Diabetes Care Improvement Packages.
Role of Primary Care

Dr Jeremy Krebs
Clinical Leader and Endocrinologist
Wellington Hospital
Diabetes Mellitus

- How big is the problem?
- Diabetes Care Improvement Packages
- Does hyperglycaemia matter?
- Management Goals
- Insulin
New Zealand Virtual Diabetes Register
end-2005 to end-2012 – latest data

Increase is in both genders, also across all ethnicities
New Zealand Diabetes Prevalance Rate as of 31 Dec 2007

European/Other
Māori
Pacific people
Indian
New Zealand Diabetes Prevalance Rate as of 31 Dec 2008

Age group

Rate (Base=Practice enrolled population)

European/Other
Māori
Pacific people
Indian
New Zealand Diabetes Prevalance Rate as of 31 Dec 2009
New Zealand Diabetes Prevalance Rate as of 31 Dec 2010

Rate (Base=Practice enrolled population)

Age group

European/Other
Māori
Pacific people
Indian
New Zealand Diabetes Prevalance Rate as of 31 Dec 2011

- European/Other
- Māori
- Pacific people
- Indian
Direct same-scale comparison of prevalence curves 2005 and 2011
VDR 2012: major points

- Diagnosed diabetes prevalence at December 2012 is 225,731, an increase of 8.5% above December 2011 (17,600, ≈ 50 per day).

- All DHBs showed increases – from 3 - 13%.

- Peak prevalence in Pacific and Asian groups is now at 45% in older adults. In Maori is now at 35% in older adults.

- The majority of diabetes (69%) is still within the European/Other community.
Diabetes Mellitus

- How big is the problem?
- Diabetes Care Improvement Packages
- Does hyperglycaemia matter?
- Management Goals
- Insulin
Traditional Model of Diabetes Care

Primary Care

Secondary Care

- Access to specialist advice / services
- Limited input to overall population
- Disparities in Access / Care
- Information sharing
How can we improve diabetes care?

◆ What? (Primary and Secondary Care)
  – Improved Communication
  – Improved Sharing of Data
  – Improved Two-way Flow of Patients

◆ How
  – Shared Care
  – Combined Community Clinics
  – More Multi-Disciplinary Approach
  – Acceleration of therapy in primary care
Diabetes Care Improvement Plan

- Prevent and slow progression of diabetic complications, especially heart disease, renal failure, impaired vision and lower limb amputations
- Reduce disparities between different population groups
- Reduced frequency of diabetes-related presentations to hospital emergency departments
- Reduce rates of hospital admission for diabetes and related complications
- Prevent or delay the onset of diabetes
The CCDHB model’s key components

- Combined Primary and Secondary Diabetes Clinical Network
- Practice population management
- Performance measures
- Collaborative case service in priority practices
- Workforce development
- Nurse practice partnership
- Self Management Groups
- Hospital specialist service focused on complex, Type 1, paediatric, gestational and renal diabetes
Key Goals

- Get quality services to the population that need it
- Foster patient self management
- Maximise the skills and confidence of the workforce
• Access to specialist advice / services
• Limited input to overall population
• Disparities in Access / Care
• Information sharing
New Model for Diabetes Management in the Wellington Region

Primary Care

Secondary Care

Outreach

Gestational DM

Paediatrics

Type 1

Self Management Groups

Clinical Network
Diabetes Mellitus

- How big is the problem?
- Diabetes Care Improvement Packages
- Does hyperglycaemia matter?
- Management Goals
- Insulin
HbA1c and Risk of Diabetes Related Complications

Target HbA1c <7%

- Retinopathy
- Nephropathy
- Neuropathy
- Microalbuminuria

Incidence rates of MI and microvascular endpoints by mean HbA$_{1c}$ (UKPDS)

Study population: white, Asian Indian, and Afro-Caribbean UKPDS patients (n = 4,585)
Adjusted for age, sex, and ethnic group

Error bars = 95% CI

UKPDS: Improving HbA$_{1c}$ Control
Reduced Diabetes-Related Complications

EVERY 1% reduction in HbA$_{1c}$

1%

Relative Risk
N=3642

- Diabetes-related deaths: 21%
- Myocardial infarctions: 14%
- Microvascular complications: 37%
- Amputations or deaths from peripheral vascular disorders: 43%

REDUCED RISK ($P<0.0001$)

UKPDF=United Kingdom Prospective Diabetes Study.
Data adjusted for age, sex, and ethnic group, expressed for white men aged 50–54 years at diagnosis and with mean duration of diabetes of 10 years.
### Figure 4: Legacy Effect of Earlier Glucose Control

