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# Using health check data to investigate cognitive function in Aboriginal and Torres Strait Islanders living with diabetes in the Torres Strait, Australia

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# Abstract

**Background:** Type 2 Diabetes (T2DM) has a subtle deleterious effect on cognition and imposes a higher lifetime risk of cognitive impairment and dementia. In populations where both T2DM and dementia are highly prevalent, understanding more about the early effects of T2DM on cognition may provide insights into the lifetime risks of this disease.

**Methods:** In 2016, 186 Australian Aboriginal and/or Torres Strait Islander residents of the Torres Strait (54% female, mean age =38.9 years, *SD* =15.9, range =15-74) participated in a community health check. The effect of diabetes (Type 1 or Type 2) on speed of thinking and working memory was assessed with the Cogstate Brief Battery (CBB) during the health check.

**Results:** One third of participants had diabetes (n = 56, 30.1%). After adjusting for age, education and previous iPad/Tablet experience, participants with diabetes had a small, yet significant reduction in accuracy on the One Back working memory task ( $\beta = -.076$ , p = .010,  $r^2 = .042$ ). The effect was most pronounced among participants with diabetes aged 20–49 years (n = 20), who also had evidence of poorer diabetes control (eg HbA1c% ≥6.5, 76.6%), relative to participants with diabetes aged 50 years and over (n = 31) (HbA1c% ≥6.5, 32.0%, p = .005).

**Conclusions:** Early and subtle decrements in working memory may be a potential complication of diabetes among Aboriginal and Torres Strait Islander residents of the Torres Strait. Several potentially influential variables were not captured in this study (eg medication and diabetes duration). Greater preventative health resources are required for this population, particularly given the emerging elevated dementia rates linked to chronic disease.

#### KEYWORDS

cognition, complications of diabetes mellitus, indigenous peoples

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# 1 | INTRODUCTION

Type 2 Diabetes (T2DM) is a major global public health concern. In 2017, T2DM was the ninth leading cause of mortality and affected 6.38% of the world's population. This represents a prevalence milestone in a rising trend that shows no signs of abating.<sup>1</sup> In Australia, T2DM was the 12th largest contributor to the country's 2015 burden of disease and affected 5.3% of adults in 2017-2018.<sup>2</sup> Among Aboriginal and Torres Strait Islander inhabitants of Australia, referred to here respectfully as Indigenous Australians, the rate of T2DM is 4.3 times higher than in the non-Indigenous population.<sup>3</sup>

For individuals, T2DM is associated with irreparable damage to multiple body organs and systems, including the brain. For older adults, it is well established that a history of T2DM is associated with a greater likelihood of cognitive impairment and an increased risk for dementia from both cerebrovascular disease and Alzheimer's Disease.<sup>4</sup> In adults without dementia, cognitive impairment associated with T2DM is subtle and expressed most reliably as decreases in processing speed,<sup>5</sup> although this may extend to executive function<sup>6</sup> and working memory.<sup>7</sup> While studies examining T2DM have been conducted mainly in older adults, qualitatively similar but quantitatively less severe cognitive impairment has been observed in adults with T2DM aged less than 60 years.<sup>8,9</sup>

For Indigenous Australians, the prevalence of dementia is 3–5 times higher than non-Indigenous Australians.<sup>10-13</sup> Elevated levels of childhood trauma, stroke, head injury, and lower levels of skilled employment have been identified as predictors of dementia among mainland Aboriginal populations, while more education has been identified as protective. Recent evidence suggests that vascular risk factors, including diabetes, may be associated with higher rates of dementia among Indigenous Australians living in the Torres Strait.<sup>13,14</sup> Understanding more about the cognitive implications of diabetes in these vulnerable populations could therefore improve understanding of the development of diabetes-related brain disease and assist with targeting preventative health activities.

The Zenadth Kes Health Partnership (ZKHP) was a communitybased health-screening program of residents aged 15-78 years, undertaken on two islands in the Torres Strait between October and December 2016.<sup>15</sup> In this population, where diabetes incidence is almost four times the general Australian population,<sup>16</sup> the purpose of the ZKHP was to provide a health service for the community and simultaneously explore the association between the metabolic syndrome and other chronic health conditions. The aim of this current study was to understand whether diabetes, defined as either Type 1 or Type 2, was having a subclinical effect on cognition in this population. It was hypothesized that speed and accuracy on cognitive tasks would reduce as a function of age and increase with years of education and iPad/Tablet experience. It was also hypothesized that participants with diabetes would have slower reaction times and lower accuracy on cognitive tasks, after accounting for age, education and iPad/Tablet experience.

# 2 | METHODS

Detailed information about the ZKHP methodology is published elsewhere.<sup>15,17</sup> A brief overview is provided below. Ethical approval for this study was granted by the Far North Queensland Human Research Ethics Committee (HREC/16/QCH/70-1059).

# 2.1 | Participants

Participants were community members aged 15 years and over who identified as being of Torres Strait Islander or Aboriginal descent. A total of 214 participants were screened and met the inclusion criteria (ie consent for both the health check and for the additional research measures). A subset of 14 people met one or more of the exclusion criteria (ie (1) non-consent, (2) insufficient responses to broader study questions, (3) time constraints or (4) having a physical or sensory disability (eg vision) preventing valid assessment. A total of 200 participants underwent cognitive assessment and the sample for the current study was limited to the 186 participants who had a complete and valid result on at least one of the cognitive tests.<sup>17</sup> The 14 participants excluded at this stage were older than those who were retained (ie mean age of 62.8 and 38.9 years, respectively, *p* < .001) and more likely to have diabetes (*p* = .002).

