Identifying potential patients with diabetes-related dementia: a descriptive approach using routinely collected data

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ABSTRACT

AIMS: Diabetes-related dementia (DRD) is a new dementia subtype associated with type 2 diabetes mellitus, first described in 2013. This study investigated data from a local New Zealand memory service to identify patients that met the criteria for DRD.

METHODS: Using routinely collected data from 2013–2021, we selected a sample of people with dementia, diabetes, and no CT evidence of Alzheimer's disease (AD), vascular dementia, or frontotemporal dementia. We compared their socio-demographic, clinical, and cognitive characteristics with a sample of patients with diabetes and Alzheimer's disease.

RESULTS: Forty (16%) of 249 patients with diabetes and dementia had "normal" CT scans (DRD subgroup), and 38 (15%) had AD (AD subgroup). Compared to NZ Europeans, disproportionally more Māori and Pacific Islanders (70.2%) were in the DRD subgroup. In the Pacific subgroup (n=31), the DRD subgroup had higher memory subscores than the AD subgroup (p=0.047), and the Kaplan–Meier plot suggested poorer survival (p=0.13). Māori patients with diabetes and dementia were more likely to meet all four criteria for DRD.

CONCLUSION: We have replicated the findings of the 2013 DRD research and have demonstrated a higher risk for the DRD subtype of dementia among the Māori and Pacific Islander patients in our sample.

Type 2 diabetes mellitus has been shown to increase the risk of cognitive decline and dementias such as Alzheimer's disease dementia (AD) and vascular dementia.[1] A number of mechanisms may be involved in the pathophysiology, including vascular disease, glucose toxicity, and changes in amyloid metabolism.[1] A research group in Japan have suggested that type 2 diabetes is also associated with another new dementia subgroup, which they have called diabetes-related dementia (DRD).[2–7] Diabetes-related dementia was first described by Fukasawa et al. in 2013.[2] Patients at a memory clinic with dementia and type 2 diabetes were categorised into four subgroups by findings on single photon emission computed tomography (SPECT) and magnetic resonance imaging (MRI): 1) those showing an AD pattern but not showing cerebrovascular disease (CVD), 2) those showing CVD only, 3) those showing AD with CVD (mixed), and 4) those without AD or CVD (which they called the DRD subgroup). The research group then examined the four groups for differences in clinical characteristics. Compared to the AD group, the DRD subgroup was characterised by higher haemoglobin A1c (HbA1c), longer duration of diabetes, higher frequency of insulin therapy, lower frequency of apolipoprotein E4 carriers (ApoE4), less severe medial temporal lobe atrophy, and cognitive assessment showed more impaired attention and executive functions but less impaired memory.

In follow-up studies on the same sample, the patients in the DRD group had a different clinical course to those in the AD group.[3,7] There were differences in SPECT on follow-up, suggesting that the underlying pathophysiology in the DRD group differs from the AD group. Patients in the AD subgroup showed a significant widespread reduction in regional cerebral blood flow (rCBF) in the parietotemporal and limbic lobes, whereas rCBF reduction in the DRD subgroup was more scattered. Patients with DRD had slower progression in cognitive decline compared to the AD group. Despite a slower decline, significantly more patients in the DRD group were admitted to hospital.[7] It is likely that more severe diabetes and a higher risk of frailty[5] contributed to higher rates of medical conditions and hospitalisation.

Based on these findings, the authors defined diabetes-related dementia (DRD) as a new subtype of dementia, with characteristics as follows:[4]

i. Type 2 diabetes mellitus: long duration and less well-controlled hyperglycemia.
ii. Impaired attention but less-impaired word recall, slow progression of cognitive impairment.
iii. No evidence of vascular lesions or medial temporal lobe atrophy on CT/MRI scan.
iv. No decreased hypoperfusion/hypometabolism in the posterior cerebral lobe on SPECT, negative or equivocal amyloid accumulation.
v. Cerebrospinal fluid: normal p-tau and normal Ab1–42 levels.
vi. ApoE4 carrier: low frequency.
vii. Exclusion of other causes of dementia (hypothyroidism, vitamin B1, B12 deficiency, head trauma, chronic alcoholism, cerebrovascular disease, other neurodegenerative diseases).

The proposed DRD subgroup has only been demonstrated by one research group so far, but has potentially important implications for New Zealand, where the prevalence of diabetes is high[8] and is projected to increase by 70–90% within the next 20 years.[9] The burden of diabetes disproportionately affects Māori and Pacific Islander populations living in New Zealand, with a prevalence two to three times higher than NZ Europeans,[9] which may be one of the reasons that the prevalence of dementia is higher among Māori and Pacific Islanders.[10] The Lancet Commission for Dementia[11,12] identified 12 modifiable risk factors which contribute to potentially reversible causes of dementia. These risk factors were less education, hypertension, obesity, alcohol, traumatic brain injury (TBI), hearing loss, smoking, depression, physical inactivity, social isolation, air pollution, and diabetes. Together they were estimated to contribute to 40% of potentially preventable dementias worldwide. Population attributable fraction (PAF) estimates vary between countries as prevalence of these risk factors differ,[13] and in New Zealand the PAF estimate exceeds worldwide estimates at 47.7%.[14] The PAF estimates for dementia are higher among Māori (51.4%) and Pacific Islanders (50.8%) compared to European (47.6%) and Asian (40.8%) peoples.[14] The findings are supported by evidence from routinely collected New Zealand national administrative health data that suggest significantly higher prevalence of *diagnosed* dementia in Māori (5.4%) and Pacific Islander (6.3%) populations compared to Asian (3.4%) and Europeans (3.7%) in the age 60+ population (with the true rate, including unidentified dementia, likely to be double these estimates).[15] The prevalence of dementia is projected to more than double by 2050, especially for Māori and Pacific Islander populations, which have more rapid demographic ageing and higher prevalence of risk factors.[10]

