### Type 1 Diabetes (T1DM)

<table>
<thead>
<tr>
<th>Trials</th>
<th>Population</th>
<th>Intervention</th>
<th>A1C Baseline (mean)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCCT</td>
<td>n=1,441</td>
<td>5 years; n=1,121</td>
<td>Intensive insulin (3 or more shots)</td>
<td><strong>Rate of A1C</strong> at 4.0% + 0.6% <strong>RRR</strong> 63%</td>
</tr>
<tr>
<td>DPTP</td>
<td>n=545</td>
<td>2.5 years; n=411</td>
<td>Intensive insulin (3 or more shots)</td>
<td><strong>Rate of A1C</strong> at 4.0% + 0.6% <strong>RRR</strong> 58%</td>
</tr>
<tr>
<td>DPP</td>
<td>n=7,834</td>
<td>3.2 years; n=6,045</td>
<td>Intensive insulin (3 or more shots)</td>
<td><strong>Rate of A1C</strong> at 4.0% + 0.6% <strong>RRR</strong> 75%</td>
</tr>
</tbody>
</table>

### Type 2 Diabetes (T2DM)

<table>
<thead>
<tr>
<th>Trials</th>
<th>Population</th>
<th>Intervention</th>
<th>A1C Baseline (mean)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVANCE</td>
<td>n=1,587</td>
<td>Intensive lifestyle</td>
<td><strong>Rate of A1C</strong> at 4.0% + 0.6% <strong>RRR</strong> 58%</td>
<td></td>
</tr>
<tr>
<td>VADT</td>
<td>n=1,370</td>
<td>Intensive lifestyle</td>
<td><strong>Rate of A1C</strong> at 4.0% + 0.6% <strong>RRR</strong> 75%</td>
<td></td>
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<tr>
<td>LEADER</td>
<td>n=1,453</td>
<td>Intensive lifestyle</td>
<td><strong>Rate of A1C</strong> at 4.0% + 0.6% <strong>RRR</strong> 63%</td>
<td></td>
</tr>
<tr>
<td>ELIXA</td>
<td>n=1,345</td>
<td>Intensive lifestyle</td>
<td><strong>Rate of A1C</strong> at 4.0% + 0.6% <strong>RRR</strong> 58%</td>
<td></td>
</tr>
<tr>
<td>REGULAR</td>
<td>n=1,274</td>
<td>Intensive lifestyle</td>
<td><strong>Rate of A1C</strong> at 4.0% + 0.6% <strong>RRR</strong> 75%</td>
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</tr>
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### Type 2 Diabetes (T2DM) - Prevention

**Type 2 Diabetes (T2DM)**

- **Intensive lifestyle control may lead to a decrease in the risk of type 2 diabetes.**
- **Weight loss (at least 5% and up to 10%)**
- **Exercise: moderate, 150 minutes/week or 30 minutes/day**
- **Diets: healthy, low calorie, low fat (<30% of total kcal & <10% saturated fat), fibre (>15g/1000kcal)**

### Macrovascular Benefits

- **Systolic blood pressure reduction:**
- **Intensive insulin therapy compared to conventional therapy**
- **Reduced risk of major adverse cardiovascular events**
- **Reduced risk of hospitalization for heart failure**

### Antiplatelet Drugs

- **Aspirin:**
- **Clopidogrel:**
- **Prasugrel:**
- **Cangrelor:**

### Lifestyle Factors

- **Diet:**
- **Physical Activity:**
- **Smoking:**
- **Alcohol Consumption:**

### Other Considerations

- **Weight Loss:**
- **Sleep:**
- **Medication:**
- **Comorbidities:**

### Summary

- **Type 2 Diabetes (T2DM)**
- **Prevention**
- **Control**
- **Management**
- **Complications**
- **Prognosis**

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**Note:** The above information is based on the references provided and may not be exhaustive. Always consult with a healthcare professional for personalized advice.
### 2hBG

