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ORIGINAL RESEARCH PAPER

ORIGINAL RESEARCH: CLINICAL

Using the Pharmaceutical Collection Database to identify patient adherence to oral hypoglycaemic medicines

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ABSTRACT

INTRODUCTION: Poor adherence to oral hypoglycaemic medicines is a key contributor to therapy failure and sub-optimal glycaemic control among people with type 2 diabetes. It is unclear how commonly non-adherence to oral hypoglycaemics occurs in the general population. This information is essential to design and implement local adherence strategies.

AIM: This study aimed to determine levels of sub-optimal adherence and identify patient groups who may need additional adherence support.

METHODS: The dispensing data of 340,283 patients from one District Health Board was obtained from the Pharmaceutical Collection Database for the period 2008–15. Of these, 12,405 patients received oral hypoglycaemic therapy during the study period. The proportion of days covered (PDC) was calculated for patients with complete data and a PDC value of ≥80% was used to indicate sufficient adherence. Patient demographics (gender, ethnicity, age, socioeconomic status) and therapy type (mono- or combination) were described.

RESULTS: Overall, 54.5% of the patients were found to have a PDC of <80% and so were considered non-adherent. Non-adherence was significantly higher in patients receiving combination oral hypoglycaemic therapy than monotherapy; in male patients; in New Zealand Māori patients; and in patients with higher socioeconomic deprivation.

DISCUSSION: In the study region, non-adherence to oral hypoglycaemic medicines was significant and widespread. Identification of such patients is important so that strategies to enhance adherence can be implemented. Prescribers need to be encouraged to optimise monotherapy before the addition of another oral hypoglycaemic, and adherence support services should be offered not only to older patients.

KEYWORDS: Pharmaceutical Collection Database; oral hypoglycaemics; adherence

Introduction

The high prevalence of type 2 diabetes continues to be of increasing international concern and it needs multiple strategies to achieve glycaemic control to avoid future complications.[1,2] Type 2 diabetes is a truly global epidemic, from both a health outcome perspective and its associated health-care costs.[3,4]

Oral hypoglycaemic medications are the mainstay therapy for type 2 diabetes in conjunction with diet and exercise modifications.[5–7] However, adherence to these medications continues to be sub-optimal, so health services are concerned with finding ways to improving patient adherence.[8–10] Abnormally high levels of HbA1c (haemoglobin A1c) are a

WHAT GAP THIS FILLS

What is already known: Poor adherence to oral hypoglycaemic medicines is a key contributor to therapy failure and sub-optimal glycaemic control. It is unclear how common non-adherence to prescribed oral hypoglycaemics is in the general population.

What this study adds: By using regional level data, the degree of adherence to oral hypoglycaemic medications can be identified. This information can inform local strategies to be implemented that will target those patients who would benefit from adherence support services.

marker for hyperglycaemia. Type 2 diabetes treatment aims to achieve glycaemic control that can be reflected by change in HbA1c. Therapeutic outcomes of oral hypoglycaemics are measured by reductions in the level of HbA1c. One driver for increasing type 2 diabetes medication adherence is that there is clear evidence that increased adherence to these medications can decrease the HbA1c level over the time.[11–13]

Inadequate adherence to long-term medication is a recognised problem that must be addressed if benefits of medication are to be achieved.[14–18] For this reason, adherence support services are increasing internationally, as individualised strategies may increase medication adherence.[19–21] In 2007, the government-funded Medication Use Review service was introduced in New Zealand; however, uptake across District Health Boards was haphazard.[22] A recent New Zealand study found that type 2 diabetic patients who received Medication Use Review adherence support improved their adherence scores and reduced their HbA1c levels.[23] However, remaining unknown are adherence levels in local populations and the number of type 2 diabetes patients who would benefit from access to this service.

Representative samples of adequate size are needed to deliver valid findings from epidemiologic observational research that is generalizable to all populations.[24,25] Administrative databases can fulfil data requirements for such research as they are the archives of health-care data obtained at a variety of occasions, including the prescription dispensing in community pharmacies, visits to physicians' offices and admissions to hospitals.[24,26] Health-care administrative data are also referred to as 'claims data', 'administrative claims data', 'administrative healthcare billing records' and 'healthcare utilization data'.[26] Their timely and systematic collection, wide coverage and large numbers are the main advantages qualifying these databases as a principal choice for epidemiological studies regarding drug utilisation.[26–28]

The proportion of days covered (PDC) is a surrogate marker for medication adherence, providing information about patients' medication possession (number of days they had medication supply). Using the Pharmaceutical Collection Database, this study aimed to estimate the PDC in patients with type 2 diabetes receiving oral hypoglycaemics over an 8-year period (2008–15), and further identify characteristics such as age, gender, ethnicity and socioeconomic status. The intent was to determine the degree of adherence in one District Heath Board (DHB) and to estimate the number of patients who could derive benefit from adherence support services.