Given the high prevalence of diabetes and dementia in New Zealand, especially in Māori and Pacific Islanders, the suggestion of the existence of a diabetes-specific subgroup of dementia (DRD) is of interest, as it may have a different prognosis and require different prevention/treatment approaches. The aim of this study is to investigate data from a local New Zealand memory service cohort to identify a group of patients that meet the criteria for DRD, and to compare their clinical and cognitive characteristics with the sample described in Japan.[2–7]

Methods

Adapted criteria for diabetes-related dementia (DRD)

We attempted to identify people with DRD guided by the seven criteria listed above.[4] We were unable to address criteria 4, 5, and 6 in our sample, as SPECT, cerebrospinal fluid, and ApoE4 carrier status are not routinely collected in the memory service. We judged that the remaining criteria would be sufficient to investigate the possibility of a subgroup with DRD using routinely collected data. We therefore used the following criteria to define DRD:

i. Type 2 diabetes mellitus, defined as HbA1c≥50 at the time of initial assessment.
ii. Impaired attention but less-impaired word recall on cognitive testing at the time of initial assessment.
iii. No evidence of vascular lesions or frontotemporal/medial temporal lobe atrophy on CT/MRI scan (defined as "normal" findings on CT scan report at the time of initial assessment).
iv. Exclusion of other causes of dementia (hypothyroidism, vitamin B1, B12 deficiency, head trauma, chronic alcoholism, cerebrovascular disease, or other neurodegenerative diseases).

Setting and sample

The sample was ascertained from consecutive referrals to Te Whatu Ora Counties Manukau Memory Service at Middlemore Hospital between 2013–2021. It extends by two years a cohort previously used to investigate the predictors of aged residential care placement in dementia.[16] The memory service accepts referrals mostly from primary care and from some secondary care services but does not assess people in residential care. The referred patients must have a primary concern of subjective and/or objective cognitive decline to meet the referral criteria for the memory service. We selected only those patients that received a new diagnosis of dementia for inclusion in this study, to attempt to capture patients at a similar clinical stage of dementia.

Study design

In our study we selected a sample of people with a new diagnosis of dementia (AD, vascular dementia [VD], mixed AD/VD, and other) and diabetes (defined as HbA1c≥50 at the time of initial assessment). We then ascertained a DRD subgroup in the sample that had "normal" CT/MRI scan reports, that is with no evidence of cerebrovascular pathology (e.g., strokes or ischaemia), and/or focal lobar atrophy in frontal, temporal and/or parietal lobes (but mild diffuse global atrophy in keeping with age was allowed), or any other abnormality such as evidence of brain tumour or subarachnoid haemorrhage. We compared the DRD subgroup with a second subgroup from the same sample who did *not* have a "normal" CT scan and had previously been given a clinical diagnosis of AD. Our aim was to investigate whether there were socio-demographic and clinical differences between these two groups (e.g., age, sex, ethnicity, HbA1c levels, cognitive profile, and mortality).

The cognitive tests we examined were the total scores, memory, and attention subscores for the Addenbrooke's Cognitive Assessment-III (ACE-III),[17] and the total scores and memory subscores for the Rowland Universal Dementia Assessment Scale (RUDAS),[18] as the RUDAS does not have an attention subtest. A higher score on either test signifies better cognitive function.

Data collection

Socio-demographic and clinical details were ascertained from routinely collected health data, including age, gender, ethnicity, HbA1c levels, CT scan reports, dementia subtypes and severity, and cognitive function. In English speakers, cognitive function was assessed using the ACE-III.[17] The RUDAS[18] was used for non-English speakers (via interpreters) or where English was the second language. Dementia diagnoses, subtypes, and dementia severity were made by clinical consensus at weekly memory service multidisciplinary team meetings, using clinical and neuroradiological information. Dementia diagnosis was made using DSM-IV criteria[19] and dementia severity utilising Clinical Dementia Rating (CDR) criteria.[20] Dementia subtyping was guided by NINCDS-ADRDA criteria for Alzheimer's disease dementia,[21,22] NINDS-AIREN criteria for vascular dementia,[23] Lewy body dementia[24,25] and frontotemporal dementia.[26] The HbA1c data, CT scan reports, and mortality data were extracted by Middlemore Hospital Health Informatics Department. This research was approved by the Northern B Health and Disability Ethics Committee (HDEC) reference number: 17/NTB/191.

Statistical analysis

All data were de-identified prior to analyses. Patient ethnicities were categorised as NZ European, Māori, Pacific Islander, and other. Dementia severity ratings were dichotomised to mild dementia or "moderate to severe" dementia. Cognitive scores on ACE-III and RUDAS were recorded as raw scores (with incomplete answers scored as zero). The total ACE-III and RUDAS scores (100 and 30, respectively) and memory subscores (26 and 8, respectively) were standardised by calculating the proportion of the score achieved by each patient concerning the total score that could be achieved in each test. We also compared the median ACE-III attention subscores across the two groups. We carried out *k*-means cluster analysis on the standardised memory scores to identify patients with high values that met criterion (ii) for DRD.

