New Zealand may finally get funded access to diabetes drugs which reduce cardiovascular events and progression of kidney disease: an audit of proposed PHARMAC criteria compared with international guidelines

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ABSTRACT

AIMS: Sodium-glucose cotransporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) agonists are classes of medications shown to reduce cardiovascular events and slow decline in renal function in people with type 2 diabetes (T2DM). They are recommended for many people as second-line agents after metformin by the American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD). PHARMAC have proposed criteria for funding in New Zealand. This clinical audit compares which patients would be eligible for treatment under each criterion.

METHODS: This retrospective audit was conducted in December 2019 of all registered patients with T2DM at three general practices within the Wellington/Porirua region. Relevant data were extracted from the electronic health records to enable assessment of eligibility under PHARMAC and ADA/EASD criteria.

RESULTS: Of the 23,517 patients enrolled, 1,160 had T2DM. Under PHARMAC criteria 399 (34.4%) patients would be eligible for funded access compared with 339 (27.2%) by the 2018 ADA/EASD criteria and 559 (48.2%) by the revised 2020 ADA/EASD criteria. Differences in eligibility relate to threshold of HbA1c and inclusion of microalbuminuria for treatment.

CONCLUSION: The proposed PHARMAC criteria will give access to these important drugs to those people with T2DM who will likely benefit the most.

Type 2 diabetes (T2DM) affects approximately 6% of the adult population in New Zealand with prevalence rising by 7% per annum.[1] The highest rates are observed in the elderly, those with higher socioeconomic deprivation and in specific ethnicities. Māori are three times more likely to have diabetes versus non-Māori, though the highest rates are in Pacific people over the age of 45 years, with one third having T2DM.[1] These groups are also more likely to experience complications due to diabetes.[1] The main cause of increased morbidity and premature mortality for people

with T2DM are vascular and renal complications.[2] Moreover the earlier the onset of diabetes, the more likely complications are to ensue, with patients diagnosed before the age of 40 having higher rates of non-fatal cardiovascular events even when adjusted for duration of diabetes.[3]

The importance of tight glycaemic control in T2DM to prevent complications is well established for microvascular disease, such as retinopathy, neuropathy and nephropathy.[4,5] Until recently the evidence for reducing macrovascular disease, including cardiovascular events, has been less clear cut. However, a series of cardiovascular outcome studies have been published in the last decade investigating three new classes of glucose lowering drugs. These include the sodium-glucose cotransporter-2 (SGLT-2) inhibitors, which act by blocking sodium and glucose reabsorption in the proximal convoluted tubules of nephrons, and glucagon-like peptide-1 (GLP-1) agonists, which increase pancreatic insulin release, decrease pancreatic glucagon release and decrease appetite.[6,7]

Large randomised controlled trials of studies of SGLT-2 inhibitors and GLP-1 agonists investigating major cardiovascular events (MACE) in people with T2DM with pre-existing atherosclerotic cardiovascular disease (ASCVD) have shown a significant reduction in events. A meta-analysis of these trials found a 14% reduction in MACE in patients with T2DM and ASCVD receiving an SGLT-2 inhibitor or GLP-1 agonist compared with placebo.[5] SGLT-2 inhibitors[8,9] and GLP-1 agonists[10–12] also reduced secondary outcomes such as heart failure and kidney disease in those with ASCVD.[9] Although this is likely due to in part to improvements in glycaemic control, alternative mechanisms are also being investigated.[5] No head-to-head studies have been conducted. However, the consistency of effect size across the published trials suggests a likely class effect for the SGLT-2 inhibitors, though there may be agent-specific effects for the GLP-1 agonists.

In light of this evidence, in 2018, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) published a consensus guideline in which an SGLT-2 inhibitor or GLP-1 agonist is recommended as the second-line agent for any person with T2DM with either ASCVD, chronic kidney disease (CKD) or heart failure (HF) and inadequate blood glucose control (HbA1c ≥53mmol/mol) on metformin.[13] In the subsequent two years, further studies of these agents have been published, with new evidence of major benefits for SGLT-2 inhibitors in those with chronic kidney disease in particular.[14] A recent meta-analysis of these trials shows a 37% reduction in combined renal outcomes, including doubling of serum creatinine, progression to dialysis or renal death. Therefore, in January 2020 the ADA/EASD published a revised guideline.[15] Important changes included the additional recommendation to treat individuals at high risk of CVD as well as those with established ASCVD independent of HbA1c. Further, that SGLT2 inhibitors are recommended in all patients with T2DM with microalbuminuria.