# 2.2 | Data collection

Demographic information, diet, health behaviours, depressive symptoms and blood samples for several routine and research blood tests were collected. Demographic data were age (years), gender (male, female), total years of education, employment status when of working age (15–64 years) defined as a person having a paid job (yes, no) and island of residence. Information on history of use of electronic devices (iPad or computer tablet (yes, no)) and hand dominance was also collected. Self-reported use of alcohol and tobacco was collected, and participants also completed a food questionnaire, which included consumption of take-away food and sugary drinks in the week preceding their health check.

Measures of cardiovascular health included heart rate, systolic and diastolic blood pressure, hypertension (ie systolic  $\geq$ 140 mmHg or diastolic  $\geq$ 90 mmHg) and urinary albumin creatinine ratio (urinary ACR). Metabolic markers were triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol, HDL/total cholesterol ratio, glucose, glycosylated haemoglobin (HbA1c%), body mass index (BMI), waist circumference (centimetres), waist/height ratio. Glucose, triglycerides, lipoproteins and cholesterol were analysed at a commercial pathology service (Sullivan Nicolaides, Cairns, Australia). A measure of omega-3 (n - 3) long-chain polyunsaturated fatty acid (LCPUFAs) was obtained by a whole blood collection on a validated dried blood spot system. Fatty acid composition was analysed by capillary gas chromatography.<sup>18</sup> An adapted Patient Health Questionnaire 9 (aPHQ-9) depression screening tool was used to measure depressive symptoms. This instrument has been specifically designed for use with Indigenous Australians in primary healthcare settings.<sup>19</sup>

# 2.3 | Diabetes

Participants were defined as having diabetes if they self-reported being treated for diabetes or had a HbA1c greater than or equal to 6.5% based on blood pathology analyses. The definition of diabetes used in this study encompassed both Type 1 and Type 2. The presence of gestational diabetes (GDM) was not captured. However, given that T2DM is highly prevalent in this population,<sup>16</sup> it likely accounted for almost all of the diabetes cases. Participants who did not report being treated for diabetes and had a HbA1c  $\geq$  6.5% were considered as 'newly diagnosed diabetes'. Information on which medication participants with diabetes had been prescribed was obtained by reviewing participant medical records. Collection of this data was limited to participants from only one of the island sites. As a result, medication information was available for approximately half of the participants with diabetes and was not included in the analyses.

## 2.4 | Cognitive assessment

Cognition was assessed in the study using the Cogstate Brief Battery (CBB), using an iPad platform, predominantly by a member of the team who was a provisional psychologist (FT). The CBB was selected as the cognitive screening tool as it has high sensitivity to cognitive dysfunction associated with dementia and MCI.<sup>20</sup> The tool also has some usability, acceptability and validity among Indigenous Australians,<sup>21-23</sup> including Indigenous residents of the Torres Strait.<sup>17</sup> Further details on the appropriateness of the CBB and its administration during the current study are described elsewhere.<sup>17</sup>

A description of the four CBB tasks and their 'built-in' Completion and Integrity Criteria is provided in Table S1. In brief, the four tasks comprise; (1) Detection, (2) Identification, which are both measures of attention and processing speed, (3) One Card Learning, a measure of visual memory and (4) One Back Learning, a visual measure of working memory. A CBB task was considered 'complete and valid' if the task was completed and the results were valid based on examiner observations and Cogstate Integrity Criteria.<sup>17</sup>

## 2.5 | Outcome measures

The primary outcome measures in this study were reaction time and accuracy on the CBB tasks. The Detection, Identification and One Back tasks provided three measures of reaction time in milliseconds and log<sub>10</sub> transformed milliseconds. The One Card Learning and One Back tasks provided two measures of accuracy as a percentage and an Arcsine transformed percentage. In addition, each participant had

a z-score derived for each of these transformed measures, using normative data in provided by Cogstate PTY LTD. The normative data comprised means and standard deviations for the four CBB tasks for males and females combined by six age groups (18–34, 35–49, 50–59, 60–69, 70–79 and 80–89). Z-scores that were one standard deviation (SD) below the respective Cogstate mean were flagged using binary yes/no variable (ie z-score < 1SD), as were z-score that were two SDs below the mean (ie z-score < 2SD). In addition, scores that were 0.5 SD below the mean were also flagged, as this cut-off has been used elsewhere as a more sensitive measure of cognitive impairment.<sup>7</sup>

For each participant, a 'cognitive speed' domain was derived (ie an average log-transformed reaction time measure from three tasks with reaction time measures). Similarly, an average Arcsine transformed accuracy measure was derived for each participant from the two tasks with accuracy measures. Only participants with complete and valid measures on these tasks had the average measures derived.

# 2.6 | Statistical analyses

All analyses were undertaken using STATA 15 Statistical software (StataCorp. 2017, College Station, TX). Prior to statistical analysis, the distribution of the data was assessed for normality assumptions and outliers. The distribution of study variables (eg demographic and cardio-metabolic) by diabetes status was tested with independent-sample t tests and rank-sum tests for parametric and non-parametric continuous data, respectively, and with Chi2 tests for categorical data (Table S2). For the CBB outcome variables, the distribution of parametric measures (ie log-transformed reaction times and Arcsine transformed accuracy) was examined by diabetes status using means and linear regressions (Table S3). Nonparametric CBB outcomes (ie untransformed reaction time and accuracy measures, number of errors and continuous z-scores) were examined by diabetes status using medians and Wilcoxon rank-sum tests. Binary variables that identified whether a Z-score was one or two standard deviations below a Cogstate mean were examined by diabetes status using proportions and Pearson chi-squared tests.

