Type Two Diabetes Mellitus Prescribing in New Zealand
- What are we dispensing?

Dr Bryan Betty
Deputy Medical Director PHARMAC
GP Cannons Creek, East Porirua
Type 2 Diabetes in NZ: The Numbers

- 250,000 patients estimated in NZ

- Māori and Pacific 3-6 times the rate of Type 2 Diabetes 40 to 60 age group compared European
  - Mortality rates 40 to 70 years of age, x7 the rate in European
  - Progression to ESRF x7 rate in European

- 11% Vote Health

- Major and growing health issue NZ
Type 2 Diabetes in NZ

1. Māori and Pacific people bear a disproportionate burden of T2DM-related disease

2. Contributing to ethnic health disparities in NZ.

3. Effective management of T2DM is critical for reducing the disease-related complications.
NZ Guidelines Recommendations

- Target HbA1c of 50-55 mmol/mol

- Tailor treatment to the individual: lifestyle interventions + medication

- Antidiabetic agents available (NZ): include:
  - metformin, sulfonylureas (glibenclamide, gliclazide, glipizide), acarbose, pioglitazone and insulin.
NZ Guidelines Recommendations

The recommended sequence of care in NZ:

1. Lifestyle interventions (eg. exercise, dietary changes)
2. Pharmacological therapies.
   i. Metformin's first-line pharmacological agent
   ii. Addition of sulfonylurea if required
   iii. Insulin

International guidelines support the use of metformin as a first-line agent:

- relatively inexpensive
- established safety profile
- possible cardiovascular protection
- no weight gain
NZ versus International

In contrast with the NZ recommendations,

- American and European guidelines support tailoring the choice of second-line therapy to the individual

Many of the agents recommended in these international guidelines are not funded in NZ:

a) sodium-glucose cotransporter-2 (SGLT2) inhibitors ($90/month)
b) dipeptidyl peptidase-4 (DPP-4) inhibitors ($110/month)
c) glucagon-like peptide-1 (GLP-1) receptor agonists ($220/month)
Study Rational

1. A number of international studies have considered prescribing patterns of antidiabetic agents

2. Using National Pharmaceutical Collection database:
   I. Describes the pattern of first- and second-line anti-diabetic dispensing (a proxy for prescribing patterns) for T2DM in NZ
   II. To assess the degree of adherence by prescribers with treatment guidelines.
How? First Line Dispensing

• Patients identified from **Pharmaceutical Collection** database

• **Collected first dispensing** for metformin, sulfonylureas, other funded anti-diabetics (acarbose and pioglitazone) +/- insulin

• Nine financial years **2007/08 to 2015/16**: complete patient identifier data was available.

• Identify T2DM (and not those with Type 1 DM): just collected insulin and not other anti-diabetic agents were excluded.

• Patient's earliest diabetes medicine dispensing date was identified.
Limitations

- As the Pharmaceutical Collection database does not record indication for medicine the analysis could not distinguish between T2DM and other conditions such as polycystic ovary syndrome (PCO) or Pre-diabetes.

- Assumed that T2DM would be vast majority of this group.
How? Second Line Dispensing

• The dataset for the patients who started diabetes medicine treatment in 2007/08 (the 2007/08 cohort) was used to investigate second-line treatments.

• The cohort was followed up until 2015/16 to see what second line agent was used.
First-line T2DM treatments used in NZ:

**Metformin**

- Total of 166,016 patients, avg. 18,446 per year, were dispensed their first T2DM treatment

- **Metformin** monotherapy was the most commonly dispensed first-line anti-diabetic

- Metformin first line **increased** from 80% in 2007/8 to 85% in 2015/16.
First-line T2DM treatments used in NZ:

**Sulfonylurea**

- Sulfonylurea monotherapy dispensing decreased over the nine years, and in 2015/16 accounted for 2% of all first-line dispensing.