Currently in New Zealand there is no funded access to either SGLT-2 inhibitors or GLP-1 agonists, despite multiple applications to PHARMAC over the last 10 years.[16] However, in response to this increasing body of evidence, and after extensive consultation, in January 2020 PHARMAC have put out a request for proposals to the pharmaceutical industry.[17] As part of this they have proposed the following eligibility criteria for funding for SGLT-2 inhibitors and GLP-1 agonists: people with T2DM, not achieving adequate glucose control of HbA1c <53mmol/mol after maximum tolerated oral antidiabetic agents and/or insulin for at least six months. Additionally, the presence of either CKD and/or microalbuminuria, or a CVD risk score ≥15%, or established cardiovascular disease (CVD) is required. Treatment is to be used as an adjunct to current therapy, with other current standard of care procedures taken to reduce cardiovascular risk.

PHARMAC have the need to balance costs and benefits across all drug treatments in the health sector. As such, it is important to optimise the access of these new drugs to those who will obtain the most benefit without excluding particular patient groups. Inadvertent exclusion of young Māori and Pacific people with T2DM, who already have poorer health outcomes, would exacerbate inequity in healthcare in New Zealand. Hence, the objective of this audit was to

determine how many patients will be eligible for treatment using both the 2018 and revised 2020 ADA/EASD criteria, and the proposed PHARMAC criteria and to compare the characteristics of those who are included or excluded.

Methods

This was a retrospective observational audit conducted in December 2019 of all registered patients with T2DM at three general practices within the Wellington/Porirua region; Karori Medical Centre (KMC), Porirua Union & Community Health Services (PUCHS) and Pacific Health Plus Porirua (PHP). These practices were chosen to span a wide range of demographic, socioeconomic, geographical and systems perspectives, particularly to ensure data were included from Māori, Pacific and patients with greater socioeconomic deprivation. When enrolling at these practices, patients gave consent for their data to be audited. As such no formal application for ethical review was required, but approval was given by the clinical governance process of each practice.

Data collection

Data were extracted onsite from MedTech Evolution, an electronic patient management system commonly used in primary care, at the three practices. Each practice coded their variables somewhat differently, which required individualising the process of extraction. Using the MedTech 'query-build function', and always limiting the search to registered patients with T2DM, each variable listed below was extracted as either a measurement, classification or comment into an Excel file. These data were then compiled into one large spreadsheet. The date of entry for each variable was also extracted. This enabled inclusion/exclusion of data based on the time restrictions below. If data weren't entered in MedTech in an easily extractable way, manual searches were made in MedTech using the patient's national health index number (NHI) and adding the relevant information to the overall Excel spreadsheet. All data were anonymised after extraction by removing patient NHI, and no names were recorded.

Data extracted were: age (years), gender, self-reported ethnicity, NZ Deprivation (quintile 1–5), weight (kg), height (cm), body mass index (BMI) (kg/m^2), smoking status, year of diagnosis and duration of T2DM (years), systolic (SBP) and diastolic (DBP) blood pressures (mmHg) and the presence of hypertension. This was defined as a SBP greater than 130mmHg.[18] The presence of any ASCVD was extracted, which included myocardial infarction (MI), transient ischaemic attack (TIA), stroke/CVA, IHD, angina, peripheral vascular disease (PVD), percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG). Other categorical variables included family history (FHx) of CVD, hypercholesterolaemia or IHD. Personal history of heart failure (HF), atrial fibrillation (AF), gout, sleep apnoea, amputations and dialysis was also collected. Other measured variables included albumin:creatinine ratio (ACR) and the presence of microalbuminuria (any measurement of ACR >2.5 or >3.5 in males and females respectively). Medications were also extracted and categorised as taking any antihypertensives, specifically taking ACE inhibitors or angiotensin II receptor blockers (ARBs), lipid lowering medication, and antiplatelets/coagulants. Detailed hypoglycaemic medications taken were also recorded for each patient. Numerical values extracted included a lipid panel: total cholesterol, triglycerides, HDL and LDL cholesterol, all measured in mmol/L and TC:HDL ratio. Moreover creatinine, eGFR (ml/min/1.73m^2), CKD (eGFR < 60 ml/min/1.73m^2), Framingham CVD risk score (%) and NZ Predict CVD risk score (%) were also recorded.

