

Dispensing patterns for antidiabetic agents in New Zealand: are the guidelines being followed?

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ABSTRACT

AIMS: Type 2 diabetes mellitus (T2DM) is a significant public health issue in New Zealand. Effective management and glycaemic control is critical for reducing diabetes-related complications. Treatment guidelines are well established in New Zealand. Using dispensing data as a proxy for prescribing data, this paper aims to describe the pattern of first- and second-line antidiabetic agent (AA) dispensing for T2DM in New Zealand and assess adherence with treatment guidelines.

METHODS: Analysis of national dispensing data for AA medications using the Pharmaceutical Collection database from 2007/08 to 2015/16.

RESULTS: Metformin monotherapy remains the most commonly prescribed first-line T2DM medication prescribed, accounting for 85% of initial agents prescribed. Sulfonylureas are the most common second-line agents used, accounting for 70% of all second-line agents.

CONCLUSION: There is a high degree of adherence with the T2DM treatment guidelines in New Zealand.

Type 2 diabetes mellitus (T2DM) is a significant and costly public health issue in New Zealand.¹⁻⁴ Māori and Pacific people bear a disproportionate burden of T2DM-related disease, contributing to ethnic health disparities in New Zealand.¹⁻⁴ Effective management of T2DM is critical for reducing the disease-related complications.^{3,5}

New Zealand guidelines recommend a target HbA1c of 50–55mmol/mol.⁶ T2DM management guidelines support tailoring treatment to the individual, drawing on lifestyle interventions and pharmacological therapies.^{6,7} Antidiabetic agents (AA) available in New Zealand include metformin, sulfonylureas (glibenclamide, gliclazide, glipizide), acarbose, pioglitazone and insulin.^{7,8} The recommended sequence of care in New Zealand is initially utilising lifestyle interventions (eg, exercise, dietary changes) followed by pharmacological therapies. The New Zealand guidelines

currently recommend metformin as a first-line pharmacological agent, followed by the addition of a sulfonylurea if required and, finally, insulin.^{6,7} International guidelines also support the use of metformin as a first-line agent as it is relatively inexpensive, has an established safety profile, provides possible cardiovascular protection and does not lead to weight gain.⁹ In contrast with the New Zealand recommendations, American and European guidelines support tailoring the choice of second-line therapy to the individual.⁹ However, many of the agents recommended in these international guidelines are not funded in New Zealand (eg, sodium-glucose cotransporter-2 (SGLT2) inhibitors, dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists).⁹

A number of international studies have considered prescribing patterns of AA.¹⁰⁻¹³ Previous New Zealand-based research has

provided a picture of diabetes medicine prescribing and concomitant self-monitoring blood glucose strip usage.¹⁵ However, national patterns of T2DM medication prescribing over time have not been researched in the New Zealand context. Using the national Pharmaceutical Collection database, this analysis describes the pattern of first- and second-line AA dispensing (a proxy for prescribing patterns) for T2DM in New Zealand to assess the degree of adherence by prescribers with treatment guidelines.

Methods

Patients were identified from the Pharmaceutical Collection database who had collected their first dispensing for metformin, sulfonylureas, other funded AA (acarbose and pioglitazone) and/or insulin during nine financial years (1 July to 30 June) from 2007/08 to 2015/16 where complete patient identifier data was available. The four-year period from 2003/04 to 2006/07, where patient identifier data was less complete, was used to exclude patients from the analysis where they were assumed to have an unknown treatment start date (ie, treatment started prior to the availability of good patient-level data). To try and best identify patients with T2DM (and not those with Type 1 DM), only those who had also collected a dispensing for an AA (at any time from 1 July 2003 to 30 June 2016) were included in the analysis, as an ostensibly

robust administrative proxy measure of true patients with T2DM.

First-line T2DM treatments used in New Zealand

Each patient's earliest diabetes medicine dispensing date was identified. Any diabetes medicine dispensing that occurred within 90 days of that date were grouped together and counted as the patient's first-line T2DM treatment. The 90-day period was chosen as it represents the lifespan of a chronic medicine prescription. As the Pharmaceutical Collection database does not routinely record indication for medicine use, the analysis could not distinguish between dispensing for T2DM and other conditions in which these agents could be used, eg, polycystic ovary syndrome or pre-diabetes. However, it was assumed that T2DM would constitute the vast majority of this group.