Univariate regression analyses were used to examine the distribution of CBB outcome variables by study variables (eg demographic, cardio-metabolic and immune markers; Table 1). As age, education and iPad/Tablet experience were all associated with CBB outcomes and diabetes status at a univariate level, these factors were adjusted for in three multivariate regression models examining the relationship between diabetes and each CBB outcome (Table 2). Specifically, Model 1–unadjusted, Model 2–adjusted for age, Model 3–adjusted for age and education, Model 4–adjusted for age, education and previous iPad/Tablet use. Effect size for the regression models was calculated using STATA's 'estat esize' post hoc command. The distribution in One Back Arcsine transformed accuracy measures with confidence intervals, by different age groups (ie 10-year age groups and three broader age groups) and

Methe         No         Mathe         Math         Math         Math			Dete	Detection Speed	beed			Iden	Identification Speed	Speed ו			One	One Back Accuracy	curacy		
opplic light formation         131	Variable	Values	z	Mean	(95%	q	d	z	Mean	(95% CI)	q	d	z	Mean	(95% CI)	q	d
(wath)         (wath)<	Demographic Information		183					181					169				
Mate         64         2.44         2.52.50.60         -0.13         0.21         2.64, 2.02         0.01         0.013        <	Age	(years)				0.002	0.000				0.002	0.000				-0.001	0.178
Female         9         223         (251.254)         -0013         (341         102         266         264.260          6         133         (130.136)         0008           Someprimary         8         263         (245.280)          9         277         268.286)          6         133         (130.136)         0008           Someprimary         6         254         (232.257)        0086         0014         54         270         268.276)        008         0009         001         123         (131.130)         0003           Secondary         50         251         250         -0.012         0.001         032         268.260         003         001         100         001         000<	Gender	Male	84	2.54	(2.52,2.56)			79	2.71	(2.69,2.72)			73	1.32	(1.29,1.36)		
Some primary         8         2.63         (2.46.2.64)          9         2.77         2.64.2.64          1         (1.2.1.4.0)         (1.2.1.4.0)           Some secondary         56         2.33         (2.46.2.64)          6         1.31         (1.2.1.4.0)         0003           Some secondary         57         2.33         (2.32.257)        0.016         0.01         57         2.66.2.69)        0.02         0.003         58         2.66.2.69)        0.023         0.003         59         2.69         2.66.2.69         0.003         50.13         2.69         0.003         0.013         0.014         0.019 <td></td> <td>Female</td> <td>66</td> <td>2.52</td> <td>(2.51,2.54)</td> <td>-0.013</td> <td>0.341</td> <td>102</td> <td>2.69</td> <td>(2.68,2.70)</td> <td>-0.019</td> <td>0.051</td> <td>96</td> <td>1.33</td> <td>(1.30,1.36)</td> <td>0.008</td> <td>0.729</td>		Female	66	2.52	(2.51,2.54)	-0.013	0.341	102	2.69	(2.68,2.70)	-0.019	0.051	96	1.33	(1.30,1.36)	0.008	0.729
Some secondary         56         24         (2.2.2.57)         -0.066         0.01         54         2.0         54         1.2         (12.81.36)         0.002           Secondary         60         251         (2.49.253)         -0.018         0.001         59         2.66.2.69)         -0.089         0.001         54         1.22         (12.81.36)         0.001           Teriary         57         2.57.253         (2.012         0.001         60         2.68.271)         -0.033         0.001         54         1.23         (12.81.36)         0.001           (w1) <sup>1</sup>	Highest education	Some primary	00	2.63	(2.46,2.80)			6	2.77	(2.68,2.86)			9	1.31	(1.23,1.40)		
Secondary         60         21         (2.49.2.53)         -0.11         0.001         5         2.68         2.66.2.69         -0.003         60         54         1.28         (1.28.1.36)         0.001           Tertiary         57         2.53         (2.50.2.55)         -0.102         0.001         5.62         5.0         56         1.38         (1.31.1.3)         0.001           (wh)         1         2         (2.50.2.55)         -0.102         0.001         0.621         -0.073         0.001         56         1.31.1.39         0.001           (wh)         1         2         (2.001         0.621         0.01         0.183         -0.013         0.013         56         1.31.1.39         0.001           (wh)         1         2         0.183         -1.23         0.183         -1.23         0.01         56         1.31.1.39         -0.023           (wh)         1         2         1         2.13         2.14         0.182         -1.23         1.21         1.21         -0.023           (wh)         1         2         2         2         2         2         2         2         2         1.23         1.23         1.31.1.31		Some secondary	56	2.54	(2.52,2.57)	-0.086		54	2.70	(2.69,2.72)	-0.063		52	1.32	(1.28,1.36)	0.003	0.964
Tertiary         57         2.53         2.50.2.55         -0.102         0.004         5.68.2.71         -0.073         0.001         5         1.31.1.39         0.003           (wf/m <sup>3</sup> ) $\times$ $\times$ 0.001         0.182 $\sim$ 0.001         0.001		Secondary	60	2.51	(2.49,2.53)	-0.119		59	2.68	(2.66,2.69)	-0.089	0.000	54	1.32	(1.28,1.36)	0.007	0.914