All variables extracted were the most recent measurements recorded by the practice up to 3 December 2019. HbA1c and ACR were only included if measured between 1 January 2018 and 3 December 2019. Medications were only included if a prescription had been issued in the last 12 months.

For eligibility calculations, part of the ADA/EASD criteria for SGLT-2 inhibitor/GLP-1 agonists included the presence of ASCVD, HF or CKD (eGFR <60ml/min/1.73m^2). The definition of ASCVD is ever having had unstable angina, MI, TIA, stroke, revascularisation procedures, PVD or CABG. The ADA/EASD 2020 criteria included all of the above as well as the presence of microalbuminuria (ACR ≥3mg/mmol) and indicators of high

ASCVD risk, defined as age ≥55 years and presence of left ventricular hypertrophy or coronary, carotid or lower extremity artery stenosis. In contrast, the proposed PHARMAC criteria require the presence of either CKD (eGFR <60ml/min/1.73m^2) and/or microalbuminuria (ACR ≥3mg/mmol), a CVD risk score ≥15%, or established CVD, defined as the presence of angina, MI, PCI, CABG, TIA, stroke or PVD.

Outcomes

The primary outcome was to ascertain how many people with T2DM would be eligible for an SGLT-2 inhibitor or GLP-1 agonist using both the proposed PHARMAC criteria and the ADA/EASD criteria. The secondary outcome was to compare the demographics of those who met or did not meet each of the criteria.

Results

The total enrolled population of the three practices was 23,517 people and the demographics are summarised, by practice and total population in Table 1A. The mean (SD) age was 35.3 (22.3) years. The majority of patients at KMC were European (73.4%), while at PHP the majority were Pacific (81.3%) and at PUCHS 68.7% were either Māori or Pacific. There was a higher level of deprivation in the PHP and PUCHS populations than KMC. The patient data of 1,160 patients with T2DM, which equates to 4.9% of the total population, were extracted from the three general practices. There are differences in prevalence of T2DM across the practices with KMC (3.2%) the lowest and PHP (9.6%) the highest. The demographics of those patients with T2DM are summarised in Table 1B. The mean (SD) age of those with diabetes was 59.5 (15.2) years, being older in KMC compared with PHP and PUCHS. Together, Māori and Pacific made up 32.7% of the overall practice populations and 56.2% of those with T2DM.

The clinical characteristics of those with T2DM are summarised in Table 2. The mean (SD) HbA1c was 63.9 (19.9) mmol/mol. Overall 17.8% had established ASCVD with similar proportions in each practice. However, more patients at PHP and PUCHS had microalbuminuria than at KMC, with over 40% overall having chronic kidney disease or microalbuminuria.

Metformin is the first-line hypoglycaemic agent recommended in the management of T2DM. In the population audited, 81.1% of those with T2DM had ever been prescribed metformin. The hypoglycaemic regimens used in the previous 12 months are summarised in Table 3. Further, 70.5% were taking an antihypertensive agent and specifically, 65.4% an ACE inhibitor or angiotensin II receptor blocker. 65.4% were on lipid lowering therapy. There were no differences in proportions of patients on these agents between practices.

Of the 1,160 people with T2DM, 399 (34.4%) are eligible to be prescribed an SGLT-2 inhibitor or GLP-1 agonist under the PHARMAC criteria, 339 (29.2%) are eligible under the 2018 ADA/EASD criteria, and 559 (48.2%) by the revised 2020 ADA/EASD criteria. The characteristics of those eligible for each criterion are shown in Table 4.