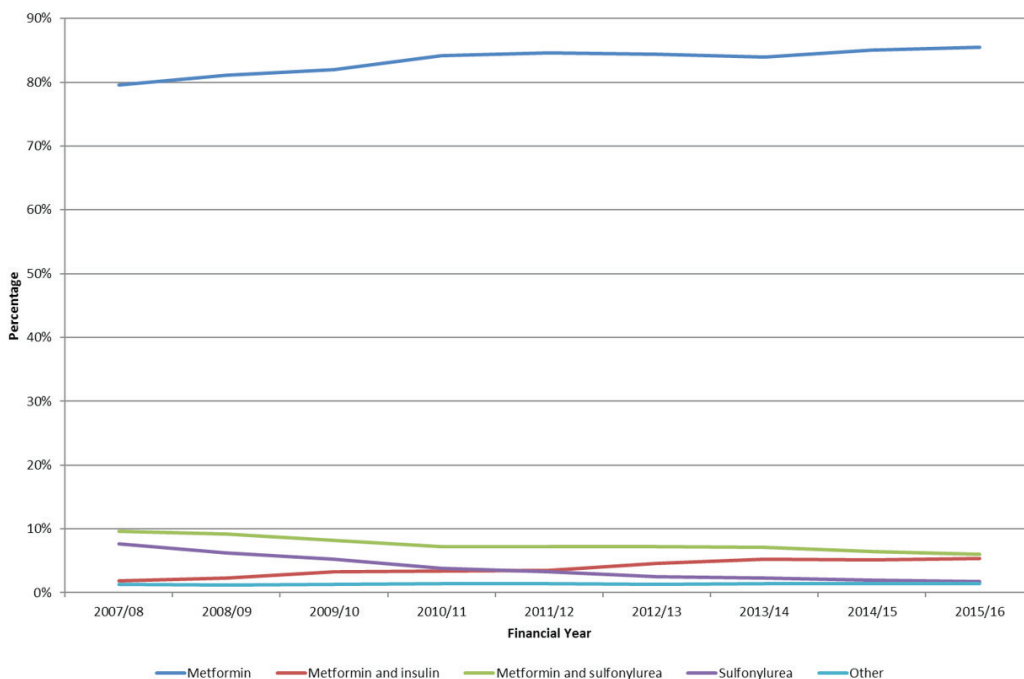
Second-line T2DM treatments used in the 2007/08 cohort

The dataset for the patients who started diabetes medicine treatment in 2007/08 (the 2007/08 cohort) was used to investigate second-line treatments. Each patient's second-line treatment was identified in a similar way to their first-line, with all diabetes medicines dispensed within 90 days of starting second-line treatment grouped together. Not all patients in the cohort could be followed up (eg, due to death), hence a discrepancy between the number first starting a T2DM treatment in 2007/08 and those analysed on follow-up.

Table 1: First T2DM medication/s dispensed in patients in New Zealand, 2007/08–2015/16.

Treatment	2007/08	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16
Metformin	14,143 (80%)	13,875 (81%)	14,788 (82%)	15,651 (84%)	15,697 (85%)	15,786 (84%)	15,646 (84%)	16,486 (85%)	16,401 (85%)
Metformin/ insulin	339 (2%)	384 (2%)	586 (3%)	640 (3%)	640 (3%)	857 (5%)	986 (5%)	994 (5%)	1,034 (5%)
Metformin/ sulfonylurea	1,704 (10%)	1,577 (9%)	1,489 (8%)	1,350 (7%)	1,346 (7%)	1,351 (7%)	1,321 (7%)	1,257 (6%)	1,162 (6%)
Sulfonylurea	1,359 (8%)	1,066 (6%)	945 (5%)	705 (4%)	618 (3%)	472 (3%)	423 (2%)	373 (2%)	331 (2%)
Other	225 (1%)	206 (1%)	236 (1%)	261 (1%)	259 (1%)	250 (1%)	263 (1%)	265 (1%)	269 (1%)
Total	17,770	17,108	18,044	18,607	18,560	18,716	18,639	19,375	19,197

Figure 1: First T2DM medication/s dispensed in patients in New Zealand, 2007/08–2015/16.



Results

First-line T2DM treatments used in New Zealand

From 2007/08–2015/16, a total of 166,016 patients, averaging 18,446 per year, were dispensed their first T2DM treatment (Table 1). Metformin monotherapy was the most commonly dispensed first-line AA in New Zealand (Figure 1). Over time its use as a first line agent increased from 80% in 2007/8 to 85% in 2015/16. Sulfonylurea monotherapy dispensing decreased over the nine years analysed and in 2015/16 accounted for 2% of all first-line dispensing. Dual AA therapy

(metformin and sulfonylurea) dispensing also trended down over time, from 10% in 2007/8 to 6% in 2015/16. However, initial dispensing of both metformin and insulin slightly increased over the period analysed (2% to 5%). Other medicines (eg, acarbose and pioglitazone) and combinations (eg, sulfonylurea plus insulin) accounted for around 1% of first-line dispensing each year. Relative to dispensing patterns in 2007/08, there was a 205% increase in metformin and insulin dispensing, contrasting with 76% and 32% reductions in sulfonylurea and metformin/sulfonylurea dispensing respectively (Figure 2).