**Dual agents**

- Dual anti-diabetic therapy (metformin and sulfonylurea) dispensing also trended down over time: 10% to 6%

- Initial dispensing of both metformin and insulin slightly increased over the period analysed: 2% to 5%
First-line T2DM treatments used in NZ:

1% of first-line dispensing each year:

- Acarbose and pioglitazone
- Other combinations (eg. sulfonylurea plus insulin)
2015/16: First Line Dispensing

Relative to dispensing patterns in 2007/08

- 205% increase in metformin and insulin dispensing
- 76% reduction in sulfonylurea
- 32% reduction in metformin/sulfonylurea dispensing (Figure 2).
Figure 2 – Changes in first T2DM agent dispensed over time relative to 2007/08

<table>
<thead>
<tr>
<th>Financial Year</th>
<th>Metformin</th>
<th>Metformin with insulin</th>
<th>Metformin with sulfonylurea</th>
<th>Sulfonylurea</th>
<th>Other</th>
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<tr>
<td></td>
<td>0%</td>
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</tr>
<tr>
<td>2007/08</td>
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<td>-7%</td>
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<tr>
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<td>205%</td>
<td>-32%</td>
<td>-76%</td>
<td>20%</td>
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<tr>
<td>2015/16</td>
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</table>
Second-line T2DM treatments used in the 2007/8 cohort

- On follow-up, the cohort of patients (N=17,206) who were prescribed their first-line T2DM agent in 2007/2008
  - 46% (N=7,958) received a second-line agent.
- Of those who received a second-line therapy, the main agents dispensed were:
  - sulfonylureas (70%),
  - insulin (14%),
  - metformin (8%)
  - other (8%)
    - Acarbose 2.4%
    - Pioglitazone 3.4%
- When metformin was the first-line agent:
  - 86% were started on a sulfonylurea as a second-line agent (Figure 3).
Figure 2 – Second-line T2DM treatment dispensing for the 2007/8 cohort
Figure 3 – Second-line T2DM treatment dispensing for the 2007/8 cohort who were initially dispensed on metformin
Implications - International comparison with guidelines adherence

The results indicate:

1. Metformin monotherapy majority of all first dispensed T2DM therapies over the nine years studied
2. Currently accounts for 85% of all dispensing.
3. First-line sulfonylurea monotherapy has decreased over time.
4. Growth in co-prescribing of metformin with insulin.

Indicate high levels of adherence with the national treatment guidelines for T2DM.
International Experience

• International studies considering T2DM prescribing patterns have not demonstrated such a high degree of adherence, (though guidelines and available treatments can differ across countries).

• Use of metformin as a first-line agent ranges from as low as 17% to (a relatively modest) 51%.

• Sulfonylurea use as first-line therapy has ranged from (a still relatively high) 18% to as high as 85%
Second Line Dispensing

- Sulfonylurea monotherapy accounted for 70% of all second-line dispensing

- 86% in those who initially started metformin for those in the 2007/8 cohort.

- Demonstrates good adherence with national T2DM treatment guidelines.

- They remain useful and effective treatments.
Second Line International Experience

- Internationally, for patients initially prescribed metformin, sulfonylureas have been used in 56% or 80% as second-line.

- Choice of second-line agent can differ across different countries
  - Treatment guidelines are different
  - In Japan recent study showed DPP-4 were the most common second line agent.
Equity

- Forthcoming analysis has looked changes in age of anti-diabetic agent dispensing by ethnicity
- Demonstrated trend to earlier prescribing of metformin particularly.
- Large differences between age of first prescribing of metformin between NZ Europeans and:
  - Māori
  - Pacific
  - Indian ethnic groups
Future:

• This analysis has identified several future research opportunities.

  • The time taken to escalate/add treatments for managing T2DM

  • Clinical Inertia attracting increasing attention within the literature, with concerns treatment is not being optimised in patients

  • Further research is warranted into this area in the NZ context, especially among differing ethnic groups
Conclusions

• High degree of adherence to the T2DM prescribing guidelines.

• Metformin and sulfonylureas are the most commonly dispensed first and second-line agents for T2DM.

• Further research is warranted into:
  • The demographic patterns of anti-diabetic prescribing
  • Treatment transition timeframes and the issue of clinical inertia (particularly if it is differential across ethnic groups) in managing patients with T2DM in NZ.
Questions