(kg/m <sup>3</sup> )         (kg/m <sup>3</sup> ) <t< td=""><td></td><td>Tertiary</td><td>57</td><td>2.53</td><td>(2.50,2.55)</td><td>-0.102</td><td>0.004</td><td>58</td><td>2.69</td><td>(2.68,2.71)</td><td>-0.073</td><td>0.001</td><td>56</td><td>1.35</td><td>(1.31, 1.39)</td><td>0.039</td><td>0.544</td></t<>		Tertiary	57	2.53	(2.50,2.55)	-0.102	0.004	58	2.69	(2.68,2.71)	-0.073	0.001	56	1.35	(1.31, 1.39)	0.039	0.544
(kg/m <sup>3</sup> )         (100)         0.001         0.021	Anthropometry																
(m)         0.001         0.189         0.001         0.180         0.002         0.001         0	Body Mass Index	(kg/m <sup>2</sup> )				0.000	0.621				0.001	0.182				-0.002	0.202
*6.5         2.3         2.5         0.182         0.182         0.103         0.002         1.2         1.2         0.020           *6.5         135         2.53         2.51,2.54         -0.052         0.015         0.012         0.415         1.29         1.21,1.37         -0.030           *6.5         135         2.53         2.51,2.54         -0.052         0.014         0.005         0.012         0.482.70         0.013         0.415         1.24         1.33         (1.30,1.36)         0.038           *6.5         135         2.532.59         0.014         0.007         5.6         2.682.70         0.039         0.014         1.35         (1.30,1.36)         0.038           Ves         135         2.55         (2.532.59)         0.014         0.007         5.6         (2.682.70)         0.017         1.18         (1.31,1.36)         0.038           Ves         2.55         (2.532.59)         0.0030         0.007         5.6         (2.682.70)         0.033         (0.013         (1.31,1.36)         0.033         (1.31,1.36)         0.033         (1.31,1.36)         0.033         (1.31,1.36)         0.033         (1.31,1.36)         0.033         (1.31,1.31)         0.033         (1.3	Waist circumference	(cm)				0.001	0.189				0.001	0.001				-0.001	0.062
26.5         23         2.52,2.64          23         2.70         2.68,2.73          21         1.29         (1.22,1.37)         0.038           <6.5	Waist/Height ratio					0.084	0.182				0.130	0.002				-0.207	0.046
26.5         23         276         2.68.2.73         21         22         22.137         22.137           6.5         135         2.51.254         -0.052         0.016         132         2.68         2.68.2.70         2.016         132         2.69         2.68.2.70         2.016         132         2.69         2.68.2.70         2.015         132         130         130         0.038           No         129         2.52         2.50.2.53         0.041         0.007         56         2.68.2.70         0.036         0.13         130         130         0.038           No         129         2.52         2.50.2.53         0.041         0.007         56         2.702.73         0.037         131         13         131	Cardio-metabolic profile																
<6.5	HbA1c (%)	≥6.5	23	2.58	(2.52,2.64)			23	2.70	(2.68,2.73)			21	1.29	(1.22,1.37)		
No         129         2.52         (2.50.2.53)         125         2.69         (2.68.2.70)         118         1.35         (1.37.1.38)           Ves         54         2.53         2.59         0.041         0.007         56         2.70         (2.68.2.70)         7.3         1.38         (1.37.1.38)           No         143         2.52         (2.53.2.59)         0.041         0.007         56         2.70         (2.002.73)         0.030         51         1.34         1.31.135           Yes         39         2.55         (2.51.2.54)         0.037         41         2.71         (2.68.2.70)         7.32         1.33         1.34         (1.31.1.36)         -0.073           YhDtratio*         00-4.5         106         2.53         (2.512.55)         0.037         61         2.68.2.70)         7.32         7.3         1.34         (1.31.1.36)         -0.033           YHDtratio*         00-4.5         106         2.53         (2.512.55)         0.037         0.56         (2.68.2.70)         7.32         1.34         (1.31.1.36)         -0.033           HDtratio*         0.0-4.5         106         2.54         (2.68.2.70)         0.013         0.124         1.34         <		<6.5	135	2.53	(2.51,2.54)	-0.052	0.016	132	2.69	(2.68,2.70)	-0.012	0.415	124	1.33	(1.30,1.36)	0.038	0.295
Yes         54         2.56         (2.53.2.59)         0.041         0.007         56         2.70,2.73)         0.030         51         1.28         (1.24,1.32)         -0.073           n         No         143         2.52         (2.51.2.54)         139         2.69         (2.68,2.70)         133         1.34         (1.31,1.36)         -0.073           Yes         39         2.55         (2.51.2.55)         0.030         0.077         41         2.71         (2.68,2.70)         0.032         35         1.31         (1.31,1.36)         -0.033           /HDLratio <sup>a</sup> 0.0-4.5         106         2.53         (2.51.2.55)         0.030         0.077         41         2.71         (2.68,2.70)         0.032         35         1.31         (1.25,1.36)         -0.033           /HDLratio <sup>a</sup> 0.0-4.5         106         2.53         (2.51,2.56)         0.009         0.579         2.69         (2.68,2.70)         0.013         (1.25,1.36)         -0.033           /HDLratio <sup>a</sup> 0.0-4.5         106         2.54         2.57         2.69         (2.68,2.70)         0.013         (1.25,1.36)         -0.033           /HDLratio <sup>a</sup> 0.0-4.5         10.6         2.51	Diabetes	No	129	2.52	(2.50,2.53)			125	2.69	(2.68,2.70)			118	1.35	(1.32,1.38)		