After median 8.5 years post-trial follow-up

<table>
<thead>
<tr>
<th>Aggregate Endpoint</th>
<th>1997</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any diabetes related endpoint</td>
<td>RRR: 12%</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td>P: 0.029</td>
<td>0.040</td>
</tr>
<tr>
<td>Microvascular disease</td>
<td>RRR: 25%</td>
<td>24%</td>
</tr>
<tr>
<td></td>
<td>P: 0.0099</td>
<td>0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>RRR: 16%</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>P: 0.052</td>
<td>0.014</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>RRR: 6%</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>P: 0.44</td>
<td>0.007</td>
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</tbody>
</table>

RRR = Relative Risk Reduction, P = Log Rank
Steno-2 Post Trial: Mortality of any cause

Numbers at risk
Conventional  Intensive
80  80  80  80
77  75  72  65
51  57  57  39
43  43  43  30
63  62  62  30
69  72  72  30
75  77  77  30
69  72  72  30
51  57  57  30
63  62  62  30
69  72  72  30
51  57  57  30
43  43  43  30
30  30  30  30

Log rank P=0.015

Gaede et al.  NEJM 2008
Steno-2 Post Trial: Any CVD events

Cumulative incidence of patients with a major CVD event during follow-up

**Numbers at risk**

<table>
<thead>
<tr>
<th></th>
<th>Conventional</th>
<th>Intensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers at risk</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Years of follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>70</td>
<td>72</td>
</tr>
<tr>
<td>1</td>
<td>60</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>46</td>
<td>61</td>
</tr>
<tr>
<td>3</td>
<td>38</td>
<td>56</td>
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<td>4</td>
<td>29</td>
<td>50</td>
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<tr>
<td>Years of follow-up</td>
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<tr>
<td>5</td>
<td>25</td>
<td>47</td>
</tr>
<tr>
<td>6</td>
<td>14</td>
<td>31</td>
</tr>
</tbody>
</table>

Cumulative incidence of CVD events (\%)

Log-rank P=0.0002

Gaede et al. NEJM 2008
<table>
<thead>
<tr>
<th>Event</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>5 patients</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>8 patients</td>
</tr>
<tr>
<td>Major cardiovascular event</td>
<td>3 patients</td>
</tr>
<tr>
<td>Progression to nephropathy</td>
<td>5 patients</td>
</tr>
<tr>
<td>Dialysis</td>
<td>16 patients</td>
</tr>
<tr>
<td>Laser treatment</td>
<td>7 patients</td>
</tr>
</tbody>
</table>

(from Gaede et al 2008 Steno 2, 13 year study)
Recent Trials of Glycaemic Control

- Advance, Accord
- 10 year post diagnosis, middle age
- Despite intensive HBA1c management have failed to show CVD benefit
Accord
The Action to Control Cardiovascular Risk in Diabetes Study Group

- **N=10,000**
  - 1/3 already on insulin
  - 1/3 prevalent CVD events
  - Age 62
  - Diabetes for 10 years
  - HbA1c 8.3

*Strategy of (ultra) intensive glycaemic control aiming for HbA1c 6 (achieved 6.3)*
The mean difference during the trial was 1.1%
Accord June 2008
Primary Outcome: First occurrence of nonfatal MI, stroke or death from Cardiovascular cause

352 vs 371 events
HR 0.9 (0.78-1.04, p=0.16)
## Primary & Secondary Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Intensive N (%)</th>
<th>Standard N (%)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>352 (6.86)</td>
<td>371 (7.23)</td>
<td>0.90 (0.78-1.04)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>257 (5.01)</td>
<td>203 (3.96)</td>
<td>1.22 (1.01-1.46)</td>
<td>0.04</td>
</tr>
<tr>
<td>Nonfatal MI</td>
<td>186 (3.63)</td>
<td>235 (4.59)</td>
<td>0.76 (0.62-0.92)</td>
<td>0.004</td>
</tr>
<tr>
<td>Nonfatal Stroke</td>
<td>67 (1.31)</td>
<td>61 (1.19)</td>
<td>1.06 (0.75-1.50)</td>
<td>0.74</td>
</tr>
<tr>
<td>CVD Death</td>
<td>135 (2.63)</td>
<td>94 (1.83)</td>
<td>1.35 (1.04-1.76)</td>
<td>0.02</td>
</tr>
<tr>
<td>CHF</td>
<td>152 (2.96)</td>
<td>124 (2.42)</td>
<td>1.18 (0.93-1.49)</td>
<td>0.17</td>
</tr>
</tbody>
</table>
Incidence of Severe Hypoglycemia per Year (1st event)
Diabetes Mellitus

- How big is the problem?
- Diabetes Care Improvement Packages
- Does hyperglycaemia matter?
- Management Goals
- Insulin
Treatment Targets
NZ Primary Care Handbook 2012

Treatment targets
Treatment targets to address risk factors.