**EXTRAS Page for Diabetes Landmark Outcome Trials: Glycemic Control & Prevention Summary**

#### T2DM “Prevention” Trials

<table>
<thead>
<tr>
<th>Pre-diabetes</th>
<th>Intervention</th>
<th>Results</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDPS 4yr, n=522 (Finnish Diabetes Prevention Study)</td>
<td>Age 40-65 (mean 55); BMI ≥25 (mean 31); IGT (a FBG = 7.8mmol/L; 2hBG ≥7.8 but &lt;11mmol/L)</td>
<td>Intensive lifestyle vs control (Lifestyle: detailed, individualized counseling with nutritionist; individualized exercise circuit. Goals: HbA1c &lt;5.5%, fat &lt;30% of all energy, fibre &gt;15g/100g/day, moderate exercise &gt;30 minutes/day.)</td>
<td>1: incident diabetes (4yrs): 11% vs 23%&lt;br&gt;RRR = 58% HR = 0.4 (0.30-0.7)&lt;br&gt;NNT=4yrs = 8&lt;br&gt;ΔBody wt: -4.2kg (4.8-1.8 - &lt;0.8kg, 1.30-0.30, cont.)&lt;br&gt;7yr follow-up: effect persists 4.3 vs 7 cases/100 person-yrs&lt;br&gt;10yr follow-up: no effect on CV or total mortality</td>
</tr>
<tr>
<td>DPP 2.8yr, n=5,234 (Diabetes Prevention Project)</td>
<td>Age ≥25 (mean 51); BMI≥24 (mean 34); IGT (FBG of 5.3-6.9mmol/L; 2hBG of 7.8-9.1mmol/L) 86%; ~45% ethnic</td>
<td>Intensive lifestyle*&lt;br&gt;Lifestyle* + MF 850mg po BID</td>
<td>1: incident diabetes (2.8yrs): 4.8 cases/100 person yrs for intensive lifestyle 7.8 cases/100 person yr MF; 11 cases/100 person yr placebo, placebo;&lt;br&gt;• NNT = 7.2/8yrs for lifestyle (RR 58%, 77% of those 60+)&lt;br&gt;• NNT = 14.2/8yrs for MF (RR 25%)&lt;br&gt;Weight loss: &lt; 5.6kg (0.9 kg, p=0.001)&lt;br&gt;10yr follow-up: delays development of diabetes by 4yr, MF by 2yr</td>
</tr>
<tr>
<td>IDPP (India) 2.8yr, n=5,531</td>
<td>Mean age 46; BMI 26 IGT – in Asian Indians</td>
<td>Lifestyle vs MF 250mg po BID vs control</td>
<td>1: incident diabetes (2.5yrs): lifestyle 39.3%, NNT=8; MF 40.5%, NNT=7; placebo 55%</td>
</tr>
<tr>
<td>Stop-NIDDM 3.3yr, n=1,429</td>
<td>Mean age 40-70 (mean 54); IGT (FBG of 6.5-7.7mmol/L)</td>
<td>Acarbose 100mg tid vs placebo (also encouraged exercise; met with dietitian)</td>
<td>1: incident diabetes (3.3yrs): 32.4% vs 41.5%;&lt;br&gt;NNT=11&lt;br&gt;GI AEs 83% vs 60% &amp; stopped Tx: 31% vs 19%</td>
</tr>
<tr>
<td>XENDOS 4yr, n=3,305</td>
<td>Age 30-60 (mean 43); BMI≥30; no CVD; 21% had IGT</td>
<td>Orlistat 120mg TID vs placebo (weight loss study also - diet &amp; physical activity encouraged)</td>
<td>1: incident diabetes (3.3yrs): 6.2% vs 9%;&lt;br&gt;NNT=36/4yrs&lt;br&gt;CV events: 2.9% vs 2.1%&lt;br&gt;CV events: 2.4% vs 1.9%&lt;br&gt;NNT=10&lt;br&gt;GI AEs 83% vs 60% &amp; stopped Tx: 31% vs 19%</td>
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<tr>
<td>DREAM-Rosi 3yr, n=5,269 (Canoe Rosiglitazone in the Prevention of Vascular Events)</td>
<td>Age ≥30 (~55%); IGT +/- IFG or IFG</td>
<td>Rosiglitazone 8mg po daily vs placebo (Trial stopped 5 months early due to: diabetes; but CV event rate approaching statistical significance.)</td>
<td>2: incident diabetes: 6.2% vs 9%;&lt;br&gt;NNT=36/4yrs&lt;br&gt;CV events: 2.9% vs 2.1%&lt;br&gt;CV events: 2.4% vs 1.9%&lt;br&gt;NNT=10&lt;br&gt;GI AEs 83% vs 60% &amp; stopped Tx: 31% vs 19%</td>
</tr>
<tr>
<td>DREAM-Rami 3yr, n=5,269 (Canoe Ramipril in the Prevention of Vascular Events)</td>
<td>No DM or CVD; weight expanded during trial</td>
<td>Ramipril 15mg po daily (start 5mg/d x2 months, then 10mg/d till 1 yr) vs placebo</td>
<td>1: incident diabetes or death: 11.6% vs 26%;&lt;br&gt;NNT=7/3yrs&lt;br&gt;CV events: 2.9% vs 2.1%&lt;br&gt;CV events: 2.4% vs 2.8%&lt;br&gt;NNT=10&lt;br&gt;GI AEs 83% vs 60% &amp; stopped Tx: 31% vs 19%</td>
</tr>
<tr>
<td>NAVIGATOR 9yr</td>
<td>IGT &amp; CV risk/disease</td>
<td>Nateglinide, no +/- prediabetes + CV event. Valsartan + diabetes treated by 4yr.</td>
<td>1: incident diabetes or death: 18.1% vs 19.5%&lt;br&gt;NNT=36/4yrs&lt;br&gt;CV event: 2.8% vs 2.4%&lt;br&gt;CV event: 2.4% vs 2.8%&lt;br&gt;NNT=10&lt;br&gt;GI AEs 83% vs 60% &amp; stopped Tx: 31% vs 19%</td>
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### Effective Options