		Yes	54	2.56	(2.53,2.59)	0.041	0.007	56	2.72	(2.70,2.73)	0.030	0.004	51	1.28	(1.24,1.32)	-0.073	0.003
Yes         39         2.55         (2.52,259)         0.030         0.077         41         2.17         (2.69,2.74)         0.024         35         1.31         (1.25,1.36)         -0030           /HDLratio <sup>a</sup> 0.0-4.5         106         2.53         (2.51,2.55)         0.030         0.579         67         2.68,2.70)         99         1.34         (1.31,1.37)         -0.030           /HDLratio <sup>a</sup> 0.0-4.5         106         2.54         (2.51,2.55)         0.0009         0.579         61         2.69         2.68,2.70)         99         1.34         (1.31,1.37)         -0.030           Fabet         No         2.54         (2.51,2.56)         0.0009         0.579         61         2.69,2.729         0.013         61         1.34         (1.31,1.37)         -0.050           Fabet         No         2.54         (2.51,2.56)         0.0009         0.579         61         2.702         0.013         61         1.25         1.33         -0.050           Fabet         Ves         136         2.57         2.0013         1.34         1.25         1.34         1.31,1.36         0.051           Fabet         Ves         136         2.56         2.569,2.73 <td>Hypertension</td> <td>No</td> <td>143</td> <td>2.52</td> <td>(2.51,2.54)</td> <td></td> <td></td> <td>139</td> <td>2.69</td> <td>(2.68,2.70)</td> <td></td> <td></td> <td>133</td> <td>1.34</td> <td>(1.31, 1.36)</td> <td></td> <td></td>	Hypertension	No	143	2.52	(2.51,2.54)			139	2.69	(2.68,2.70)			133	1.34	(1.31, 1.36)		
HDL ratio <sup>a</sup> 0.0-4.5         106         2.51,2.55         100         5.69         2.68,2.70         99         1.34         (1.31,1.37)           >4.5         60         2.54         (2.51,2.56)         0.009         0.579         61         2.09         7.39         1.39         (1.31,1.37)           Tablet         No         2.54         (2.51,2.56)         0.009         0.579         61         2.09         54         1.29         (1.35,1.33)         -0.050           Tablet         No         46         2.77         2.69         (2.69,2.72)         0.013         6190         54         1.29         (1.25,1.33)         -0.050           Tablet         No         46         2.77         2.69         (2.68,2.70)         0.013         1.31         1.34         (1.31,1.36)         0.050           Tablet         No         2.52         (2.50,2.53)         -0.048         0.003         9.027         0.013         1.31         1.34         (1.31,1.36)         0.031           dex         7         2.69         2.692,2.70         0.012         0.013         1.31         1.34         (1.31,1.36)         0.031		Yes	39	2.55	(2.52,2.59)	0.030	0.077	41	2.71	(2.69,2.74)	0.024	0.032	35	1.31	(1.25,1.36)	-0.030	0.298
>4.5         60         2.54         (2.51,2.56)         0.009         0.579         61         2.70         (2.69,2.72)         0.013         0.190         54         1.29         (1.25,1.33)         -0.050           Tablet         No         46         2.57         2.702         2.69         (2.50,2.74)         38         1.30         (1.25,1.36)         -0.050           Ves         136         2.52         (2.50,2.53)         -0.048         0.003         135         2.69         (2.68,2.70)         -0.013         131         1.34         (1.31,1.36)         0.031           dex         0.009         0.128         0.012         0.012         0.013         131         1.34         (1.31,1.36)         0.031	Cholesterol/HDL ratio <sup>a</sup>	0.0-4.5	106	2.53	(2.51, 2.55)			102	2.69	(2.68,2.70)			66	1.34	(1.31, 1.37)		
Tablet     No     46     2.57     (2.53,2.60)     46     2.72     (2.70,2.74)     38     1.30     (1.25,1.36)       Yes     136     2.52     (2.50,2.53)     -0.048     0.003     135     2.69     (2.68,2.70)     -0.027     0.013     131     1.34     (1.31,1.36)     0.031       dex     0.009     0.128     0.128     0.012     0.001     0.001     0.001     -0.001		>4.5	60	2.54	(2.51,2.56)	0.009	0.579	61	2.70	(2.69,2.72)	0.013	0.190	54	1.29	(1.25,1.33)	-0.050	0.048
et No 46 2.57 (2.53,2.60) 46 2.72 (2.70,2.74) 38 1.30 (1.25,1.36) Yes 136 2.52 (2.50,2.53) -0.048 0.003 135 2.69 (2.68,2.70) -0.027 0.013 131 1.34 (1.31,1.36) 0.031 0.009 0.128 0.012 0.001 -0.027 0.001 -0.001 -0.003	Other factors																
Yes 136 2.52 (2.50,2.53) -0.048 0.003 135 2.69 (2.68,2.70) -0.027 0.013 131 1.34 (1.31,1.36) 0.031 0.009 0.128 0.012 0.001 0.012 0.001 -0.001 -0.003	Used iPad/Tablet	No	46	2.57	(2.53,2.60)			46	2.72	(2.70,2.74)			38	1.30	(1.25,1.36)		
0.009 0.128 0.012 0.001 -0.003		Yes	136	2.52	(2.50,2.53)	-0.048		135	2.69	(2.68,2.70)	-0.027	0.013	131	1.34	(1.31, 1.36)	0.031	0.259
	Omega 3 Index					0.009	0.128				0.012	0.001				-0.003	0.753