• should be appropriate for and agreed with the individual patient

• glycaemic control target: HbA1c 50–55 mmol/mol
  or as individually agreed

• blood pressure target: <130/80 mm Hg. Evidence suggests a
  BP target <120 mm Hg may be harmful. Care should be taken
  to estimate likely treatment response for patients when BP approaches
  the target of <130 mm Hg

• lipids target: triglycerides <1.7 mmol/L; total cholesterol <4.0 mmol/L.
Less than 50% of Adults With Type 2 Diabetes Have Achieved HbA$_1c$ Goals

**US Population**

- **HbA$_1c$ level <7%**
  - 44.3%
  - NHANES 1999–2000 (n=370)
  - 37.0%

- **Blood pressure <130/80 mmHg**
  - 29.0%
  - NHANES 1999–2000 (n=370)
  - 35.8%

- **Total cholesterol <200 mg/dl**
  - 33.9%
  - NHANES 1999–2000 (n=370)
  - 48.2%

- **Achieved all 3 treatment goals**
  - 5.2%
  - NHANES 1999–2000 (n=370)
  - 7.3%

Adapted from Saydah SH et al. *JAMA*, 2004;291:335–342.
Glycaemic Control

Target HbA1c 48-58 mmol/mol
(6.5 - 7.5%)

Management Strategy

Diet and Lifestyle

Oral Hypoglycaemics

Monotherapy

Combination therapy

Insulin
Natural History of Type 2 Diabetes

Cross-sectional, median values

Conventional

Intensive

HbA1c (%)

Years from randomisation

6.2% upper limit of normal range
Clinical Inertia

- **Metformin monotherapy (n=513 episodes)**
- **Sulfonylurea monotherapy (n=3394 episodes)**

<table>
<thead>
<tr>
<th>Treatment Status</th>
<th>Metformin</th>
<th>Sulfonylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>First HbA(_1c) on Treatment</td>
<td>8.2</td>
<td>7.6</td>
</tr>
<tr>
<td>Best HbA(_1c) on Treatment</td>
<td>7.7</td>
<td>7.1</td>
</tr>
<tr>
<td>Last HbA(_1c) before Switch</td>
<td>8.8</td>
<td>9.1</td>
</tr>
<tr>
<td></td>
<td>(35\textsuperscript{b} months)</td>
<td>(27\textsuperscript{b} months)</td>
</tr>
</tbody>
</table>

- ADA goal: 7.7%
- EASD goal: 8.2%

\(\text{HbA}_{1c}\) values are in percentages.

\(^{a}\)US Physicians; 1994–2002

\(^{b}\)Mean number of months that elapsed until a new or additional treatment was started.

\(^{c}\)Monotherapy switched to another agent or additional agent added.

Traditional Type 2 Diabetes Management: A “Treat-to-Fail Approach”

Published Conceptual Approach

- Mean HbA1c of patients
- Duration of Diabetes
- Time

OAD=oral anti-hyperglycaemic drug.
The Therapeutic Challenge in Managing Type 2 Diabetes

We need treatments that:

- Additive to traditional treatments
- Can be used in presence of complications (eg kidney failure, heart disease)
- Acceptable to patients
- Minimise rather than worsen complications of diabetes
- (preferably) not increase weight
- (ideally) not cause hypos
Pathogenesis of Type 2 Diabetes: Insulin Resistance and β-cell dysfunction

Genetic Susceptibility
Obesity, Sedentary Lifestyle

Insulin Resistance
↓ glucose uptake
↑ hepatic glucose production

Type 2 Diabetes

β-cell Dysfunction
impaired insulin secretion

Major Targeted Sites of Oral Drug Classes

- **Pancreas**: Impaired insulin secretion
  - Sulfonylureas
  - GLP-1 mimetics
  - DPP-4 inhibitors

- **Liver**: Hepatic glucose overproduction
  - Biguanides
  - TZDs
  - GLP-1 mimetics
  - DPP-4 inhibitors

- **Muscle and fat**: Insulin resistance
  - TZDs
  - Biguanides

- **Gut**: Glucose absorption
  - α-Glucosidase inhibitors
  - Biguanides

DPP-4=dipeptidyl peptidase 4; TZDs=thiazolidinediones.
Type 2 Diabetes Algorithm

Diet and Lifestyle

Metformin

- Oral agent
  - Good evidence
  - But weight gain, heart failure, fractures, bladder cancer, IHD risk

- Oral agent
  - No hypos
  - But Gl side effects

- Weight neutral
  - Oral agent
  - No hypos

- Weight loss
  - No hypos
  - But Injectable

SU

Glitazone

Acarbose

DPPIV Ant

GLP-1 Agon

Insulin
Diabetes Mellitus

- How big is the problem?
- Diabetes Care Improvement Packages
- Does hyperglycaemia matter?
- Management Goals
- Insulin
Insulin Therapy

Pro’s

- Feel Better
  - More energy
  - Less infections
- Better HbA1c
  - ↓ Microvascular
  - ? Macrovascular
- Flexibility

Con’s

- Injections
- Weight gain
- More hypo’s
- Driving issues
- Needle phobias
Trade off of Intensifying Insulin therapy

Hypoglycaemia/complications (%)

Risk of developing hypoglycaemia/complications (%)

HbA1C

DCCT Research Group.
Insulin and Type 2 Diabetes: The Who?