Figure 2: Changes in first T2DM agent dispensed over time relative to 2007/08.

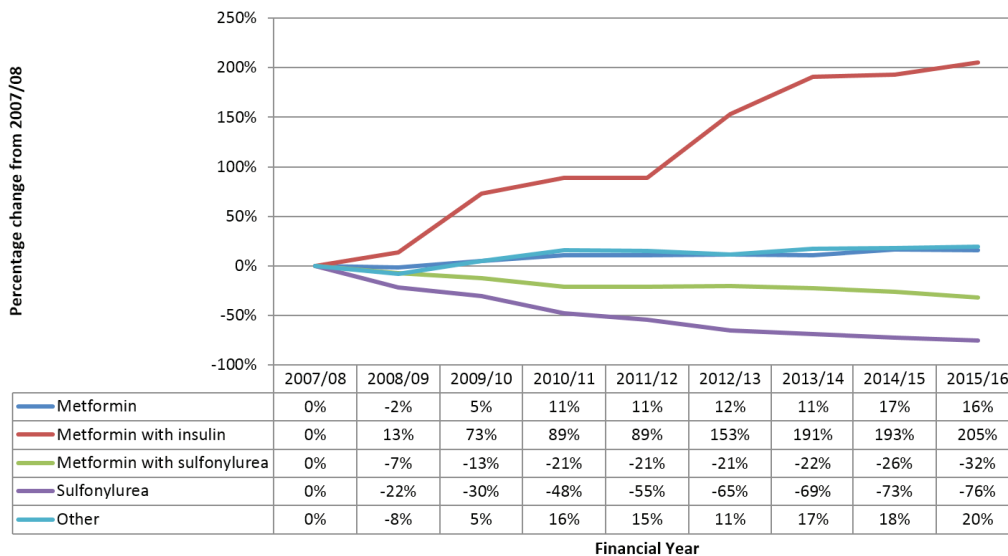
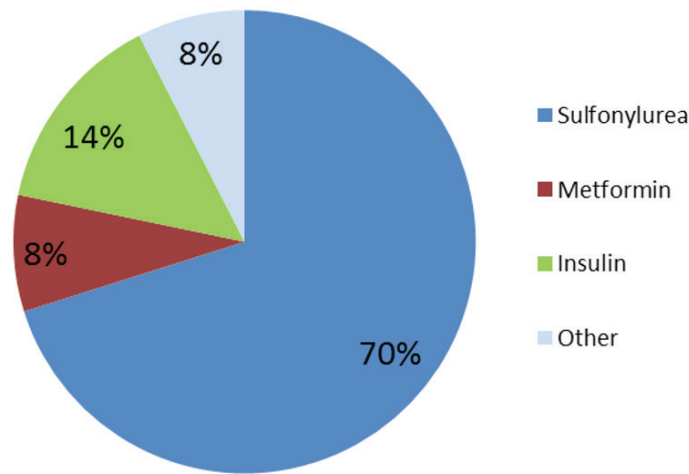


Figure 3: Second-line T2DM treatment dispensing for the 2007/8 cohort.

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 as monotherapies were sulfonylureas (70%), followed by insulin (14%), metformin (8%) and other (8%) (Figure 3). Acarbose and pioglitazone were dispensed as second-line agents (as monotherapy or in combination with other agents) in 2.4% and 3.4% of this cohort, respectively. In patients who were dispensed metformin as a first-line agent, 86% were started on a sulfonylurea as a second-line agent (Figure 4).

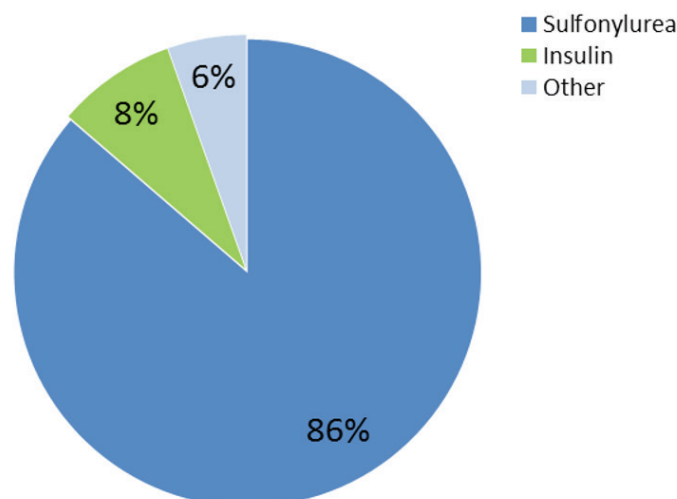
Discussion

This analysis describes the AA dispensing patterns for T2DM in New Zealand using the national Pharmaceutical Collection database, specifically the choice of first- and second-line agent.