TABLE 1 Performance on selected Cogstate Brief Battery tasks by selected study variables, among 186 Torres Strait Islanders who attended the 2016 Zenadth Kes Health Partnership

<sup>a</sup>Ratio of Total Cholesterol and High-Density Lipoprotein (HDL) cholesterol.

		<b>Detection Speed</b>	Speed			Identifica <sup>-</sup>	Identification Speed			One Back	One Back Accuracy		
		Model 1		Model 4		Model 1		Model 4		Model 1		Model 4	
Variable	Values	b <sup>a</sup>	рª	pa	p <sup>a</sup>	pa	b <sup>a</sup>	рª	p <sup>a</sup>	pa	p <sup>a</sup>	b <sup>a</sup>	ьª
Diabetes	No												
	Yes	0.041	0.007	0.013	0.436	0.030	0.004	0.002	0.836	-0.073	0.003	-0.076	0.010
Demographic Information	tion												
Age	(years)	0.002	0.000	0.002	0.002	0.002	0.000	0.002	0.000	-0.001	0.178	0.000	0.889
Education	Some secondary (reference)	(reference)											
	Secondary	-0.044	0.009	-0.044	0.005	-0.035	0.002	-0.033	0.002	0.004	0.879	0.009	0.762
	Tertiary	-0.027	0.116	-0.039	0.017	-0.019	0.105	-0.029	0.007	0.037	0.194	0.050	0.078
iPad/Tablet	No (ref)												
	Yes	-0.048	0.003			-0.027	0.013	-0.003	0.762	0.031	0.259	0.008	0.791
Other measures													
Body Mass Index	(kg/m <sup>2</sup> )	0.000	0.621	-0.001	0.216	0.001	0.182	0.001	0.386	-0.002	0.202	-0.001	0.776
Waist/Height ratio		0.084	0.182	-0.027	0.683	0.130	0.002	0.063	0.131	-0.207	0.046	-0.084	0.483
HbA1c (%)		0.013	0.007	0.006	0.285	0.007	0.030	0.003	0.364	-0.005	0.531	0.008	0.451
Hypertension	No (reference)												
	Yes	0:030	0.077	0.006	0.724	0.024	0.032	0.006	0.560	-0.030	0.298	-0.019	0.527
Total Chol/HDL ratio <sup>b</sup>		-0.002	0.791	0.000	0.976	0.003	0.474	0.003	0.342	-0.017	0.080	-0.019	0.055
Omega 3	Index	0.009	0.128	-0.006	0.306	0.012	0.001	0.003	0.489	-0.003	0.753	0.014	0.196
Handedness	Left (reference)												
	Right	-0.071	0.003	-0.068	0.003	-0.015	0.370	-0.017	0.262	-0.022	0.599	-0.037	0.393
aPHQ Referred <sup>c</sup>	No (reference)												
	Yes	0.007	0.755	0.035	0.126	-0.010	0.525	0.010	0.463	0.023	0.555	0.007	0.871

TABLE 2 Multivariate Regression models of selected Cogstate Brief Battery tasks by selected study variables, among 186 Torres Strait Islanders who attended the 2016 Zenadth Kes Health

b b in in <sup>a</sup>Beta coefficient.

<sup>b</sup>p-value.

<sup>c</sup>Ratio of Total Cholesterol and High-Density, Lipoprotein (HDL) cholesterol.

<sup>d</sup>Adapted Patient Health Questionnaire 9.

Endocrinology, Diabetes

diabetes status, is provided in Figure 1 and Figure S1. Interaction terms were used to analyse the effect of diabetes on One Back outcomes, within each of these age groups, unadjusted and adjusted for education and previous iPad/Tablet use. p Values < 0.05 were considered statistically significant.

# 3 | RESULTS

## 3.1 | Participants

There were 186 participants (54% female, mean age = 38.9 years, SD = 15.9, range = 15-74). Approximately one third (n = 56, 30.1%) had diabetes (Table S1), either as an existing condition (n = 49) or newly diagnosed (n = 7) at assessment. Compared to people without diabetes, those with diabetes were approximately 17 years older (p < .001), more likely to have tertiary education (40.0% and 28.7%, respectively, p = .015), had higher BMI (M = 34.6 and 30.6, respectively, p < .001), greater waist/height ratio (M = 0.70 and 0.61, respectively, p < .001), higher urinary ACR (Table S2), and less likely to have previous iPad/Tablet experience (60.7%) than those without (79.8%, p = .006). The number of CBB tasks completed was equivalent between the groups.

# 3.2 | Univariate analyses

When performance on CBB tasks was examined in univariate analyses, participants with diabetes were significantly slower on all reaction time measures and had significantly lower accuracy on the One Back task (Table 1). Reaction times on the three measures increased as a function of age and decreased with years of education. Previous experience with an iPad/Tablet was associated with faster response times. Accuracy on One Card Learning task was not related to any study variables and these results are not tabled.

#### 3.3 | Multivariate analyses

After adjusting for age, education and previous iPad/Tablet experience (Model 4), none of the three reaction time measures were significantly associated with diabetes status (Table 2) and neither was the derived 'cognitive speed' domain (data not tabled). Participants with diabetes had significantly lower accuracy on the One Back task after adjusting for age, education and previous iPad/Tablet experience (Model 4). Post hoc effect size estimates showed diabetes accounted for approximately 4% of the variance in One Back accuracy in this model. As shown in Table S3, the median number of errors on

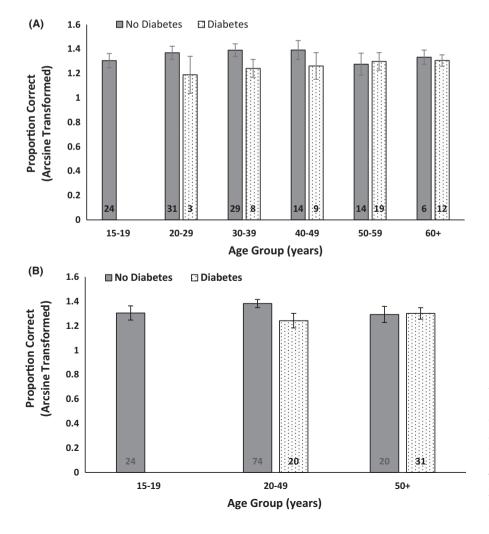


FIGURE 1 Arcsine transformed proportion of correct responses to the Cogstate Brief Battery One Back working memory test with 95% confidence intervals, by 10-year age group (Figure 1A) and three age groups (Figure 1B) by diabetes status with number of participants displayed, among Torres Strait Islanders attending the 2016 Zenadth Kes Health Partnership health screen.

the One Back task was higher in the diabetes group compared to the no diabetes group (3 and 2, respectively, p = .008) and the median z-score for accuracy on the One Back task was lower among participants with diabetes (-0.39 and 0.09, respectively, p = .002). The proportion of participants with a z-score  $\leq 0.05$  standard deviations below the age normative mean was also higher among people with diabetes (47.1% and 30.2%, respectively, p = .039; Table S3). There were no significant differences in z-score measures on the other tasks. Other cardiovascular risk factors, HbA1c, health behaviours, depression and gender were not related to Cogstate outcomes during univariate and/or multivariate modelling (Table 2).