Anyone!

- Poor glycaemic control (HbA1c >60 mmol/mol)
- Symptoms of hyperglycaemia

But consider:

- Is it realistic
  - Self inject?
  - ↑ Risk of hypoglycaemia
  - Age and Co-morbidities
"It wasn’t really insulin. You don’t have diabetes yet. It was just a warning shot."
Progressive Decline in Insulin Secretion

Insulin Therapy: The What?

- ? Once daily intermediate acting insulin
- ? Twice daily intermediate acting insulin
- ? Mixed insulins
- ? Basal bolus regimen
- ? Regular or analogue

Little evidence to support one over another in Type 2.
How to Decide on What?

◆ Pattern of hyperglycaemia
  • Fasting vs Post-prandial
  • Morning vs Evening

◆ What will the patient do?
  • Inject once or several times per day?
  • Willing to test glucose levels?
  • Able to interpret result and modify insulin?
Role of Self Monitoring of Blood Glucose

◆ *Type 2 DM on lifestyle alone/Metformin*
  – Useful intermittently to establish effect of food/exercise on glycaemia
  – Useful to examine pattern of glucose elevation to aid commencement of further treatment

◆ *Type 2 DM on oral hypoglycaemic agents*
  – As above, plus
  – Monitoring for hypoglycaemia

◆ *Type 1 DM and Type 2 on insulin*
  – Needed to rationally adjust insulin doses, plus
  – Factors above
Glucose Focused Testing Examples
Actionable information for informed decision-making

Pattern Testing …
Multi-point BG profiles for a specific duration to use pattern analysis to identify problem areas for remediation.

Paired Testing …
Testing to explore cause and effect BG variance related to life events or activities, such as food, lifestyle, and current medication. Supports patient self-learning and engagement.

Adjustment Testing …
BG testing to support activities to determine dose adjustment.
Types of Insulin

◆ Basal Insulins
  • Isophane (Protophane, Humulin N)
  • Analogs (Glargine, Detimir)

◆ Bolus Insulins
  • Actrapid, Humulin R
  • Analogs (Novorapid, Humalog, Apidra)

◆ Mixed Insulins
  • Penmix 30/70,
  • Humalog Mix 25 and 50
Insulin comparisons

- Aspart, lispro (4–6 hr)
- Regular (6–10 hr)
- NPH (12–20 hr)
- Extended zinc insulin (18–24 hr)
- Glargine (20–24 hr)
To normalise blood glucose both FPG and PPG must be reduced

Most insulin is initiated when HbA$_{1c}$ >8.5%

Adapted from Monnier L et al. Diabetes Care 2003;26:881–5
Success Comes From Using the Most Appropriate Tools
What about the oral agents?

Continue or Stop?

- **Metformin**
  - Good evidence to continue

- **Glitazones**
  - Some evidence but increased risk of heart failure

- **Sulphonylureas**
  - Often continue in short-term
  - No real benefit to continue in the long-term?
Most Commonly

- Add in once daily intermediate or long acting insulin (NPH insulin or Glargine).
- Evening if FPG > 6mmol/L
- Morning if hyperglycaemia mostly later in day

- May need to look at twice daily insulin
  - Wean off sulphphonylurea
Insulin Therapy: The When?

- Poor Glycaemic control:
  - HbA1c > 53mmol/mol (7.0%) despite maximal tolerated oral therapy?

- Symptomatic
Insulin Therapy: The When?

♦ Prepare patient in advance.
  • Progressive disease. Likely to be needed at some stage.

♦ Don’t use insulin as a threat!
  • If you don’t exercise you will need insulin….

♦ When the patient is ready!
  • Optimised diet and lifestyle
  • Optimised oral hypoglycaemics
  • Compliance
  • Home glucose monitoring
Insulin Therapy: Summary

◆ Why?
  • DCCT and UKPDS. Reduced complications

◆ Who?
  • All with Type 1 diabetes
  • Anyone with Type 2 diabetes, but…

◆ What?
  • Anything goes. Start with once daily NPH insulin (protophane/humulin N) or Glargine. Continue Metformin.

◆ When?
  • Consider when HbA1c > 53 mmol/mol (7.0%) despite optimal other care
  • When the patient is ready