We reviewed CT/MRI reports closest to time of acceptance by the memory service and classified findings into "normal" or "abnormal" based on criteria (iii) above. The CT scan reports were checked independently by two of the authors (CGP, SC) to classify referrals, and discrepancies were discussed to reach a consensus opinion.

Wilcoxon Rank-Sum Test, t-Tests and Fisher's exact tests were used with a significance level of 5%. $P<0.05$ was considered statistically significant. All statistical analyses were made using statistical software R 4.2.1 version.[27]

Results

Between 2013–2021, there were 3,950 referrals to the memory service for dementia assessment. Of these, 2,250 had a clinical assessment by the memory service. Around half were diagnosed with dementia, of whom 1,077 had a *new* diagnosis of dementia. Patients with a new diagnosis of dementia were classified by HbA1c level (where available, n=1071). Table 1 compares patients with a new diagnosis of dementia and HbA1c ≥50 mmol/mol (n=249) and patients with a new diagnosis of dementia and HbA1c<50 mmol/mol (n=822). There were a higher proportion (60.3%) of Māori and Pacific Islanders in the high HbA1c group and proportionally more European people (56.4%) in the low HbA1c group. Alzheimer's disease was more common in the low HbA1c group (40.1%), and vascular dementia was more common in the high HbA1c group (53.4%). Dementia subtypes in Table 1 were the clinical diagnoses given *prior* to this study; the study was designed to identify those that would meet criteria for the new dementia subtype of DRD.

The 249 patients with high HbA1c levels were then classified by their CT scan report findings. Forty of the 249 patients' CT scan reports were classified as "normal", and we called this group the DRD subgroup, of whom 36/40 had cognitive data (RUDAS or ACE-III). The comparison group was 38 patients with high HbA1c, an "abnormal" CT scan report, and a clinical diagnosis of Alzheimer's disease (AD subgroup), of whom 35/38 had cognitive data. In the DRD subgroup, we used the *k*-means algorithm on standardised memory scores to identify 17 patients who met the HbA1c, neuroradiological, *and* cognitive (less impaired memory subscore) criteria for DRD. Figure 1 shows the process of ascertaining the AD and DRD subgroups. Table 2 describes the characteristics of the subsamples at each stage to establish the DRD subgroup. Māori and Pacific Islanders made up the highest proportion of patients with high HbA1c and "normal" CT scans (70%), and Pacific Islanders had the highest mean HbA1c levels. Of patients with a new diagnosis of dementia, Māori were four to eight times more likely to meet all four criteria for DRD compared to other ethnic groups. The sample size was too small to test the statistical significance.

Socio-demographic and clinical characteristics of DRD and AD

Table 3 shows the socio-demographic variables and cognitive scores comparing DRD and AD subgroups for all ethnic groups (n=78) and for the Pacific Islander subgroup (n=31).

All ethnicities

Patients in the DRD subgroup were significantly younger than patients in the AD subgroup (p<0.001), but this may be due to confounding, as the majority in the DRD subgroup were Māori or Pacific Islanders (70.2%) and patients from these ethnic groups have a younger overall mean age compared to Europeans. The mean HbA1c level was slightly higher in the DRD subgroup, but did not reach statistical significance (p=0.290). Standardised and raw total scores on cognitive tests and memory subtests (ACE-III and RUDAS) were higher in the DRD subgroup than in the AD subgroup, but these also did not reach statistical significance. The median ACE-III memory subscore was 12/26 in the DRD subgroup and 10/26 in the AD subgroup (p=0.112), but we found no difference in the ACE-III attention subscores between the two groups (p=0.730). The median total RUDAS score was 19/30 in the DRD group and 15/30 in the AD subgroup (p=0.068), and the median RUDAS memory subscore was 2/8 in the DRD subgroup and 0/8 in the AD subgroup (p=0.304). Regarding missing data, it is important to note the following instances: for dementia severity, six patients in the DRD subgroup and one patient in the AD subgroup had missing data; concerning cognitive scores, there were no cognitive data available for four out of 40 patients in the DRD subgroup and three out of 38 patients in the AD subgroup. Additionally, one patient in the AD subgroup lacked total ACE-III scores, while four patients in the DRD subgroup and two patients in the AD subgroup did not have RUDAS memory subscores. These instances of missing data are denoted in Table 3 with asterisks (* and **).

Pacific subgroup

As ethnic differences may cause heterogeneity and spurious findings, we stratified by ethnicity and examined the findings for the largest subgroup (Pacific, n=31). There were 19 Pacific Islanders in the DRD group and 12 in the AD subgroup, of whom 29/31 had cognitive test data. Pacific Islanders in the DRD group were slightly younger than in the AD subgroup, but this was not significant (p=0.215). The total standardised cognitive score (ACE-III and RUDAS) was higher in the DRD group (p=0.013). Most Pacific Islander patients were tested with the RUDAS (21/31) rather than ACE-III (8/31). Compared to the AD subgroup, the total RUDAS

Table 1: Socio-demographic variables by HbA1c status.