When comparing the PHARMAC criteria to the 2020 ADA/EASD criteria, 364 patients meet both (Figure 1). Interestingly, 195 of 559 patients (34.8%) meet only the 2020 ADA/EASD criteria, whereas 35 of 399 (8.7%) meet only the PHARMAC criteria. The characteristics of patients that meet one criterion but not the other are shown in Table 5. Figure 1 also illustrates that the principal reason for those meeting 2020 ADA/EASD criteria and not PHARMAC is the removal of the HbA1c threshold. The majority (145/195 (74.4%)) patients included by the 2020 ADA/EASD guideline, but excluded by PHARMAC have an HbA1c below 53mmol/mol. Most (73.3%) of those excluded by PHARMAC have microalbuminuria, but are excluded because their HbA1c is <53mmol/mol. Conversely, of those 35 patients included by PHARMAC but not the 2020 ADA/EASD criteria, 21 (60.0%) have a calculated CVD risk above 15%. A calculated CVD risk score is not a specific component of the ADA/EASD criteria.

The main change in the 2020 ADA/EASD criteria is the removal of an HbA1c treatment threshold and the inclusion of microalbuminuria as an indication for treatment. All of the patients eligible under the 2018 criteria (n=339) remain eligible under the 2020 criteria (n=559). Of the additional 220 patients included by the 2020 criteria, 80% had microalbuminuria. Moreover the mean HbA1c of these 220 people was 55mmol/mol, and 160 of the

Table 1: Demographics of total practice populations (A) and those with type 2 diabetes (T2DM) (B).

A: Total practice	**KMC**	**PHP**	**PUCHS**	**Total**
Number of patients	14,682	2,234	6,601	23,517
Demographics. Mean (SD)				
Age (years)	38.5 (22.7)	29.3 (20.3)	30.2 (20.5)	35.3 (22.3)
NZ Dep Quintile	1.8 (1.0)	4.5 (1.1)	4.4 (1.2)	2.7 (1.7)
Gender				
Female	7,639 (52.0%)	1,120 (50.1%)	3,415 (51.7%)	12,174 (51.8%)
Male	7,042 (48.0%)	1,114 (49.9%)	3,182 (48.2%)	11,338 (48.2%)
Ethnicity				
Asian	1,875 (12.8%)	94 (4.2%)	777 (11.8%)	2,746 (11.7%)
European	10,772 (73.4%)	81 (3.6%)	627 (9.5%)	11,480 (48.8%)
Indian	653 (4.4%)	37 (1.7%)	278 (4.2%)	968 (4.1%)
NZ Māori	718 (4.9%)	164 (7.3%)	1,399 (21.2%)	2,281 (9.7%)
Pacific	459 (3.1%)	1,817 (81.3%)	3,138 (47.5%)	5,414 (23.0%)
Other	204 (1.4%)	34 (1.5%)	377 (5.7%)	615 (2.6%)
B: Patients with T2DM	**KMC**	**PHP**	**PUCHS**	**Total**
Number of patients	467	214	479	1,160
% of practice with T2DM	3.2%	9.6%	7.3%	4.9%
Demographics. Mean (SD)				
Duration of DM (years)	10.8 (7.6)	7.2 (7.6)	10.0 (7.6)	9.3 (7.6)
Age (years)	64.1 (13.6)	54.7 (13.1)	57.1 (14.0)	59.5 (14.2)
NZ Dep Quintile	1.8 (1.1)	4.4 (1.1)	4.4 (1.3)	3.4 (1.7)
Gender				
Female	220 (47.1%)	107 (50.0%)	259 (54.1%)	586 (50.5%)
Male	247 (52.9%)	107 (50.0%)	220 (45.9%)	574 (49.5%)
Ethnicity				
Asian	79 (16.9%)	6 (2.8%)	36 (7.5%)	121 (10.4%)
European	243 (52.0%)	1 (0.5%)	22 (4.6%)	266 (22.9%)
Indian	69 (14.8%)	3 (1.4%)	21 (4.4%)	93 (8.0%)
NZ Māori	23 (4.9%)	9 (4.2%)	78 (16.3%)	110 (9.5%)
Pacific	46 (9.9%)	194 (90.7%)	302 (63.0%)	542 (46.7%)
Other	7 (1.5%)	0 (0.0%)	20 (4.2%)	27 (2.3%)

Table 2: Clinical characteristics of patients with diabetes.