Methods

In New Zealand, each patient has a unique health identifier (the National Health Index (NHI) code). All medicines dispensed for individual patients under the government supply schedule are held in a central database, maintained by the Ministry of Health. In New Zealand, there are 20 DHBs that divide the country into 20 non-overlapping geographical areas, and each DHB has a degree of autonomy in providing health services. This study was set in one DHB and involves the population it covers in an area of 12,231 km^2. Records for a total of 340,283 patients were accessed. This region was chosen as it is one of the few DHBs providing Medicines Use Review adherence support services to patients.

Data

We made a request to the Ministry of Health to access the Pharmaceutical Collection Database for the study region, for the period 2008–15 (inclusive). In the data we obtained, individual patients' information was irreversibly de-identified, but individual level data were used as an encrypted NHI was

provided. De-identification and encryption occurred before the data were sent to the research team so the data could not be linked back to identify individual patients. The study data included patients' encrypted identity, age, gender, ethnicity, and medication dispensing dates, quantity dispensed, daily dose, total number of days' supply, and chemical and therapeutic medication classification. All patients receiving oral hypoglycaemic medications within the study period were included. The Pharmaceutical Collection Database records only government-subsidised oral hypoglycaemic medications and has no information about non-subsidised ones.

Outcomes

There were two categories of information: (1) patient characteristics including gender, ethnicity, age group, age range and socioeconomic deprivation index; (2) type of therapy (monotherapy or combination of two or three medications).

The type of therapy consistently dispensed during the study period was included and categories of monotherapy or combination of therapy were based on counts of oral hypoglycaemic medications not in the therapeutic category of oral hypoglycaemic. A change or substitution of oral hypoglycaemic medication was not considered as long as the type of therapy stayed the same. Medication non-adherence in combination therapy was related to the count of oral hypoglycaemics and not individual drugs in the combination.

Adherence to the oral hypoglycaemics was the primary outcome of interest, assessed by calculating the PDC for each patient. The nature of medication refill is highlighted by this ratio, as it shows how often patients refill their medications.

The PDC in a year with oral hypoglycaemic medication was calculated using the following equation:[29]

$$\text{PDC} = \frac{\text{D} \times 100}{365 - 1}$$

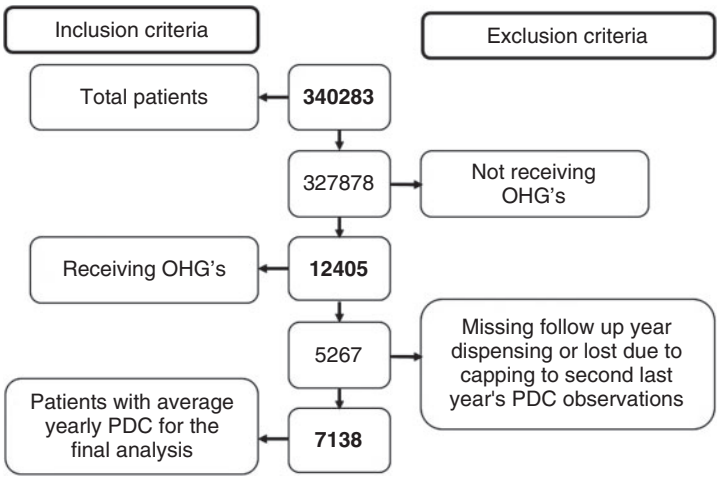
In this equation, 'D' is days on which the patient has the medication available (total days' supply including any overlapping supply from earlier fills); '–1' is for a day of last dispensing. Most published literature observes the PDC of ≥80% as indicating adherence and patients with a PDC >90% achieve maximum benefit from their medication.[14,16,29–33] A PDC of <50% indicates insufficient medication supply to achieve therapeutic benefits. Therefore, we categorised PDCs <50% as 'extremely non-adherent', PDCs 50–79.99% as 'non-adherent', PDCs 80–89.99% as 'adherent' and PDCs ≥90% as completely adherent.