		High HbA1c	Low HbA1c	p-value
Variable		Mean (SD)		
Age (years)		80.2 (7.4)	82.8 (8.1)	<0.001
	Category	n/249 (%)	n/822 (%)	
Gender	Female	142 (57.0)	457 (55.6)	0.716
	Male	107 (43.0)	365 (44.4)	
Ethnicity	European	61 (24.5)	463 (56.4)	<0.001
	Māori	35 (14.1)	76 (9.2)	
	Pacific Islander	115 (46.2)	207 (25.2)	
	Other	38 (15.2)	76 (9.2)	
Dementia subtype	Alzheimer's disease (AD)	62 (24.9)	330 (40.1)	<0.001
	Vascular dementia (VD)	133 (53.4)	299 (36.4)	
	Mixed dementia (AD/VD)	13 (5.2)	35 (4.3)	
	Other dementias	41 (16.5)	158 (19.2)	

Table 2: Dementia group status by ethnic group.

	Patient category							
Ethnicity	**All (n=1077)**		**Dementia and HbA1c≥50 (n=249)**		**Dementia, HbA1c≥50, and normal CT scan (n=40)**		**Meeting all four DRD criteria* (n=17)**	
	n (%)	**HbA1c mmol/mol Mean (SD)**	**n (%)**	**HbA1c mmol/mol Mean (SD)**	**n (%)**	**HbA1c mmol/mol Mean (SD)**	**n (%)**	**HbA1c mmol/mol Mean (SD)**
European	527 (48.9)	42.1 (10.5)	61 (24.5)	65.9 (14.1)	7 (17.5)	66 (22.3)	5 (29.4)	59.4 (9.4)
Māori	111 (10.3)	47.8 (14.0)	35 (14.1)	63.5 (15.0)	9 (22.5)	59 (9.14)	7 (41.2)	59.6 (10.1)
Pacific	325 (30.2)	53.0 (21.4)	115 (46.2)	75.4 (21.7)	19 (47.5)	76.1 (22.4)	4 (23.5)	80.2 (27.6)
Other	114 (10.6)	48.1 (13.7)	38 (15.3)	63.6 (13.1)	5 (12.5)	58.2 (6.91)	1 (5.9)	61.0 (-)

*DRD criteria defined as dementia, diabetes, “normal” CT scans, and less impaired memory subscore.

Table 3: Socio-demographic variables by DRD and AD for all ethnicities and for Pacific subgroup.

		All ethnicities (n=78)			Pacific subgroup (n=31)		
		DRD (n=40)	AD (n=38)	p-value	DRD (n=19)	AD (n=12)	p-value
		Mean (SD)			Mean (SD)		
Age (years)		77.7 (7.9)	83.6 (6.9)	0.001	77.4 (9.0)	80.2 (8.4)	0.215
HbA1c level (mmol/mol)		68.2 (19.8)	64.2 (12.9)	0.290	76.1 (22.4)	66.2 (17.8)	0.128
		n/40 (%)	n/38 (%)		n/19 (%)	n/12 (%)	
Gender	Female	26 (65.0)	24 (63.2)	1.000	12 (63.2)	8 (66.7)	1.000
	Male	14 (35.0)	14 (36.8)		7 (36.8)	4 (33.3)	
Ethnicity	European	7 (17.5)	15 (39.5)	0.174			
	Māori	9 (22.5)	6 (15.8)				
	Pacific	19 (47.7)	12 (31.6)				
	Other	5 (12.5)	5 (13.1)				
Dementia severity*	Mild	26 (84.6)	22 (60.61)	0.139	9 (64.3)	6 (54.5)	0.697
	Mod–Severe	8 (15.4)	15 (39.39)		5 (35.7)	5 (45.5)	
Cognitive scores (Mean and median scores)**		**ACE-III (n=19) RUDAS (n=17)**	**ACE-III (n=20) RUDAS (n=15)**	**p-value**	**ACE-III (n=5) RUDAS (n=12)**	**ACE-III (n=3) RUDAS (n=9)**	**p-value**
Total cognitive score, ACE-III or RUDAS (standardised)	Mean (SD)	0.64 (0.12)	0.59 (0.14)	0.159	0.63 (0.09)	0.51 (0.14)	0.013
Total ACE-III score (max 100)	Median (IQR)	67 (59.5, 72.5)	65.5 (55.8, 69.5)	0.693	58 (55, 60)	55 (49.5, 65)	0.881

Table 3 (continued): Socio-demographic variables by DRD and AD for all ethnicities and for Pacific subgroup.