	KMC	PHP	PUCHS	Total
Total number of patients	467	214	479	1,160
Patient characteristics. Mean (SD)				
Weight (kg)	86.9 (22.8)	102.5 (23.3)	97.8 (22.8)	94.3 (25.1)
BMI (kg/m^2)	31.0 (7.9)	36.3 (7.2)	35.5 (8.2)	33.9 (7.9)
HbA1c (mmol/mol)	58.0 (19.8)	72.7 (20.1)	65.9 (19.8)	63.9 (19.9)
Systolic (mmHg)	138 (16)	134 (17)	131 (14)	134 (16)
Diastolic (mmHg)	80 (9)	82 (9)	81 (10)	81 (9)
Smoking status				
Yes	27 (5.8%)	48 (22.4%)	106 (22.1%)	181 (15.6%)
Never	328 (70.2%)	108 (50.5%)	238 (49.7%)	674 (58.3%)
Past	109 (23.3%)	58 (27.1%)	135 (28.2%)	302 (26.1%)
Comorbidities				
ASCVD	74 (15.8%)	47 (22.0%)	86 (18.0%)	207 (17.8%)
CKD	195 (41.8%)	49 (22.9%)	247 (51.6%)	491 (42.3%)
Microalbuminuria	163 (34.9%)	114 (53.3%)	224 (46.8%)	501 (43.2%)
Cardiovascular risk factor. Number (%)				
NZ Predict ≥15%	58 (12.4%)	32 (15.0%)	87 (18.2%)	177 (15.3%)
Māori or Pacific with NZ Predict ≥15%	6 (1.3%)	31 (14.5%)	80 (16.7%)	117 (10.1%)

Table 3: Medications taken by patients with diabetes in the last 12 months.

	KMC	PHP	PUCHS	Total
Total number of patients	467	214	479	1,160
Hypoglycaemics				
Metformin only	145 (31.0%)	65 (30.4%)	116 (24.2%)	326 (28.1%)
Metformin ever	388 (83.1%)	162 (75.7%)	389 (81.2%)	940.6 (81.1%)
Metformin + sulfonylurea	77 (16.5%)	56 (26.2%)	60 (12.5%)	193 (16.6%)
Metformin + any oral hypoglycaemic agent	120(25.7%)	61 (28.5%)	130 (27.1%)	311 (26.8%)
Insulin only	14 (3.0%)	7 (3.3%)	28 (5.8%)	49 (4.2%)
Insulin + metformin	70 (15.0%)	57 (26.6%)	74 (15.4%)	201 (17.3%)
Insulin + any oral hypoglycaemic agent	74 (15.8%)	59 (27.6%)	82 (17.1%)	215 (18.5%)
Other medications				
Any antihypertensive	318 (68.1%)	158 (73.8%)	342 (71.4%)	818 (70.5%)
ACE or ARB	300 (64.2%)	142 (66.4%)	317 (66.2%)	759 (65.4%)
Lipid lowering	318 (68.1%)	138 (64.5%)	303 (63.3%)	759 (65.4%)
Anticoagulant	78 (16.7%)	58 (27.1%)	70 (14.6%)	206 (17.8%)

Table 4: Eligibility of patients with diabetes for SGLT-2 inhibitors/GLP-1 agonists by different criteria.