- **DREAM**
  - **XENDOS**
  - **IDPP** (India)
  - **FDPS** (Finnish Diabetes Prevention Study)

### Pharmacological Options

1. **Metformin** (MF - 250-850mg po BID (Meta-analysis))
   - 6 trials, n=3119, abd obesity, IGT, family hx: time to diabetes onset ≤ 3yrs; NNT=12.5 95% CI: 9.1-20 (Most effect if age >60yrs)
   - Orlistat 120mg po TID: Effective if able to tolerate GI side effects, high cost (not placebo)
   - Acarbose 100mg po TID (CV benefit did not persist)
   - Effective if able to tolerate GI side effects, high cost (not placebo)

2. **Not Effective or Harm/Outcome Concerns**
   - **Rami**
   - **Glibotazone** (Ros & Pi-glibotazine, CTV 25mg/1000kcal) effective after D/C; concerns (W, edema, HF, infection & CV Risk) 31;30
   - Nateglinide: ↑ risk of hypoglycemia without any benefits
   - Prevention strategies utilizing drugs have potential to harm otherwise healthy people: knowledge of long-term efficacy, safety & impact on healthcare resources need to be established.

### Other Trials of Interest


- **IRIS**: pioglitazone after stroke in patients with insulin resistance. For every 100 patients with recent history of stroke, transient ischemic attack (TIA) and insulin resistance, but NOT diabetes, giving pioglitazone 45mg daily for ~5 years will result in approximately 3 less cases of stroke or MI, 4 less cases of diabetes, 2 extra cases of serious bone fracture, 7 extra cases of weight gain > 13.6kg, and 11 extra cases of edema. (Note – those with various degrees of heart failure, pitting edema, etc. were excluded.) Link to trial summary: http://www.rxfiles.ca/rxfiles/uploads/documents/IRIS-Trial-Summary.pdf

- **RECORD**: n=4447, ~5.5yr; T2DM (A1C mean ~7.9% vs 7.4-7.9%); open label; MF or SU + rosiglitazone vs MF + SU. No difference in CV death, MI, HF & fracture.

### Upcoming Trials in Diabetes/CV Risk Prevention:

- **NAVIGATOR** (Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research) - NEJM Mar/10
- **TRANSCEND** (Telmsartan Randomized Assessment Study in aC Intolerant subjects with cardiovascular Disease) - RAPSOADI (rabinan in diabetes prevention) - CANOE (rosiglitazone 2mg bid & metformin 500mg bid in diabetes prevention)

### Prediabetes

- Includes: 1) **Impaired Fasting Glucose** (8hr fasting BG between 5.6-6.9mmol/L) & 2) **Impaired glucose tolerance** (Postprandial BG of 7.8-11.0mmol/L 2hrs post 75g oral glucose challenge)

### Risk factors: family hx, obesity – especially around waist, age >45, hypertension, gestational diabetes hx, sedentary lifestyle. Screening recommendations vary; USPSTF recommends screening particularly if BP ≥135/80. Oral Glucose Challenge most recommended, but A1c screen also advocated by some.