		All ethnicities (n=78)			Pacific subgroup (n=31)		
		DRD (n=40)	AD (n=38)	p-value	DRD (n=19)	AD (n=12)	p-value
		Mean (SD)			Mean (SD)		
Cognitive scores (Mean and median scores)**		**ACE-III (n=19) RUDAS (n=17)**	**ACE-III (n=20) RUDAS (n=15)**	**p-value**	**ACE-III (n=5) RUDAS (n=12)**	**ACE-III (n=3) RUDAS (n=9)**	**p-value**
Total ACE-III score	Mean (SD)	63.6 (11.4)	63.3 (11.8)	0.932	52.9 (9.3)	58 (15.7)	0.638
Total RUDAS score (max 30)	Median (IQR)	19 (16, 21)	15 (13, 17)	0.068	20 (18.8, 21)	15 (12, 16)	0.014
Total RUDAS score	Mean (SD)	18.4 (4.1)	15.7 (4.3)	0.083	19.4 (3.0)	14.7 (3.9)	0.008
Total memory score: ACE-III or RUDAS (standardised)	Mean (SD)	0.37 (0.24)	0.31 (0.26)	0.285	0.32 (0.20)	0.19 (0.27)	0.232
ACE-III memory sub-score (max 26)	Median (IQR)	12 (9.5, 14)	10 (6, 13)	0.112	9 (9, 10)	12 (11, 12)	0.089
ACE-III memory sub-score	Mean (SD)	11.9 (4.5)	9.9 (4.1)	0.13	9 (3.3)	12 (1.2)	0.054
RUDAS memory sub-score (max 8)	Median (IQR)	2 (0, 2)	0 (0, 0)	0.304	2 (1.5, 2.5)	0 (0, 0)	0.047
RUDAS memory sub-score	Mean (SD)	1.7 (2.0)	1.4 (2.8)	0.75	2.3 (2.0)	0.8 (2.1)	0.054
ACE-III attention sub-score (max 18)	Median (IQR)	13 (11, 14)	13 (11, 16)	0.730	13 (11, 13)	12 (11.5, 14)	0.815
ACE-III attention sub-score	Mean (SD)	12.5 (2.0)	12.9 (3.4)	0.67	11.9 (2.0)	13 (2.7)	0.55

Figure 1: Flowchart showing the finding of the DRD and AD subgroups.

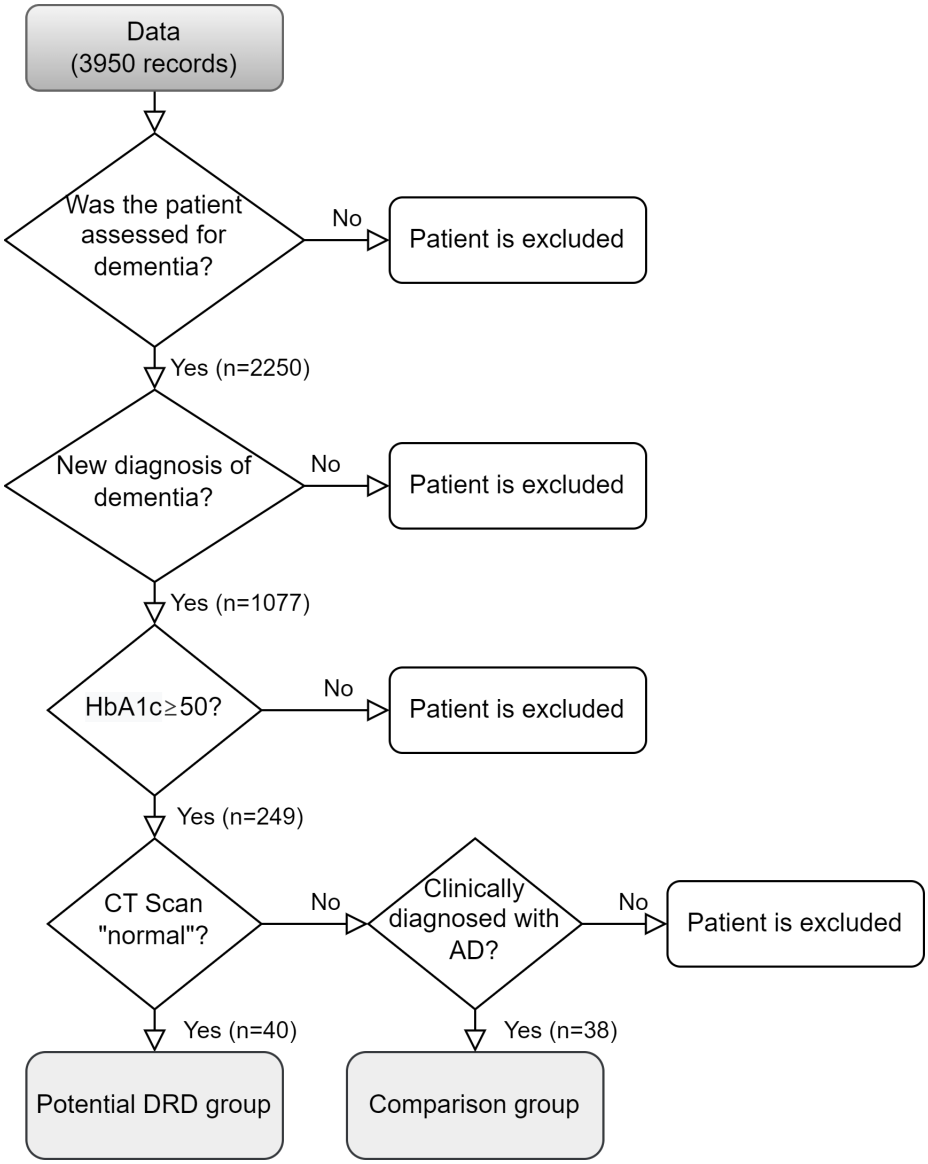
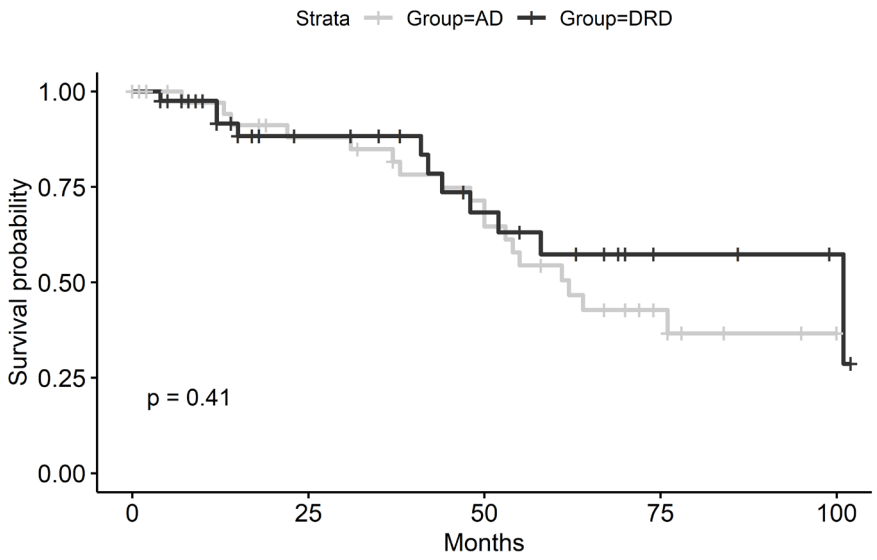
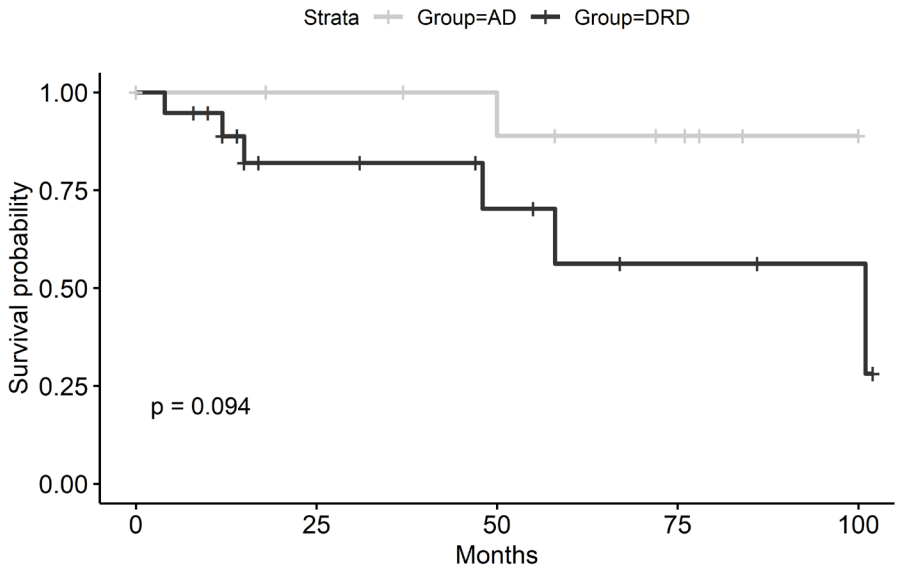