	KMC	PHP	PUCHS	Total
Total number of patients	467	214	479	1,160
ADA 2018				
Total eligible overall	130 (27.8%)	53 (24.8%)	157 (32.8%)	339 (29.2%)
ASCVD	39 (8.4%)	33 (15.4%)	46 (9.6%)	118 (10.2%)
CKD/HF	111 (23.8%)	33 (15.4%)	142 (29.6%)	286 (24.7%)
Māori or Pacific	23 (4.9%)	50 (23.4%)	131 (27.3%)	204 (17.6%)
Age (years)	64.1 (14.5)	58.4 (14.6)	58.1 (14.1)	61.0 (14.1)
Quintile	1.9 (1.6)	4.3 (1.4)	4.5 (1.7)	3.5 (1.7)
Duration (years)	12.9 (7.9)	10.5 (7.4)	12.4 (7.6)	12.4 (7.6)
HbA1c (mmol/mol)	67.7 (20.6)	78.4 (20.2)	75.7 (19.7)	73.4 (19.8)
Microalbuminuria	100 (21.4%)	37 (17.3%)	132 (27.6%)	269 (23.2%)
ADA 2020				
ASCVD	60 (12.8%)	40 (18.7%)	73 (15.2%)	173 (14.9%)
CKD/HF/microalbuminuria	164 (35.1%)	125 (58.4%)	210 (43.8%)	499 (43.0%)
Total eligible overall	193 (41.3%)	136 (63.6%)	230 (48.0%)	559 (48.2%)
Māori or Pacific	30 (6.4%)	133 (62.1%)	193 (40.3%)	356 (30.7%)
Age (years)	66.0 (14.1)	54.9 (14.5)	59.1 (14.1)	60.8 (14.1)
Quintile	1.9 (1.7)	4.5 (1.6)	4.5 (1.7)	3.6 (1.7)
Duration (years)	12.3 (7.6)	8.2 (7.6)	12.3 (7.6)	11.3 (7.6)
HbA1c (mmol/mol)	60.6 (20.0)	72.9 (20.1)	67.7 (19.8)	66.6 (19.9)
Microalbuminuria	143 (30.6%)	112 (52.3%)	191 (39.9%)	444 (38.3%)
PHARMAC				
CVD	37 (7.9%)	27 (12.6%)	47 (9.8%)	111 (9.6%)
CKD/microalbuminuria	103 (22.1%)	88 (41.1%)	154 (32.2%)	345 (29.7%)
CVD risk ≥15%	28 (6.0%)	17 (7.9%)	48 (10.0%)	93 (8.0%)
Total eligible overall	128 (27.4%)	96 (44.9%)	175 (36.5%)	399 (34.4%)
Māori or Pacific	23 (4.9%)	95 (44.4%)	146 (30.5%)	264 (22.8%)
Age (years)	65.3 (14.1)	56.5 (14.5)	59.7 (13.9)	60.7 (14.1)
Quintile	1.9 (1.7)	4.6 (1.6)	4.5 (1.7)	3.7 (1.7)
Duration (years)	13.3 (7.6)	10.1 (7.6)	13.0 (7.6)	12.4 (7.6)
HbA1c (mmol/mol)	67.0 (19.9)	79.5 (20.1)	75.0 (19.6)	73.5 (19.9)
Microalbuminuria	93 (19.9%)	83 (38.8%)	143 (29.9%)	319 (27.5%)

Figure 1: Patients with type 2 diabetes eligible for SGLT2 inhibitors/GLP-1 agonists by criteria.

