6.0)</td>
<td>1.6</td>
<td>0.78 (0.66–0.93)</td>
<td>0.007</td>
</tr>
<tr>
<td>Death from noncardiovascular causes</td>
<td>162 (3.5)</td>
<td>0.9</td>
<td>169 (3.6)</td>
<td>1.0</td>
<td>0.95 (0.77–1.18)</td>
<td>0.66</td>
</tr>
<tr>
<td>Myocardial infarction§</td>
<td>292 (6.3)</td>
<td>1.6</td>
<td>339 (7.3)</td>
<td>1.9</td>
<td>0.86 (0.73–1.00)</td>
<td>0.046</td>
</tr>
<tr>
<td>Fatal§</td>
<td>17 (0.4)</td>
<td>0.1</td>
<td>28 (0.6)</td>
<td>0.2</td>
<td>0.60 (0.33–1.10)</td>
<td>0.10</td>
</tr>
<tr>
<td>Nonfatal</td>
<td>281 (6.0)</td>
<td>1.6</td>
<td>317 (6.8)</td>
<td>1.8</td>
<td>0.88 (0.75–1.03)</td>
<td>0.11</td>
</tr>
<tr>
<td>Silent§</td>
<td>62 (1.3)</td>
<td>0.3</td>
<td>76 (1.6)</td>
<td>0.4</td>
<td>0.86 (0.61–1.20)</td>
<td>0.37</td>
</tr>
<tr>
<td>Stroke§</td>
<td>173 (3.7)</td>
<td>1.0</td>
<td>199 (4.3)</td>
<td>1.1</td>
<td>0.86 (0.71–1.06)</td>
<td>0.16</td>
</tr>
<tr>
<td>Fatal§</td>
<td>16 (0.3)</td>
<td>0.1</td>
<td>25 (0.5)</td>
<td>0.1</td>
<td>0.64 (0.34–1.19)</td>
<td>0.16</td>
</tr>
<tr>
<td>Nonfatal</td>
<td>159 (3.4)</td>
<td>0.9</td>
<td>177 (3.8)</td>
<td>1.0</td>
<td>0.89 (0.72–1.11)</td>
<td>0.30</td>
</tr>
<tr>
<td>Transient ischemic attack§</td>
<td>48 (1.0)</td>
<td>0.3</td>
<td>60 (1.3)</td>
<td>0.3</td>
<td>0.79 (0.54–1.16)</td>
<td>0.23</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>405 (8.7)</td>
<td>2.3</td>
<td>441 (9.4)</td>
<td>2.5</td>
<td>0.91 (0.80–1.04)</td>
<td>0.18</td>
</tr>
<tr>
<td>Hospitalization for unstable angina pectoris</td>
<td>122 (2.6)</td>
<td>0.7</td>
<td>124 (2.7)</td>
<td>0.7</td>
<td>0.98 (0.76–1.26)</td>
<td>0.87</td>
</tr>
<tr>
<td>Hospitalization for heart failure</td>
<td>218 (4.7)</td>
<td>1.2</td>
<td>248 (5.3)</td>
<td>1.4</td>
<td>0.87 (0.73–1.05)</td>
<td>0.14</td>
</tr>
<tr>
<td>Microvascular event</td>
<td>355 (7.6)</td>
<td>2.0</td>
<td>416 (8.9)</td>
<td>2.3</td>
<td>0.84 (0.73–0.97)</td>
<td>0.02</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>106 (2.3)</td>
<td>0.6</td>
<td>92 (2.0)</td>
<td>0.5</td>
<td>1.15 (0.87–1.52)</td>
<td>0.33</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>268 (5.7)</td>
<td>1.5</td>
<td>337 (7.2)</td>
<td>1.9</td>
<td>0.78 (0.67–0.92)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

* Hazard ratios and P values were estimated with the use of a Cox proportional-hazards model with treatment as a covariate.
† The primary composite outcome in the time-to-event analysis consisted of the first occurrence of death from cardiovascular causes (181 patients in the liraglutide group vs. 227 in the placebo group), nonfatal (including silent) myocardial infarction (275 vs. 304), or nonfatal stroke (152 vs. 163). The P value is for superiority.
‡ The expanded composite outcome included death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or hospitalization for unstable angina pectoris or heart failure.
§ This analysis was not prespecified.
Primary and Exploratory Outcomes

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical type 2 diabetes</td>
<td>Low calorie/low carbohydrate diet + metformin + GLP1 analogues</td>
</tr>
<tr>
<td>Insulinopenic diabetes (lean type 2 diabetes)</td>
<td>Insulin</td>
</tr>
<tr>
<td>Hyperinsulinaemic diabetes</td>
<td>Gastric bypass/GLP1 analogues</td>
</tr>
<tr>
<td>Latent autoimmune diabetes in adults (LADA)</td>
<td>A recent Cochrane analysis states that insulin is the first drug of choice</td>
</tr>
<tr>
<td>Prednisolone-induced diabetes</td>
<td>Prandrial insulin treatment or GLP1 analogues</td>
</tr>
<tr>
<td>Type 2 diabetic subjects with pancreatitis</td>
<td>Often needs insulin as first drug of choice. Glucagon-like peptide-1 analogues and dipeptidyl peptidase IV inhibitors may be contraindicated</td>
</tr>
<tr>
<td>Mature onset diabetes of the young (MODY)</td>
<td>MODY 1+3: Sulfonylurea (not insulin) MODY 2: Lifestyle changes only</td>
</tr>
<tr>
<td>Characterisation of glucose-lowering drugs in type 2 diabetes</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>Effect on blood glucose (HbA1c)</strong></td>
<td><strong>Effect on the cardiovascular system</strong></td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Sulfonylurea</td>
<td>+++ (2 years only)</td>
</tr>
<tr>
<td>Metformin</td>
<td>++</td>
</tr>
<tr>
<td>DPPIV inhibitors</td>
<td>+</td>
</tr>
<tr>
<td>GLP1 analogues</td>
<td>+++</td>
</tr>
<tr>
<td>Insulin</td>
<td>+++</td>
</tr>
<tr>
<td>SGLT2 inhibitors</td>
<td>++</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>++</td>
</tr>
</tbody>
</table>
Treatment strategy in patients with newly diagnosed type 2 diabetes

Classification

Classical type 2 diabetes (WHO)

Hypocaloric/low carbohydrate diet + ↑ physical activity

or

Gastric bypass (sleeve surgery)

Metformin

GLP1 analogue

or

Insulin (lean type 2 diabetes)

Other types:
- LADA
- MODY
- Steriod-induced diabetes mellitus
- Secondary diabetes mellitus

Lifestyle intervention and treatment of the patophysiological background of hyperglycaemia

OUH
Odense Universitetshospital
Coworkers

Jacob Volmer Stidsen
Jan Erik Henriksen
Michael Hecht Olesen
Klára Berencsi
Reimar Wernich Thomsen
Henrik Toft Sørensen
Jens Steen Nielsen
Allan Vaag
Jens Sandahl Christiansen
Jørgen Rungby
Type 2 diabetes er en heterogen sygdom med mange forskellige årsager til hyperglykæmi.

Test patienter med familiær anamnese for type 2 diabetes for MODY.

Behandl årsagen til hyperglykæmi og ikke kun blodglukose.