Figure 2: Kaplan–Meier plots for survival by DRD group and AD subgroup.

Whole group, all ethnicities (n=78).



Pacific subgroup (n=31).



score was higher in the DRD group (p=0.014), and mean RUDAS memory subscores were also higher (p=0.047). There were no significant differences in ACE-III scores, probably due to the small sample size. Regarding missing data, it is noteworthy that five patients in the DRD subgroup and one patient in the AD subgroup had missing data for dementia severity. Furthermore, for cognitive data, there were no available records for 2 out of 31 patients. Additionally, missing data were observed for RUDAS memory subscores, with four patients in the DRD subgroup and one patient in the AD subgroup affected. These instances of missing data are indicated in Table 3 using asterisks (* and **).

Survival

Figure 2 shows the Kaplan–Meier plots comparing survival curves for the whole group and for the Pacific subgroup classified into DRD or AD subgroups. In total (for all ethnicities), 18 patients died in the DRD group (47.4%), and 11 died in the AD subgroup (27.5%). The median survival time for the DRD group was 101 months, as opposed to 62 months for the AD subgroup, which means that although there were more deaths in the DRD group, their survival time was longer. However, this was not statistically significant (p=0.56), even after adjustment for the difference in mean age and severity between the two groups at baseline (p=0.42).

In the Pacific DRD subgroup 6/19 patients died (31.6%), and 1/12 died in the AD subgroup (8.3%). The Kaplan–Meier plot for the Pacific subgroup suggests a difference in survival but is not statistically significant (p=0.09), possibly due to small sample size and inadequate statistical power.

Discussion

Our study used routinely collected data to examine the potential existence of a group of patients meeting the criteria for diabetes-related dementia (DRD). Of 249 patients with dementia and diabetes, we found a mixed ethnicity group (40/249) who met the CT scan criteria for DRD. This group had higher memory scores and higher mortality compared to the AD subgroup, but these findings were not statistically significant. This may have been due to the heterogeneity, as the differences *were* statistically significant in the smaller Pacific subgroup. The Pacific subgroup who met criteria for DRD had higher total cognitive score and memory subscore compared to the subgroup with diabetes and AD, and their risk of dying was higher. These findings replicate those of the research group in Japan,[2–7] in that the DRD group had higher mean HbA1c, less impaired memory, and a higher risk of death than the AD subgroup. There were 17/249 patients that met HbA1c, CT scan *and* cognitive (memory) criteria for DRD; compared to the source population of people with dementia, disproportionally more of these (up to eight-fold higher) were Māori.