### QDscore diabetes risk calculator:

### Insulin Analogues Systematic Review/Reports, 2008:

### Tight glucose control in critically ill hospitalized pts may ↑ mortality & ↑ risk of hypoglycemia: JAMA 08; 40 Non-Sugar NNH=3860day
Q&A: Limitations & Unanswered Questions Regarding A1C Control and Clinical Outcome - Benefits or Risks

There are some important qualifiers on the commonly quoted observational data that “with every 1% drop in A1C the risk of developing long-term diabetes complications decreases”. (Concept originally based on observational data driven by an eye-related microvascular endpoint in the UKPDS). **RCT evidence does not support this assumption!**

- Most recently the **ACCORD** trial (established, higher risk T2DM) was halted after looking at whether a A1C target of <6% would result in beneficial clinical outcomes compared to 7-7.9%. According to the preliminary results still awaiting publication, it would appear from this RCT, in this population group, the extra 1.1% drop in A1C seen in the intensive group was actually associated with **increased all cause death compared to the standard group.** **Explanations for this are still pending; some possibilities noted with 5yr follow-up discussion below.**
  

- 5 year **ACCORD** follow-up results published Mar 2011. A1C lowering intensiveness relaxed for balance of study period; participants continued in BP or lipid lowering arms; A1C at 5 yrs ~ 7.2% vs 7.6%.  
  
  1. ↑ death sustained in intensive glucose lowering group 5.5% vs 4.5%  
  2. ↓ non-fatal MI, but fatal CV ↑
  3. severe hypoglycaemia equivalent in follow-up period;
  4. those most at risk of ↑ death were those with baseline A1C > 8%;
  5. possible explanations for harm with intensive glucose lowering:
     - **A)** different outcomes associated with different drugs or drug combinations?;  
     - **B)** impact of ↑ wt gain?;  
     - **C)** impact of intense BG lowering.

- With the current RCT evidence with rosiglitazone, there is some concern that lowering A1C does not necessarily result in CV event reductions? With the limited evidence, it appears to at best be neutral, and at worst, harmful in RCTs/durations studied so far (e.g. up to 5.6 year RCTs.). Patients studied, agents used & study limitations such as dropout may affect the benefit/risk balance.

- The **UKPDS-33**, ~ 10 year trial saw reductions predominantly in the microvascular events (predominantly photocoagulation), with stroke and heart related endpoints not significant, but trending favorably and contributing to the composite endpoint benefit. (Exception: metformin had all-cause death reduction in obese T2DM in UKPDS-34)

- In **UKPDS 34**, with noted a mortality benefit for metformin in obese T2DM, there is inconsistency in the association of A1C & outcomes (less A1C difference but more benefit)

- In **UKPDS 34** Metformin + Sulfonylurea combination led to a lower A1C than Sulf alone (7.7 vs 8.2) but had higher incidence of DM death and all cause death (perhaps due to design issues and a several year delay in moving to combination therapy).

- The **UKPDS** epidemiologic evidence for the 1% drop in A1C did not control for obesity/BMI/waist circumference. **UKPDS 35**

- In **ADOPT**, rosiglitazone decreased A1C more than metformin or glyburide, but glyburide had the lowest rate of CV outcomes.

- In **VADT**, a 1.5% reduction (6.9% intensive vs 8.4% standard) in A1C for an average follow-up of 5.6 years resulted in no benefit (microvascular or macrovascular) but increased serious adverse events (predominantly hypoglycaemia).

**Meta-analysis** 2011 of Intensive ↓ BG RCTs in T2DM: 13 trials, n=34,500. Endpoints: mortality, no difference; ↓RR=1.04, 95%CI 0.91-1.19); CV death, no difference; ↓RR=1.10, 95%CI 0.91-1.32); non-fatal MI, ↓RR=0.85, 95%CI 0.74-0.96)

- **Severe hypoglycaemia**: ↑↑ (RR=2.33, 95%CI 1.62-3.36) 1.9-8.6% of patients required tx for severe hypoglycaemia over 5 years. If only high quality studies included, no longer a ↓ in non-fatal MI & there was an ↑ in HF.

- **Microvascular effects**: no difference, but heterogeneity; rate of retinopathy (0.85, 0.71-1.03); photocoagulation (0.91, 0.71-1.17), ↓vision or blindness (1.00); neuropathy 0.99, 0.95-1.03; renal failure or 2x SCR (1.03, 0.98-1.08).