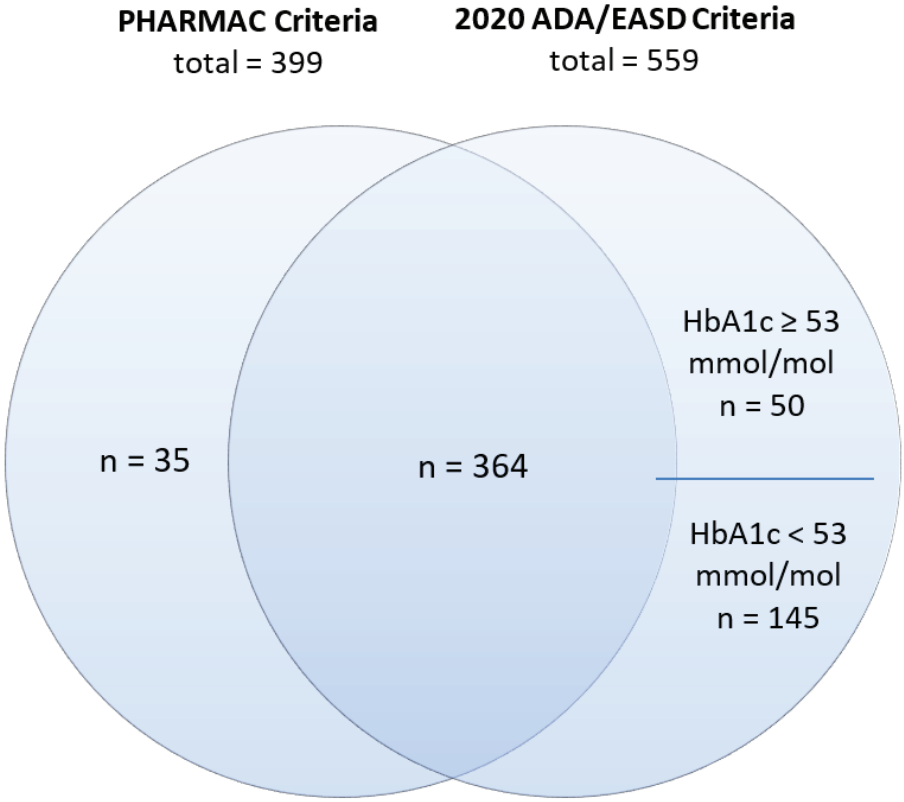

Table 5: ADA/EASD 2020 vs PHARMAC: which patients are excluded for an SGLT-2 inhibitor/GLP-1 agonist by criteria.

	KMC	PHP	PUCHS	Total
Excluded by ADA/EASD 2020				
Total	8	3	24	35
Māori or Pacific	1 (12.5%)	3 (100.0%)	20 (83.3%)	24 (68.6%)
Age (years)	67.3 (19.4)	61.0 (8.7)	65.1 (12.3)	65.2 (13.7)
Quintile	1.5 (0.9)	4.3 (1.2)	4.5 (1.3)	3.8 (1.7)
Duration (years)	13.0 (8.9)	6.0 (2.6)	14.8 (8.8)	13.6 (8.7)
HbA1c (mmol/mol)	57.5 (5.7)	88.0 (35.5)	68.3 (17.9)	67.5 (18.9)
ACE or ARB	7 (87.5%)	2 (66.7%)	17 (70.8%)	26 (74.3%)
Microalbuminuria	3 (37.5%)	1 (33.3%)	15 (62.5%)	19 (54.3%)
CVD risk >15%	6 (75.0%)	2 (66.6%)	13 (54.2%)	21 (60.0%)
Excluded by PHARMAC				
Total	73	43	79	195
Māori or Pacific	8 (11.0%)	41 (95.3%)	67 (84.8%)	116 (59.5%)
Age (years)	68.7 (13.5)	53.6 (14.7)	60.9 (13.3)	62.2 (14.8)
Quintile	1.8 (1.0)	4.3 (1.2)	4.6 (1.0)	3.5 (1.7)
Duration (years)	10.7 (8.0)	3.8 (5.1)	11.8 (8.1)	9.6 (8.1)
HbA1c (mmol/mol)	49.6 (12.3)	60.2 (23.2)	48.8 (11.7)	51.8 (16.0)
ACE or ARB	54 (74.0%)	26 (60.5%)	59 (74.7%)	139 (71.3%)
Microalbuminuria	52 (71.2%)	29 (67.4%)	62 (78.5%)	143 (73.3%)

additional 220 (73%) patients had an HbA1c below the previous treatment threshold of 53mmol/mol, still a requirement of PHARMAC.

Discussion

This audit of patients with T2DM from three different primary care practices in the greater Wellington region compared different criteria for eligibility for treatment with an SGLT-2 inhibitor or GLP-1 agonist as a second-line therapy after metformin, by the 2018 and 2020 ADA/EASD guideline or those proposed by PHARMAC for potential funding of these agents in New Zealand. Using the proposed PHARMAC criteria 34.4% patients with T2DM would be eligible compared to the 2018 ADA/EASD criteria, which would recommend their use in 27.2% patients and 48.2% by the revised 2020 ADA/EASD criteria.

This audit was conducted before the publication of the 2020 revised ADA/EASD criteria. The additional 110 patients included under the PHARMAC criteria compared with 2018 ADA/EASD are predominantly Māori or Pacific, younger and 86% had microalbuminuria. However, once microalbuminuria was included as an indication and the HbA1c threshold was removed in the 2020 ADA/EASD guideline, there are now 160 more patients in total who meet the 2020 ADA/EASD guideline than would be funded under PHARMAC criteria. This is an important change in focus of the utility of these agents from predominantly glucose lowering therapy to prevention of cardiovascular events and diabetic kidney disease. The removal of an HbA1c threshold by 2020 ADA/EASD was largely driven by the REWIND trial which showed the same reduction of MACE for a GLP-1 agonist in patients with an HbA1c above and below 55mmol/mol.[19] Furthermore, studies where there was minimal difference in HbA1c seen between placebo and GLP-1 agonist treatment arms, showed significant reduction in MACE with the GLP-1 agonist.