Figure 1 shows the Arcsine transformed proportion of correct responses by diabetes status and age group on the One Back working memory task. Younger participants with diabetes tended to perform worse than participants without diabetes in all age groups up to 50 years. From 50 years of age onward, the accuracy was comparable irrespective of diabetes status. The same trend was evident when average One Back Accuracy z-scores were graphed by age groups (Figure S1). Multiple regression analyses of One Back accuracy with interaction terms for diabetes and the different age groupings were used to further examine the trends in Figure 1. After adjustment for education and iPad/Tablet experience, there were significant associations in the 20–29, 30–39 and 40–49 age groups, albeit with wide confidence intervals and small cell sizes, compared to the reference group 50 years and over (data not tabled). A post hoc power calculation using G\*Power software indicated these analyses were underpowered (ie  $1-\beta = 68.7\%$ ). Using three age groups instead, there was a significant association in the 20-49 year age group ( $\beta = -.16$ , 95% CI: -0.27, -0.05, p = .005) and a post hoc power calculation was adequate (ie >80%). This suggests the effect of diabetes on One Back accuracy in this younger age group was significantly different compared to the reference group 50 years and over (data not tabled). Other interaction analyses were not significant.

Table 3 shows younger participants with diabetes (ie 20–49 years, n = 21) had higher levels of morbidity compared to older participants with diabetes (ie 50+ years, n = 31). Specifically, younger participants with diabetes were more likely to be current smokers (65% and 9.7%, respectively, p < .001) and to have consumed a sugary drink in the preceding week (80.0% and 38.7%, respectively, p = .004). They were also more likely to be newly diagnosed with diabetes (25.0% and 6.4%, respectively), have a HbA1c greater than 6.5% (76.5% and 32.0%, respectively, p = .005) and have a higher Total/HDL ratio (4.82 and 3.85, respectively p = .011).

# 4 | DISCUSSION

This study examined relationships between diabetes and cognition, measured by the speed and accuracy of performance on a standardized test battery, in Indigenous Australians living in the Torres Strait. After accounting for age, education and previous iPad/Tablet experience, participants with diabetes had significantly lower accuracy on a task of working memory compared to those without, although the absolute difference between the groups and effect size was both very small. Younger participants (ie 20–49 years of age) with diabetes had lower accuracy scores on this task and evidence of greater morbidity compared to participants 50 years and older with diabetes. As hypothesized, age, education and iPad/Tablet experience were associated with reaction time measures for all participants. There were no differences in speed measures between the participants with and without diabetes after adjusting for these variables.

The One Back task used in the current study is a measure of working memory, which is a cognitive ability underpinned by executive functioning.<sup>24</sup> Our results therefore correspond with research showing lower working memory<sup>7</sup> and executive function<sup>6,25</sup> among people with T2DM. As the reduction we observed was primarily among participants in their young to mid-adult life (ie 20–49 years), our results are most consistent with findings from a recent metaanalysis of 12 studies that showed working memory and executive functioning decrements are observable in midlife among people with T2DM.<sup>9</sup> Our study supports a growing consensus that cognition may be affected in early to mid-adulthood during T2DM and adds to existing knowledge by showing this may represent a potential complication of diabetes for Indigenous residents of the Torres Strait.

The magnitude of reduction observed in One Back accuracy was much lower than reported elsewhere. For example, while Pelimanni and Jehkonen<sup>9</sup> reported medium effect sizes, in our study, the effect was small. Diabetes status accounted for approximately 4% of the variance in One Back performance and participants with diabetes made, on average, one additional error on this task compared to participants without diabetes. This very modest reduction in performance would be considered, at most, a "diabetes associated cognitive decrement".<sup>4</sup> These are subtle decrements that may give rise to selfreported complaints, but are unlikely to affect social or occupational functioning or diabetes self-management.<sup>26</sup> These decrements have been noted to progress slowly over many years,<sup>27,28</sup> particularly in the context of chronically elevated blood glucose.<sup>6,29</sup> While this may eventually lead to deficits that are clinically or practically important for everyday functioning,<sup>30</sup> it remains unclear whether dementia represents an 'end point' on the same continuum.<sup>4</sup> Among older Indigenous residents of the Torres Strait, vascular risk factors such as diabetes have been identified as potential drivers of the elevated dementia rates.<sup>14</sup> The results of the current study may provide some evidence of the detrimental effect of a vascular risk early in this process. However, this proposition remains far from conclusive given the small effect size in our study and the broader uncertainty about the continuum between diabetes-associated cognitive decrements and later dementia.

The difference in One Back accuracy between participants with and without diabetes was most evident in younger age groups and became less pronounced with older age. There may be several study design reasons for this finding. First, Indigenous Australians have an earlier age of mortality, which has resulted in a healthy survivor effect in other research.<sup>31,32</sup> In our study, older participants with diabetes were relatively healthy compared to their younger diabetes counterparts in terms of cardio-metabolic indicators. Our results TABLE 3 Comparison of Zenadth Kes Health Partnership participants with diabetes who completed the One Back Cogstate Brief Battery task, by age group, 2016 (n = 51).