Strengths and limitations

The key strength of this research is that it covers the majority of New Zealand's pharmaceutical dispensing (hence prescribing) patterns and trends at a national level, as the Pharmaceutical Collection dataset includes all government-subsidised dispensing data. This allows for an almost complete picture of dispensing over time.

However, there are a number of limitations to this analysis. Firstly, the Pharmaceutical

Figure 4: Second-line T2DM treatment dispensing for the 2007/8 cohort who were initially dispensed on metformin.

Collection dataset records all dispensing of medications. Dispensing of a T2DM treatment has been used as proxy for patients having true T2DM. This analysis therefore excludes those with T2DM who are not on any medicines and may capture those with impaired glucose tolerance who are treated with diabetic medication.

Secondly, given changes in the dataset over time, the analysis could not reliably extend retrospectively further than 2007/8.

Thirdly, the analysis could not describe the time to transition between first- and second-line treatments to allow assessment of clinical inertia within diabetes management in New Zealand.^{16,17} Further research is warranted into this issue.

Fourthly, the data are dispensing-based, not based on prescription-at-doctor-visit nor patient end-use. Dispensing-based data (rather than prescription-at-doctor-visit or patient end-use) do not capture end-use (ie, whether medicines dispensed are taken by the patient—wastage and suboptimal treatment), nor prescriber intent (since not all prescriptions are necessarily dispensed and captured in the data).

Fifthly, diabetes diagnoses are by inference and will include other conditions where diabetes medicines are used, including polycystic ovary syndrome;¹⁸ however, the numbers of these cases are likely to be relatively small compared with the T2DM population.

Finally, the analysis has not attempted to link dispensing usage with laboratory data such as HbA1c measurements of glycaemic control, nor has it considered the full range of demographic and clinical information—socioeconomic deprivation, region, type of diabetes, macrovascular and microvascular complications, use of other medicines (eg, inhibitors, statins), etc.—to better elucidate key patterns and gaps in the treatment of patients with diabetes.

Implications—international comparison with guidelines adherence

Despite the above limitations, when considering the choice of AA, this is the first analysis we are aware of that has explicitly explored the nationwide dispensing patterns in New Zealand for initial and second-line AAs (hence by implication, prescribing

patterns) over an extended time period. The results indicate that metformin monotherapy has accounted for the majority of all first dispensed T2DM therapies over the nine years studied and currently accounts for 85% of all dispensing. First-line use of sulfonylurea monotherapy has decreased over time. Furthermore, though be it small, there has been a growth in coprescribing of metformin with insulin.

These results indicate high levels of adherence with the national treatment guidelines for T2DM.^{6,7} 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 has ranged from as low as 17% to (a relatively modest) 51%.^{10–14,19–24} Sulfonylurea use as first-line therapy has also ranged from (a still relatively high) 18% to as high as 85%.^{20,22,25,26}

Sulfonylurea monotherapy accounted for 70% of all second-line dispensing (or 86% in those who initially started metformin) for those in the 2007/8 cohort. Again, this demonstrates good adherence with national T2DM treatment guidelines. While concerns have been expressed in the use of sulfonylureas, they remain useful and effective treatments.^{27,28} Internationally for patients initially prescribed metformin, sulfonylureas have been used in 56% or 80% as second-line.^{29,30} However, the choice of second-line agent can differ across different countries, with a recent study finding dipeptidyl peptidase-4 inhibitors were the most common utilised second-line agent in Japan.²⁴

Future research

This analysis has identified several future research opportunities.

Firstly, there is a need to consider the pattern of AA prescribing by key demographic features (particularly age, gender and ethnicity) to see if there are differences between populations in New Zealand. This is the topic of forthcoming analysis.³¹

Secondly, this analysis could not address the time taken to escalate/add treatments for managing T2DM; this information is critical for addressing the issue of clinical inertia. This topic is attracting increasing attention within the literature, with concerns treatment is not being optimised in patients.^{16,17} Further research is warranted

into this area in the New Zealand context, particularly if there is differential clinical inertia between ethnic groups.

Conclusions

This analysis of dispensing patterns for AA in New Zealand indicates that there is a high degree of adherence to the T2DM prescribing guidelines. Metformin and

sulfonylureas are the most commonly dispensed first- and second-line agents for T2DM respectively. Further research is warranted into the demographic patterns of AA prescribing, treatment transition timeframes and the issue of clinical inertia (particularly if it is differential across ethnic groups) in managing patients with T2DM in New Zealand.

Competing interests:

The authors are (or were at the time of writing) employees of PHARMAC; the views expressed do not necessarily represent those of PHARMAC.

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