The main weakness of our study is that the final sample was relatively small and was unlikely to have statistical power to test for significant differences. However, the findings that the Pacific subgroup displayed the cognitive criteria for DRD and that there were proportionally more Māori in the group that met all four criteria for DRD are of interest, as, compared to NZ Europeans, Māori and Pacific Islanders living in New Zealand have a higher prevalence of diabetes and dementia. These findings may suggest a potential avenue for dementia prevention in populations that already suffer health inequalities. The findings are hypothesis-generating and may warrant further investigation in a larger, more representative, community-based sample.

Due to the limitations of using routinely collected data (rather than research data), we were only able to approximate the research diagnostic criteria described by Hanyu et al. in 2015.[4] However, the use of routinely collected administrative data is a cost-effective way of examining research questions of importance to the New Zealand population, and our findings suggest that there may indeed be a group of patients with dementia who have DRD. Another limitation is the relatively blunt nature of cognitive screening tests, which may not capture the more subtle or complex aspects of cognition. The study also relied on CT reports rather than a thorough review of CT scan images themselves, which could have led to some inaccuracies in the ascertainment of dementia subtype.

The broader question is whether DRD is a real phenomenon, or, given the potential harmful impact of hyperglycaemia on cognition, is this a potentially reversible stage of cognitive decline? Several studies have demonstrated that diabetes causes cognitive deficits in older adults without dementia,[28] and this process is likely to be on a continuum through cognitive decline to mild cognitive impairment, and then to various dementias including Alzheimer's disease and vascular dementia.[29] A 2018 meta-analysis[30] suggested that

treatment with metformin lowered the risk of dementia in type 2 diabetes, and a recent study in China[31] found that cognitive function of actively treated older diabetic patients was better than that of patients without diabetes. The main clinical priority then is to ensure adequate treatment of people with type 2 diabetes in order to prevent the onset of cognitive decline and dementia. The current cost of dementia in New Zealand is $2.5 billion NZD, and due to the rapid rise in prevalence, this will increase to $6 billion NZD by 2050.[10] In Māori, Pacific, and Asian populations, much of the cost is borne by families who provide most of the dementia care, increasing the financial burden on those who already have high socioeconomic deprivation. Thus, we should prioritise those population groups most at risk, both in terms of individual and population-level approaches to prevent diabetes and dementia, and by developing culturally appropriate dementia prevention strategies as part of diabetes health education.

Conclusion

We have replicated the 2013 findings of a research group in Japan who described a new diabetes-related dementia subtype that did not have features of Alzheimer's disease or vascular dementia, and we have demonstrated a higher risk for this subtype of dementia among the Māori and Pacific Islander patients in our sample. This may represent a potentially reversible form of dementia. Further research is required to examine the effect of anti-diabetic treatments and prevention strategies on cognitive function as an important outcome in these populations.

COMPETING INTERESTS
Nil.

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REFERENCES
1. Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P. Risk of dementia in diabetes mellitus: a systematic review. Lancet Neurol. 2006 Jan;5(1):64-74. doi: 10.1016/S1474-4422(05)70284-2.
2. Fukasawa R, Hanyu H, Sato T, Shimizu S, Koyama S, Kanetaka H et al. Subgroups of Alzheimer's disease associated with diabetes mellitus based on brain imaging. Dement Geriatr Cogn Disord. 2013;35(5-6):280-90. doi: 10.1159/000348407.
3. Fukasawa R, Hanyu H, Shimizu S, Kanetaka H, Sakurai H, Ishii K. Identification of diabetes-related dementia: Longitudinal perfusion SPECT and amyloid PET studies. J Neurol Sci. 2015 Feb 15;349(1-2):45-51. doi: 10.1016/j.jns.2014.12.023.
4. Hanyu H, Hirose D, Fukasawa R, Hatanaka H, Namioka N, Sakurai H. Guidelines for the Clinical Diagnosis of Diabetes Mellitus-Related Dementia. J Am Geriatr Soc. 2015 Aug;63(8):1721-3. doi: 10.1111/jgs.13581.
5. Hirose D, Hanyu H, Fukasawa R, Hatanaka H, Namioka N, Sakurai H. Frailty in diabetes-related dementia. Geriatr Gerontol Int. 2016 May;16(5):653-5. doi: 10.1111/ggi.12566.
6. Nakabeppu Y, Ninomiya T, editors. Diabetes Mellitus: A risk factor for Alzheimer's Disease. Singapore: Springer Singapore; 2019. p. 147-60.
7. Inagawa Y, Takenoshita N, Shimizu S, Fukasawa R, Sato T, Kanetaka H et al. Clinical Course of Diabetes-Related Dementia. J Alzheimer's Neurodegen Dis. 2020;6(036). doi: 10.24966/AND-9608/100036.
8. Te Whatu Ora Health New Zealand. Virtual Diabetes Register and web tool [Internet]. Wellington: Te Whatu Ora Health New Zealand; 2022 [cited 2022 Nov 4]. Available from: https://www.tewhatuora.govt.nz/our-health-system/digital-health/virtual-diabetes-tool/
9. PwC New Zealand. The Economic and Social Cost of Type 2 Diabetes [Internet]. Wellington: PwC; 2021 [revised 2021 Mar 1; cited 2022 Nov 4]. Available from: https://healthierlives.co.nz/wp-content/uploads/Economic-and-Social-Cost-of-Type-2-Diabetes-FINAL-REPORT.pdf
10. Ma'u E, Cullum S, Yates S, Te Ao B, Cheung G, Burholt V et al. Dementia Economic Impact Report 2020. Auckland: The University of Auckland; 2021 [cited 2022 Nov 4]. Available from: https://cdn.alzheimers.org.nz/wp-content/uploads/2021/09/Dementia-Economic-Impact-Report-2020.pdf
11. Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D et al. Dementia prevention, intervention, and care. Lancet. 2017 Dec 16;390(10113):2673-2734. doi: 10.1016/S0140-6736(17)31363-6.
12. Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet. 2020 Aug 8;396(10248):413-446. doi: 10.1016/S0140-6736(20)30367-6.
13. Mukadam N, Sommerlad A, Huntley J, Livingston G. Population attributable fractions for risk factors for dementia in low-income and middle-income countries: an analysis using cross-sectional survey data. Lancet Glob Health. 2019 May;7(5):e596-e603. doi: 10.1016/S2214-109X(19)30074-9.
14. Ma'u E, Cullum S, Cheung G, Livingston G, Mukadam N. Differences in the potential for dementia prevention between major ethnic groups within one country: A cross sectional analysis of population attributable fraction of potentially modifiable risk factors in New Zealand. Lancet Reg Health West Pac. 2021 Jul 5;13:100191. doi: 10.1016/j.lanwpc.2021.100191.
15. Cheung G, To E, Rivera-Rodriguez C, Ma'u E, Chan AHY, Ryan B et al. Dementia prevalence estimation among the main ethnic groups in New Zealand: a population-based descriptive study of routinely collected health data. BMJ

