Complications of Diabetes: Screening and Prevention

Dr Steve Cleland
Consultant Physician
GGH and QEUH

Diabetes Staff Education Course
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Diabetic Complications

**Microvascular:**
- Retinopathy
- Nephropathy
- Neuropathy
- Erectile dysfunction

**Macrovascular:**
- Coronary heart disease (CHD)
- Cerebrovascular disease (CVD)
- Peripheral vascular disease (PVD)
Type 2 diabetes is NOT a mild disease

Diabetic Retinopathy
Leading cause of blindness in working age adults\(^1\)

Stroke
2 to 4 fold increase in cardiovascular mortality and stroke\(^3\)

Cardiovascular Disease
8/10 diabetic patients die from CV events\(^4\)

Diabetic Nephropathy
Leading cause of end-stage renal disease\(^2\)

Diabetic Neuropathy
Leading cause of non-traumatic lower extremity amputations\(^5\)
Macrovascular disease at diagnosis in Type 2 diabetes

- Cerebrovascular disease: 1%
- Abnormal ECG: 18%
- Hypertension: 35%
- Absent foot pulses: 13%
- Intermittent claudication: 3%

75% of all deaths in people with Type 2 diabetes are due to cardiovascular disease.

Retinopathy

- Specific for diabetes
- Type 1 and Type 2 diabetes
- Related to duration of diabetes and control
- Individual risk factors (?genetic)
- Most common cause of preventable blindness <65 year old

Other Diabetic Eye Diseases

- Cataracts
- Glaucoma
Retinopathy - Prevention

Good diabetes control
  Type 1 diabetes (DCCT, 1993)
  Type 2 diabetes (UKPDS, 1998)

ACE inhibitors
  Type 1 diabetes (Lewis et al, 1993)
  Type 2 diabetes (HOPE, 2000)

Good BP control

STOP SMOKING

Regular attendance at Retinal Screening
  Referral to ophthalmologist when appropriate
DCCT - New Retinopathy

Conventional

Intensive

P<0.001

NEJM 1993;329:977-86
DCCT - Progressive Retinopathy

Percentage of Patients

Year of Study

Conventional

Intensive

P<0.001

NEJM 1993;329:977-86
Nephropathy

- Specific for diabetes
- Type 1 and Type 2 diabetes
- Related to duration of diabetes and control
- Associated with retinopathy
- Commonest cause of ESRD
- Progressive

- Microalbuminuria (30-300mg/24hr)
- Albuminuria (>300mg/24hr)
- Renal impairment (eGFR <60mL/min)
- Dialysis
  (Transplantation)
Natural history of diabetic nephropathy

![Graph showing the natural history of diabetic nephropathy with stages and GFR, Systolic BP, and Proteinuria over time.](image)

Adapted from Mogensen et al, Diabetologia 1979; 17: 71-76
Nephropathy - Prevention

Good diabetes control
  Type 1 diabetes (DCCT, 1993)
  Type 2 diabetes (UKPDS, 1998)

Good blood pressure control (esp. ACEI)
  Type 1 diabetes (Lewis et al, 1993)
  Type 2 diabetes (HOPE, 2000)

Target BP <140/80
  (<130/70 if presence of microalbuminuria)

CKD Guidelines - referral
DCCT - New Microalbuminuria

Percentage of Patients

Year of Study

Conventional
Intensive

P<0.04

NEJM 1993;329:977-86
Neuropathy

Clinical Syndromes

- Chronic sensory neuropathy
- Acute painful neuropathy
- Proximal motor neuropathy (amyotrophy)
- Diffuse motor neuropathy
- Focal neuropathy
- Autonomic neuropathy
Neuropathy - Prevention

Good diabetes control (DCCT, UKPDS)

Neuropathy - Treatment

Improve diabetes control
Anti-depressants (amitriptyline, duloxetine)
Anti-epileptics (gabapentin, pregabalin)
Opiates
Axain cream
Lidocaine patches
Acupuncture
Macrovascular Disease

Coronary Heart Disease (CHD)
• Angina
• Myocardial infarction
• PTCA
• CABG
• Heart failure

Cerebrovascular Disease (CVD)
• Stroke
• TIA

 Peripheral Vascular Disease (PVD)
• Intermittent claudication
• Ulceration
• Gangrene
• Amputation
Cardiovascular Disease

The Framingham Study Kannel and McGee. Circulation 1979
Glycaemic Control
Meta-analysis of CV outcome RCTs

- n=33040
- HbA$_{1c}$ 10 mmol/mol (0.9%) difference (intensive v conventional)
- Odds ratio:
  - Fatal MI $0.83$ (0.75–0.93)
  - CHD $0.85$ (0.77–0.93)
  - Stroke $0.93$ (0.81–1.06)
  - All-cause mortality $1.02$ (0.87–1.19)

CV=cardiovascular; RCT=randomised controlled trials; MI=myocardial infarction; CHD=coronary heart disease.
Ray KK et al Lancet 2009; 373: 1765-72
Meta-analysis of intensive glucose control in T2DM: major CV events including heart failure

<table>
<thead>
<tr>
<th>Event</th>
<th>Number of events</th>
<th>Difference in HbA1c (%)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>378, 370</td>
<td>-0.88</td>
<td>0.96 (0.83, 1.10)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>730, 745</td>
<td>-0.88</td>
<td>0.85 (0.76, 0.94)</td>
</tr>
<tr>
<td>Hospitalisation for or death from heart failure</td>
<td>459, 446</td>
<td>-0.88</td>
<td>1.00 (0.86, 1.16)</td>
</tr>
</tbody>
</table>