Another important change in the 2020 ADA/EASD criteria was the inclusion of people at high risk of CVD as well as those with established disease. The PHARMAC criteria include this whereas the 2018 ADA/EASD criteria did not. It must be noted that there are two CVD risk calculations commonly used by GP practices: the Framingham five-year CVD risk and the NZ predict five-year CVD risk calculator. The NZ predict calculation generally gives more conservative estimates of CVD risk and was used for this audit. Practices which use the Framingham risk calculator are likely to identify more patients meeting the PHARMAC criteria. Standardisation of the CVD risk calculator to the diabetes specific Predict equation may be an important component of the roll out of the PHARMAC criteria.

Because of higher rates of diabetes-related kidney disease, the inclusion of microalbuminuria by PHARMAC as an indication for funding gave greater access to Māori and Pacific patients than the 2018 ADA/EASD guideline, actively reducing inequity. However, comparison with the 2020 guideline this advantage is lost. Under the 2020 ADA/EASD, 356 Māori and Pacific people would be eligible (30.7% of all those with diabetes and 54.6% of the Māori and Pacific people with diabetes) and by the PHARMAC criteria 264 would be eligible (22.8% of all those with diabetes and 40.5% of Māori and Pacific people with diabetes).

Based on the the 2020 ADA/EASD guideline, where an HbA1c threshold has been removed, an argument could be made to follow similar open criteria. However, consultation between PHARMAC and clinicians, including endocrinologists, cardiologists and renal physicians, helped to develop a recommendation that is evidence-based, current and most importantly will include more of the New Zealand population who have the worst diabetes outcomes. Following clinical trial data these groups should have the greatest benefits to improve health equity within the fiscal reality. As more data become available we may gain further clarity on which patients are best managed with SGLT-2s vs GLP-1 agonists. Current data would suggest a funding priority for the SGLT-2 class, particularly with greater benefits in heart failure and nephropathy, at approximately 50% of the cost of GLP-1 agonists. This is especially relevant for younger Māori and Pacific patients who are most at risk of developing diabetic nephropathy.

There are limitations to this research. While care was taken to ensure all information is as accurate as possible, large

amounts of data were extracted manually. Each practice coded information differently, with variability in quality of data by variable. Where data were missing, calculations were performed with the most conservative estimate, which may result in underestimation of CVD risk. Moreover, when using the NZ Predict CVD calculator any ethnicities that weren't listed were calculated using 'Asian' ethnicity, as it was the most conservative estimate of CVD risk. Therefore, it is possible that unlisted ethnicities have higher CVD risks. Furthermore, the overall population included in this audit is somewhat unbalanced compared with the total New Zealand population. The audit attempted to include patients with the greatest burden of T2DM and inequity. Hence almost half (46.7%) of the people with T2DM were Pacific, which is a higher proportion than the overall New Zealand population, but does capture high-needs patients.

Conclusion

This clinical audit of three primary care practices in the greater Wellington region of New Zealand highlights that the proposed eligibility criteria from PHARMAC for SGLT-2 inhibitors and GLP-1 agonists will give funded access to these drugs for 34.4% of those with T2DM. While this is fewer patients than would be eligible if the 2020 ADA/EASD criteria were employed (48.2%), this is a long awaited and very welcome development. Importantly, the PHARMAC criteria captures Māori and Pacific people with microalbuminuria at high risk of developing CVD and renal complications. Based on clinical trial evidence, the availability of these agents to New Zealanders with T2DM will reduce cardiovascular events, heart failure and progression of kidney disease and from our analysis will likely reduce health inequity, which is of priority for the New Zealand health system. This outcome strongly supports the ongoing active interaction between PHARMAC and specialist medical communities to facilitate the optimum availability of medications for New Zealanders. It will now be critical to ensure that primary care are supported to deliver these new medicines to those who are eligible and ensure uptake for Māori and Pacific patients and those with greatest deprivation.

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