- **Microalbuminuria**: ↓(0.90, 0.85-0.96), AFR 0.7%-3.1%; NNT=142-32. **OVERALL**: for hard clinical endpoints, no benefit, but increased severe hypoglycaemia requiring tx. However, note heterogeneity in trials, different tx approaches, different definitions of “intensive lowering”, etc. Nevertheless, the more trials, the more evidence that just lowering BG does not equate automatically to beneficial clinical outcomes, but does carry hypoglycaemia risk.

There is some discordance between randomized trial outcome evidence and the frequently reported “1% A1C...” benefit. One thing that has growing certainty is that the risks and benefits of drug regimens that lower A1C is more complex than what was previously commonly accepted. While a high A1C is not good, some methods of lowering A1C in some patient groups, are also harmful. While we do not want to be lazy in addressing glucose control, the evidence suggests that we do not assume a net benefit for all A1C lowering interventions in all Type 2 diabetes patients. (Let the target serve the patient, and not the patient the target.)

See also: Yudkin JS, Lipska KJ, Montori VM. The idolatry of the surrogate. BMJ. 2011 Dec 28;343:d7995. [http://www.bmj.com/content/343/bmj.d7995](http://www.bmj.com/content/343/bmj.d7995)

**Multifactorial intervention** - blood pressure, lipids, possibly ASA, lifestyle – in addition to glucose control, is essential in reducing macrovascular endpoints!

References - Diabetes Trials: Landmark Outcome and Prevention (www.RxFiles.ca)


9. Salpetier SR, Buckley NS, Kahn JA, Salpetier EE. Meta-analysis: metformin treatment in persons at risk for diabetes mellitus. Ann Med. 2006;38:149-157. (InfoPOEMS: Using metformin to treat patients at risk for diabetes decreases their likelihood of developing diabetes over a 3-year period. Longer studies are needed to determine whether the likelihood of diabetes is truly decreased or simply delayed. We have no research to tell us whether, in the long run, patients live longer or live better if they are treated at this stage of pre-diabetes. (LOE = 1a)).


11. DeFronzo Ralph A., Tripathy Devjit, Schwenneke Dawn C., et al. for the ACT NOW Study. Pioglitazone for Diabetes Prevention in Impaired Glucose Tolerance. N Engl J Med 2011;364:3104-114. (ACT-NOW: Upgression to TZD (annual incidence of diabetes was 2.1 vs 7.6%/yr; NNT=19 yr) but Tweight (3.9kg vs 0.7kg) & edema (12.9 vs 6.4%).


Zoungas S, de Galan BE, Ninniyira T, et al. for the Diabetes Prevention Program. The combined effects of routine blood pressure lowering and intensive glucose control on macrovascular and microvascular outcomes in patients with type 2 diabetes: new results from ADVANCE. Diabetes Care. 2009 Aug 3. [Epub ahead of print] The effects of routine blood pressure lowering and intensive glucose control were independent of one another and when combined produced additional reductions in clinically relevant outcomes.

Zoungas S et al. Severe hypoglycemia and risks of vascular events and death (ADVANCE). N Engl J Med 2010 Oct 7; 363:1410. During a median follow-up period of 5 years, 231 patients (2.1%) had at least one severe hypoglycemic episode; 150 had been assigned to intensive glucose control (2.7% of the 5571 patients in that group), and 81 had been assigned to standard glucose control (1.6% of the 5569 patients in that group).


UGDP.

Duckworth W, Abraira C, Moritz T, et al. Glucose Control and Vascular Complications in Veterans with Type 2 Diabetes. N Engl J Med. 2008 Dec 17. (VADT study) Intensive glucose control in patients with poorly controlled type 2 diabetes had no significant effect on the rates of major cardiovascular events, death, or microvascular complications. (InfoPOEMs Mar09: Like the ACCORD and ADVANCE studies, this trial provides additional evidence that intensive glucose control does not improve outcomes in patients with type 2 diabetes mellitus. It is important to note that these patients had well-controlled hypertension (mean blood pressure = 126/88) and well-controlled hyperlipidemia (mean low-density lipoprotein = 80 mg/dL.)