- Meta-analysis of 27,049 participants and 2370 major vascular events from:
  - ADVANCE
  - UKPDS
  - ACCORD
  - VADT

HR, hazard ratio; CV, cardiovascular
Turnbull FM et al. Diabetologia 2009;52:2288–2298
## Meta-analysis of intensive glucose control in T2DM: mortality

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Number of events More intensive</th>
<th>Number of events Less intensive</th>
<th>Difference in HbA1c (%)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>980</td>
<td>884</td>
<td>-0.88</td>
<td>1.04 (0.90, 1.20)</td>
</tr>
<tr>
<td>CV death</td>
<td>497</td>
<td>441</td>
<td>-0.88</td>
<td>1.10 (0.84, 1.42)</td>
</tr>
<tr>
<td>Non-CV death</td>
<td>476</td>
<td>432</td>
<td>-0.88</td>
<td>1.02 (0.89, 1.18)</td>
</tr>
</tbody>
</table>

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Blood Pressure Control
Summary of BP trials in T2D

- HOT: Lancet 98;351:1755-62
- SHEP: JAMA 91;265:3255-64
- UKPDS: BMJ 00;321:412-9
- HOPE: Lancet 01;358:2130-1
- Syst Eur: Lancet 97;350:757-64
- PROG: Lancet 01;358:1033-41
- ADV: Lancet 07;370:829-40
- ABCD: Diabetologia 96;39:1646-54
- IDNT: NEJM 01;345:861-9
- RENAAAL: NEJM 01;345:861-9
Systolic Pressures (mean ± 95% CI)

Mean # Meds
Intensive: 3.2 3.4 3.5 3.4
Standard: 1.9 2.1 2.2 2.3

133.5 mmHg Standard vs. 119.3 mmHg Intensive

ACCORD BP trial: NEJM 2010; 362: 1575-85
# Primary & Secondary Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Intensive Events (%/yr)</th>
<th>Standard Events (%/yr)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td>208 (1.87)</td>
<td>237 (2.09)</td>
<td>0.88 (0.73-1.06)</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>Total Mortality</strong></td>
<td>150 (1.28)</td>
<td>144 (1.19)</td>
<td>1.07 (0.85-1.35)</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>Cardiovascular Deaths</strong></td>
<td>60 (0.52)</td>
<td>58 (0.49)</td>
<td>1.06 (0.74-1.52)</td>
<td>0.74</td>
</tr>
<tr>
<td><strong>Nonfatal MI</strong></td>
<td>126 (1.13)</td>
<td>146 (1.28)</td>
<td>0.87 (0.68-1.10)</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>Nonfatal Stroke</strong></td>
<td>34 (0.30)</td>
<td>55 (0.47)</td>
<td>0.63 (0.41-0.96)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Total Stroke</strong></td>
<td>36 (0.32)</td>
<td>62 (0.53)</td>
<td>0.59 (0.39-0.89)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**ACCORD BP trial**: *NEJM* 2010; 362: 1575-85
Aspirin use in patients with diabetes
# Events Avoided or Caused per 1000 Individuals Treated with Aspirin for 5 Years

<table>
<thead>
<tr>
<th>10 year risk of CHD event</th>
<th>Avoided</th>
<th>Caused</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CHD event</td>
<td>Ischaemic stroke</td>
</tr>
<tr>
<td>&lt;10%</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>10-20%</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Secondary</td>
<td>25-50</td>
<td>25-50</td>
</tr>
</tbody>
</table>

ATTC, *BMJ* 2002;324:71-86
Lipid Control
On-Treatment LDL and CHD Events in Statin Trials

LDL-C achieved, mg/dL (mmol/L)

Event rate (%)

Secondary Prevention

Primary Prevention

Adapted from Rosenson RS. Expert Opin Emerg Drugs. 2004;9:269-279.
The Diabetic Foot

Feet are at risk from microvascular (neuropathy) and/or macrovascular disease (PVD)

Remember loss of protective sensation

Foot screening – assessment of risk (SCI Diabetes)

- Skin condition (infection, ulceration, callus)
- Deformity (claw toes, Charcot joint)
- Peripheral pulses (dorsalis pedis, posterior tibial)
- Fine touch (10g monofilament)
- (Vibration -tuning fork, neurosesthesiometer)
- (Ankle reflexes)
- Footwear
Screening for complications (1)

- Retinal screening
  - Digital camera
  - Grading system
  - Automatic call and recall
  - Varying locations
  - Optician
  - Ophthalmology clinic

- Foot screening
  - Suitably trained HCP
  - Pulses and sensation using 10g monofilament

- HbA1c
  - Aiming for <58mmol/mol
  - Likely to need escalating medication over time
Screening for complications (2)

- BP control
- Urinary ACR/PCR; U&E /eGFR
- Smoking cessation advice
- Cardiovascular risk assessment - statins
- Lifestyle factors – exercise, diet, weight loss (GWMS referral)
my diabetes my way is the NHS Scotland interactive diabetes website to help support people who have diabetes and their family and friends. You'll find leaflets, videos, educational tools and games containing information about diabetes. You can now also use this website to view your own up-to-date diabetes clinic results, to help you manage your condition more effectively.

Diabetes (known formally as Diabetes Mellitus) is a long term condition where the amount of glucose in the blood is too high because the body cannot use it properly. There are over 250,000 people with diabetes in Scotland - that's around one person in every twenty.

In the case of an emergency, view the emergency contact leaflet here.
Summary

• Prevention always better than treatment
• Importance of tackling lifestyle factors from beginning and throughout
• Recognition of the natural progression of the condition and need for escalation of therapies
• Importance of attending screening opportunities
• Empowering patient to make choices about the things they can control
• Enabling patients to access information and data