As this study was over a defined period, the actual date of therapy initiation for each patient was unknown when it was before 1 January 2008. For consistency, we considered the first recorded dispensing of oral hypoglycaemic as index dispensing. Not all patients had their index dispensing on 1 January of every calendar year. Some patients had their index dispensing in the middle of the year and last dispensing extending over a period of years or months. To ensure that all analysis was consistent, the Pharmaceutical Collection data records were combined from 2008 to 2015 and days between different dispensings were added cumulatively. Dividing this cumulative total by 365 days produced the yearly analysis. Others have used different timeframes to measure adherence, and the most frequently used is 12 months.[34] In the last study year, the cumulative days may be less than 365, as dispensing records may be available for only a few months. Incomplete data may lead to the calculation of false PDCs in the last year of study, and it may influence the average value of the PDCs for overall study years. Hence, the proportion of days that covered the analysis period was capped up to the last full year to avoid false medication adherence reports. A summary of the data filtering process is shown in Figure 1.

Data analysis

Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) and IBM SPSS Statistics version 23 (SPSS Inc., Chicago, IL, USA) were used to collate and analyse the data. The test of the difference between two proportions was used for all comparisons. First, patients receiving and not receiving oral hypoglycaemics were compared, then further non-adherent (PDC <80%) and adherent (PDC ≥80%) patients were compared. Statistical significance was taken to be $P < 0.05$.

Figure 1. Inclusion and exclusion criteria to select the patients receiving oral hypoglycaemics (OHGs) for the final analysis. PDC, proportion of days covered.



Results

The demographics of patients receiving and not receiving oral hypoglycaemics is shown in Table 1. Use of oral hypoglycaemics was higher in male patients (52.0% vs. 47.4%, $P < 0.001$), patients of New Zealand Māori ethnicity (27% vs. 20.3%, $P < 0.001$), patients aged 41–80 years and in patients living in areas with higher socioeconomic deprivation (deprivation index 8–10, $P < 0.001$). There were 12,405 patients receiving oral hypoglycaemic therapy. Of these patients, 1775 (14.3%) were excluded from further analysis as they had only one dispensing recorded and no follow-up dispensing (to calculate PDCs there should be at least two dispensing records). There were 3492 patients excluded while capping the observation period to the last complete year. Finally, the data for 7138 patients were analysed (Fig. 1).

The range of PDCs for every dispensing year in patients receiving oral hypoglycaemics is summarised in Table 2. Extreme non-adherence (PDC <50%) was significantly higher in the eighth year than the first year (31.1% vs. 26.0%; $P < 0.001$), whereas complete adherence (PDC ≥90%) was significantly higher in the first year than the eighth year (46.2% vs. 17.6%; $P < 0.001$).

The range of PDCs in patients receiving oral hypoglycaemics ($n = 7138$) is summarised in Table 3. We found that 54.5% of patients dispensed oral hypoglycaemics were non-adherent (PDC <80%). Based on the type of therapy – monotherapy, combination of two and combination of three oral hypoglycaemics – non-adherence was 34.5%, 74.7% and 92.3% respectively. Extreme non-adherence (PDC <50%) was significantly ($P < 0.001$) higher in patients with combinations of three (41.9%) and two (19.4%) oral hypoglycaemics when compared to monotherapy (5.5%). Complete adherence (PDC ≥90%) was significantly ($P < 0.001$) higher in monotherapy (37.3%) when compared with combinations of three (8.6%) and two (1.0%) oral hypoglycaemics.

The demographics of the sub-sets of patients with PDC <80% and PDC ≥80% is shown in Table 4. Of the 3892 people in the sample who were non-adherent (PDC <80%), 54.0% were men and 33.3% were of New Zealand Māori ethnicity.

Discussion

We found that males, people aged 41–80 years, people of NZ Māori ethnicity and people living in socioeconomically deprived areas had higher use of oral hypoglycaemics than the general population of this DHB. Of the patients receiving oral hypoglycaemics, half were non-adherent (PDC <80%). In this group of patients, non-adherence was significantly higher in the eighth year than the first year, indicating a decrease in adherence level with time. Patients on monotherapy, combinations of two oral hypoglycaemics, and combinations of three oral hypoglycaemics, had successively higher levels of non-adherence, suggesting that increased medication burden may decrease adherence. Non-adherence was significantly higher in the NZ Māori ethnic group, in young and the middle aged (21–60 years) and in patients with low socioeconomic status, and correspondingly, adherence was significantly higher in the NZ European ethnic group and for people aged ≥61 years. This is an important finding as many adherence support services target patients aged >65 years when there may be a more pressing need for adherence support for people in the middle-aged bracket.