10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes. (UKPDS-80). N Engl J Med 2008;359:1-13. ([SU/Insulin vs control]; MI 19.6±0.86 per 1000 patient-yrs; RR=0.58 (CI: 0.74-0.49)); Death 30.3±29.8 per 1000 patient-yrs (RR=0.53 (CI: 0.74-0.39)); MI vs control; MI, 21.1±14.8 per 1000 patient-yrs (RR=0.71 (CI: 0.51-0.96)); Death 33.1±25.9 per 1000 patient-yrs (RR=0.63 (CI: 0.52-0.78)). (Daily POEM: The advantages of tight blood sugar control seen in the United Kingdom Prospective Diabetes Study (UKPDS) trial were maintained and to some extent extended during a 10-year nonrandomized follow-up period, even though all patients quickly had similar glycohemoglobin levels. The benefit was most pronounced with metformin. Note that in the "intensive therapy" group had a mean glycohemoglobin of approximately 8% at the end of the randomized portion of the study, and the recent ACCORD study found that more aggressive control offered no benefit and may be harmful (N Engl J Med 2008;358:2545-59, POEM #100825). LOE = 2/7)


Canadian Pharmacological Prescribing & Utilization Service (COMPASS), Current Topics, Diabetes. http://care.diabetesjournals.org/content/37/Supplement_1.toc

Canadian Optimal Medication Prescribing & Utilization Service (COMPASS), Current Topics, Diabetes. http://content.nejm.org/cgi/content/full/NEJMoa072561


Montori VM, Balsells M. Glycemic Control in Type 2 Diabetes: Time for an Evidence-Based Approach? Ann Intern Med 2009; 150(11). Available at: http://www.aannals.com/cgi/content/full/0000605-20090620-00119v1

Salpeter SR, Buckley NS, Kahn JA. Salpeter EE. Meta-analysis: metformin treatment in persons at risk for diabetes mellitus. Am J Med 2008;121:149-156. (infoPOEMS: Using metformin to treat patients at risk for diabetes decreases their likelihood of developing diabetes over a 3-year period. Longer studies are needed to determine whether the likelihood of diabetes is truly decreased or simply delayed. We have no research to tell us whether, in the long run, patients live longer or live better if they are treated at this stage of (pre)diabetes. (LOE = 1A)


Montori VM, Balsells M. Glycemic Control in Type 2 Diabetes: Time for an Evidence-Based Approach? Ann Intern Med 2009; 150(11). Available at: http://www.aannals.com/cgi/content/full/0000605-20090620-00119v1

Wiener RS, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis. JAMA. 2008 Aug 27;300(8):933-44. In critically ill adult patients, tight glucose control is not associated with significantly reduced hospital mortality but is associated with an increased risk of hypoglycemia.


New Trials Post-2015


Additional References

ADA-American Diabetes Association Guidelines—Standards of Medical Care in Diabetes—2014 http://care.diabetesjournals.org/content/37/Supplement_1#toc


Targeting intensive glycaemic control reduced the risk of microvascular complications while increasing the risk of hypoglycaemia. Furthermore, intensive glycaemic control might reduce the risk of fatal myocardial infarction in trials exclusively dealing with glycaemic control in usual care settings.


Hemmingsen B, Sonne DP, Metzdorf MJ, et al. Dipeptidyl-peptidase (DPP)-4 inhibitors and glucagon-like peptide (GLP)-1 analogues for prevention or delay of type 2 diabetes mellitus and its associated complications in people at increased risk for the development of type 2 diabetes mellitus. Cochrane Database Syst Rev. 2017 May 10;5:CD012204. There is no firm evidence that DPP-4 inhibitors or GLP-1 analogues compared mainly with placebo substantially influence the risk of T2DM and especially its associated complications in people at increased risk for the development of T2DM. Most trials did not investigate patient-important outcomes.


Milly G, Mowinckel M. Treating prediabetes with metformin: systematic review and meta-analysis. Can Fam Physician. 2009 Apr;55(4):363-9. Metformin decreases the rate of conversion from prediabetes to diabetes. This was true at higher dosage (850 mg twice daily) & lower dosage (250 mg twice or three times daily); in people of varied ethnicity; & even when a sensitivity analysis was applied to the data. The number needed to treat was between 7 & 14 for treatment over a 3-year period.


Orrozco LJ, Buchleitner AM, Glinzinger A, Roqui IF, Majcher B, Mauricio D. Exercise or exercise and diet for preventing type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD003054. DOI: 10.1002/14651858.CD003054.pub3. Interventions aimed at increasing exercise combined with diet are able to decrease the incidence of type 2 diabetes mellitus in high risk groups (people with impaired glucose tolerance or the metabolic syndrome). There is a need for studies exploring exercise only interventions and studies exploring the effect of exercise and diet on quality of life, morbidity and mortality, with special focus on cardiovascular outcomes.