Open. 2022 Sep 7;12(9):e062304. doi: 10.1136/bmjopen-2022-062304.
16. Cullum S, Varghese C, Yates S, Kalauta L, Appleton J, Knell R et al. Predictors of Aged Residential Care Placement in Patients Newly Diagnosed with Dementia at a New Zealand Memory Service. J Long-Term Care. 2021 Jan:24-32. doi: 10.31389/jltc.46.
17. Hsieh S, Schubert S, Hoon C, Mioshi E, Hodges JR. Validation of the Addenbrooke's Cognitive Examination III in frontotemporal dementia and Alzheimer's disease. Dement Geriatr Cogn Disord. 2013;36(3-4):242-50. doi: 10.1159/000351671.
18. Storey JE, Rowland JT, Basic D, Conforti DA, Dickson HG. The Rowland Universal Dementia Assessment Scale (RUDAS): a multicultural cognitive assessment scale. Int Psychogeriatr. 2004 Mar;16(1):13-31. doi: 10.1017/s1041610204000043.
19. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Arlington, VA: American Psychiatric Publishing, Inc.; 1994.
20. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. Int Psychogeriatr. 1997;9 Suppl 1:173-6; discussion 177-8. doi: 10.1017/s1041610297004870.
21. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology. 1984 Jul;34(7):939-44. doi: 10.1212/wnl.34.7.939.
22. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR Jr, Kawas CH. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011 May;7(3):263-9. doi: 10.1016/j.jalz.2011.03.005.
23. Román GC, Tatemichi TK, Erkinjuntti T, Cummings JL, Masdeu JC, Garcia JH et al. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology. 1993 Feb;43(2):250-60. doi: 10.1212/wnl.43.2.250.
24. McKeith IG, Galasko D, Kosaka K, Perry EK, Dickson DW, Hansen LA et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology. 1996 Nov;47(5):1113-24. doi: 10.1212/wnl.47.5.1113.
25. McKeith IG, Dickson DW, Lowe J, Emre M, O'Brien JT, Feldman H et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. Neurology. 2005 Dec 27;65(12):1863-72. doi: 10.1212/01.wnl.0000187889.17253.b1.
26. Englund B, Brun A, Gustafson L, Passant U. Clinical and neuropathological criteria for frontotemporal dementia. J Neurol Neurosurg Psychiatry. 1994 Apr;57(4):416-8. doi: 10.1136/jnnp.57.4.416.
27. R Core Team. R: A Language and Environment for Statistical Computing. Austria: R Foundation for Statistical Computing; 2022.
28. Nandipati S, Luo X, Schimming C, Grossman HT, Sano M. Cognition in non-demented diabetic older adults. Curr Aging Sci. 2012 Jul;5(2):131-5. doi: 10.2174/1874609811205020131.
29. Sinclair A, Abdelhafiz A. Cognitive dysfunction in older adults with type 2 diabetes: links, risks, and clinical implications. Clin Geriatr Med. 2020 Aug;36(3):407-417. doi: 10.1016/j.cger.2020.04.002.
30. Campbell JM, Stephenson MD, De Courten B, Chapman I, Bellman SM, Aromataris E. Metformin use associated with reduced risk of dementia in patients with diabetes: a systematic review and meta-analysis. J Alzheimers Dis. 2018;65(4):1225-1236. doi: 10.3233/JAD-180263.
31. Wu K, Liu H, Zheng J, Zou L, Gu S, Zhou R et al. Diabetes treatment is associated with better cognitive function: the age disparity. Front Aging Neurosci. 2022 Jan 6;13:753129. doi: 10.3389/fnagi.2021.753129.