Previously reported research from the study evaluating the influence of a Medication Use Review service found that the type 2 diabetes patients who received adherence support improved their

Table 1. Demographic profile of patients with and without oral hypoglycaemic medication

	Patients with oral hypoglycaemic (*n* = 12,405)		Patients without oral hypoglycaemic (*n* = 327,878)	
	Frequency	%	Frequency	%
Gender				
Female	5952	48.0	172,450	52.6
Male	6453	52.0	155,428	47.4
Ethnicity				
NZ European	6722	54.2	202,924	61.9
Other European	1020	8.3	26,446	8.1
NZ Māori	3354	27.0	66,407	20.3
Indian	510	4.1	6504	2.0
Index age range (years)				
21–30	530	4.3	39,565	12.1
31–40	992	8.0	39,760	12.1
41–50	1940	15.6	40,801	12.4
51–60	2916	23.5	36,430	11.1
61–70	3023	24.4	29,209	8.9
71–80	2048	16.5	17,490	5.3
81–90	681	5.5	8164	2.5
91–100	52	0.4	1166	0.5
NZ Deprivation Index 2013				
1	115	1.0	5868	1.9
2	592	5.1	19,990	06.4
3	313	2.7	14,259	4.7
4	680	5.9	24,321	7.8
5	1080	9.3	35,440	11.4
6	962	8.3	30,525	9.8
7	1404	12.1	42,226	13.6
8	1929	16.6	46,185	14.9
9	2208	19.1	47,603	15.3
10	2303	19.9	44,126	14.2

NZ (New Zealand).
NZ deprivation index 2013: 1 = high socioeconomic status; 10 = low socioeconomic status.

adherence scores and subsequently reduced their HbA1c levels.[23] However, the number of other type 2 diabetes patients who would benefit from access to this service was unknown and neither did we previously know the overall oral hypoglycaemic medication adherence level in the local population. By using centrally held data and applying the PDC algorithm as a surrogate marker of medication adherence in this study, we were able to assess medication adherence in a real-world population.[35–42]

Continued treatment with oral hypoglycaemic medication is desirable for optimal outcomes of chronic type 2 diabetes treatment, and an important finding of this study is that the adherence rate was significantly higher in the first year but decreased over time. The significant rate of non-adherence in

Table 2. Proportion of days covered (PDC) for every dispensing year in patients receiving oral hypoglycaemics

Year of dispensing	Patient (%) with respective PDC range						Yearly patient count (*n*)
	Non-adherence zone				Adherence zone		
	<50	50.00 – 59.99	60.00 – 69.99	70.00 – 79.99	80.00 – 89.99	90.00 – 100	
First	26	3.8	5.5	10.5	8.0	46.2	10,207
Second	27.3	3.9	7.4	15.6	10.9	34.9	7446
Third	26.5	4.2	7.5	14.2	12.0	35.6	6411
Fourth	25.7	3.9	7.5	14.5	12.6	35.9	5409
Fifth	27.8	4.0	6.8	14.6	13.0	33.9	4573
Sixth	25.8	4.4	7.3	14.2	12.9	35.3	3755
Seventh	27.5	3.7	7	15.7	13.3	32.8	3010
Eighth	31.1	5.7	11.1	22.1	12.4	17.6	2264

Table 3. Proportion of days covered (PDC) values in patients receiving oral hypoglycaemics (n = 7138)

Patient characteristics	Patient count with respective PDC range (*n*, %)						Total
	Non-adherence zone				Adherence zone		
	<50	50.00 – 59.99	60.00 – 69.99	70.00 – 79.99	80.00 – 89.99	90.00 – 100	
All patients receiving oral hypoglycaemics	905 (12.7)	697 (9.8)	961 (13.5)	1329 (18.6)	1593 (22.3)	1653 (23.1)	7138
Patients grouped as per treatment type							
Oral hypoglycaemic as monotherapy (a)	201 (5.5%)	168 (4.6)	320 (8.8)	566 (15.6)	1020 (28.1)	1357 (37.3)	3632
Combination of two oral hypoglycaemics (b)	660 (19.4)	517 (15.2)	616 (18.1)	747 (22.0)	566 (16.6)	295 (8.6)	3401
Combination of three oral hypoglycaemics (c)	44 (41.9)	12 (11.4)	25 (23.8)	16 (15.2)	7 (6.7)	1 (1.0)	105

patients with low socioeconomic status may reflect a reluctance for low-income patients to refill their medications due to financial barriers. Primary healthcare accessibility is influenced by ethnicity and socioeconomic status in New Zealand.[43,44] Reduced income may also affect dietary choices, particularly for low nutritional, low-cost food options, which may trigger high blood glucose levels.[44] Non-adherence by patients aged 31–60 years is concerning, as these patients are of 'actively working' age. Poor glycaemic control will affect their working ability and productivity and may lead to hospitalisation and additional healthcare costs. We found that patients aged ≥60 years were reasonably adherent to oral hypoglycaemic therapy, as other studies have previously reported.[45] Such patients may have become accustomed to their medications over a longer time, with established routines to remind them to take their medication.[46] A meta-analysis has also shown that adherence can be better in older patients.[45]

Considering the chronic nature of type 2 diabetes, treatment intensification may demand an additional one or more drugs to the initial monotherapy. This additional oral hypoglycaemic medication may trigger treatment non-adherence, as the study demonstrated that the spread of non-adherence was higher in therapy with combinations of two and three medications than monotherapy. This non-adherence may complicate the disease's progression, raise the chances of comorbidity, invite expensive health management and lead to death.[33]

Table 4. Demographics of oral hypoglycaemic patients with a proportion of days covered (PDC) <80 and a PDC ≥80%

	PDC <80% (*n* = 3892)		PDC ≥80% (*n* = 3246)	
	Frequency	%	Frequency	%
Gender				
Female	1788	46.0	1517	46.7
Male	2103	54.0	1729	53.3
Ethnicity				
NZ European	1879	48.3	2090	64.4
Other European	297	7.6	295	9.1
NZ Māori	1295	33.3	651	20.1
Indian	185	4.8	92	2.8
Index age range (years)				
21–30	83	2.1	23	0.7
31–40	281	7.2	76	2.3
41–50	728	18.7	331	10.2
51–60	1083	26.7	693	21.3
61–70	967	24.9	1017	31.3
71–80	599	15.4	833	25.7
81–90	169	4.3	249	7.7
91–100	7	0.2	19	0.6
NZ Deprivation Index 2013				
1	20	0.5	13	0.4
2	191	5.1	185	6.0
3	78	2.1	76	2.4
4	191	5.1	246	7.9
5	366	9.9	307	9.9
6	305	8.2	251	8.1
7	434	11.7	369	11.9
8	656	17.7	546	17.6
9	720	19.4	530	17.1
10	749	20.2	582	18.7

NZ (New Zealand).
NZ deprivation index 2013: 1 = high socioeconomic status; 10 = low socioeconomic status.

Different tools to enhance medication adherence range from self-management to integrated care interventions.[47–52] Pharmacist intervention has been well researched and shown to improve medication adherence and treatment outcomes (glycaemic control) in type 2 diabetes patients.[23,53–59] Support services that provide structured patient education and counselling about type 2 diabetes, prescribed medications, proper dosage, possible side-effects and importance of medication adherence have been investigated.[53,54] A common approach is to combine an educational with a behavioural strategy to optimise the use of oral hypoglycaemic medications.[2,9,56,58] With 54.5% of type 2 diabetes patients in the current study not fully adhering to oral hypoglycaemic medication adherence, support services may be warranted in the study DHB.

This study has some limitations. The Pharmaceutical Collection data records medication dispensing funded by the Ministry of Health, but it does not collect data about medicines paid for privately. This study was conducted within a single DHB, and may not reflect the situation in other DHBs. A small number of patients will be receiving oral hypoglycaemic medication for conditions other than diabetes (e.g. metformin for polycystic ovary syndrome, and some type 1 diabetes patients receive oral hypoglycaemic in addition to insulin), but adherence is still important in those clinical conditions. The Pharmaceutical Collection data represents only information about the collection of medication. The fate of dispensed drugs is still unknown as there is no information about its administration; therefore, the results of this study may underestimate true non-adherence. This study could not account for patients receiving a prescription that was not presented for dispensing and patients who collected a single script, but did not persist with treatment for a full year. The accuracy of the data source is important for reliable results. Short-term analysis (<90 days) may result in bias and imprecise outcomes.[59] People with type 2 diabetes may also have other chronic illnesses. Declining adherence with combination therapy could also indicate additional morbidities and addition of medicines other than oral hypoglycaemic for managing those conditions. The current study could not account for this as a confounding factor.

Not all patients can receive adherence support services, so use of a large dataset such as the Pharmaceutical Collection Database can provide insights into how widespread the adherence issue is and how many may benefit from adherence support. Knowing the characteristics of non-adherent patients is important so that strategies to enhance the adherence can be implemented. Prescribers could be encouraged to optimise monotherapy before the addition of another oral hypoglycaemic medication, and adherence support services should not only be offered to older patients.

Conclusion

This study showed how the degree of adherence to oral hypoglycaemic medications can be established using regional level data from the Pharmaceutical Collection Database. This information can inform local strategies to target patients who would benefit from adherence support services.

Competing interests

The authors declare that they have no conflicts of interest.

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