		Diabet	es (20–49 years	old)	Diabet	es (50+years)		
Variable	Values	No.	(%),mean	(95% CI)	No.	(%),mean	(95% CI)	р
Demographics	Total	20			31			
Gender	Female	13	(65.0)	(43.6, 86.4)	20	(64.5)	(47.3, 81.8)	.972
Education	At least some primary			(0.0, 0.0)	4	(12.9)	(0.8, 25.0)	.374
	Some secondary	4	(21.1)	(2.3, 39.8)	5	(16.1)	(2.9, 29.4)	
	Completed secondary	7	(36.8)	(14.6, 59.1)	8	(25.8)	(10.0, 41.6)	
	Tertiary	8	(42.1)	(19.3, 64.9)	14	(45.2)	(27.2, 63.1)	
Risk Behaviours	Consumes alcohol	15	(75.0)	(55.6, 94.4)	16	(51.6)	(33.6, 69.6)	.095
Smoker	Never	2	(10.0)	(-3.5, 23.5)	10	(32.3)	(15.4, 49.1)	.000
	Former	5	(25.0)	(5.6, 44.4)	18	(58.1)	(40.3, 75.9)	
	Current	13	(65.0)	(43.6, 86.4)	3	(9.7)	(-1.0, 20.3)	
	Takeaway (prev. week)	7	(35.0)	(13.6, 56.4)	9	(29.0)	(12.7, 45.4)	.654
	Sugary drink yesterday	16	(80.0)	(62.0, 98.0)	12	(38.7)	(21.1, 56.3)	.004
Anthropometry	Body Mass Index (h/kg <sup>2</sup> )	20	34.78	(31.9, 37.6)	31	35.45	(33.5, 37.4)	.682
	Waist/Height ratio	20	0.69	(0.6, 0.7)	30	0.71	(0.7, 0.7)	.221
Cardio-metabolic	HbA1c (%) ≥6.5	13	(76.5)	(55.7, 97.2)	8	(32.0)	(13.2, 50.8)	.005
	Hypertension	5	(26.3)	(6.0, 46.6)	10	(32.3)	(15.4, 49.1)	.656
	Total Cholesterol	18	4.93	(4.4, 5.5)	27	4.38	(4.0, 4.8)	.087
	HDL Cholesterol <sup>d</sup>	18	1.09	(0.9, 1.2)	27	1.21	(1.0, 1.4)	.144
	LDL Cholesterol <sup>a</sup>	17	2.64	(2.2, 3.1)	27	2.33	(2.0, 2.7)	.255
	Total/HDL Ratio <sup>b</sup>	18	4.82	(4.0, 5.6)	27	3.85	(3.4, 4.3)	.011
	Omega 3 Index	20	5.94	(5.4, 6.4)	31	7.06	(6.6, 7.6)	.001
Other factors	aPHQ (referred) <sup>c</sup>	2	(10.0)	(-3.5, 23.5)	1	(3.2)	(-3.1, 9.6)	.315
	Used iPad/Tablet	14	(70.0)	(49.4, 90.6)	18	(58.1)	(40.3, 75.9)	.389
	ONB Accuracy - Trans.	20	(1.2)	(1.2, 1.3)	31	(1.3)	(1.3, 1.4)	.105
Other		No.	Median	(IQR)	No.	Median	(IQR)	р
	ONB Accuracy - Untrans.	20	0.91	(0.81, 0.94)	31	0.94	(0.86, 0.97)	.116
	ONB Errors (No.)	20	3.00	(2.00, 7.50)	31	2.00	(1.00, 5.00)	.148

<sup>a</sup>High-Density Lipoprotein (HDL).

<sup>b</sup>Low-Density Lipoprotein (LDL) cholesterol.

<sup>c</sup>Ratio of Total Cholesterol and HDL cholesterol.

<sup>d</sup>Adapted Patient Health Questionnaire 9.

suggest a healthy survivor effect could extend to cognition, at least in terms of working memory. Our results may have also been influenced by selection bias, where older residents with diabetes and cognitive difficulties may have been less likely to self-select into a community health screen initially. We also excluded data from 14 participants who were unable to complete any of the CBB tasks, most of whom were older and had diabetes. Had these participants been retained and appropriately supported to undertake the CBB tasks, as noted elsewhere,<sup>17</sup> then poorer performance on the One Back task among people with diabetes may have also been observed in the older age groups.

In addition to study design factors, the lower performance of younger participants with diabetes on the One Back task may reflect their increased morbidity relative to their older counterparts. Poorer glycaemic control in the younger group, as evidenced by higher HbA1c, was particularly evident. A systematic review of 86 articles indicated that high HbA1c had a weak negative association with cognitive function in older people (ie 51–85 years of age) with T2DM without dementia.<sup>33</sup> Our study adds to the body of knowledge by suggesting this effect may also be present among younger people who have both diabetes and notable indicators of morbidity. Our limited sample size of 51 people with diabetes, unfortunately, prevented us from exploring this with further modelling.

In contrast to many studies,<sup>9</sup> we found no difference in processing speed, as measured by the Detection and Identification tasks, by diabetes status. The requirements of the CBB tasks may be a reason for these contrary results. While these tasks have criterion validity with traditional measures of processing speed, such as the Symbol Digit Modality Test (SDMT) and Grooved Pegboard,<sup>34</sup> there are notable differences. For example, the CBB speed measures lack an 'executive function' component, which is present in the SDMT, in the form of working memory and associative learning memory.<sup>35</sup> The CBB measures also have a relatively minor 'motor' component, which is a notable domain measured by the Grooved Pegboard test.<sup>25</sup> Further research would be required to examine this possibility. In the absence of this evidence, the current results suggest the CBB tasks are unlikely to be appropriate to detect the early processing speed decrements often seen in diabetes.

In terms of strengths, the examiner was blinded to the diabetes status of participants, which reduced the chance of assessment bias. We obtained diabetes status from both self-report and HbA1c measures. The results of this study suggest that targeted education for younger people with diabetes and improved diabetes monitoring and management may be valuable in terms of protecting later cognitive health, particularly in contexts where there are higher rates of dementia linked to chronic disease. To our knowledge, this is the first study to indicate a detrimental effect of diabetes using a brief computer-based cognitive screen. Further research in other communities would be required to verify these early findings.

There were several study limitations. As noted, the high likelihood of selection bias would mean the sample might not be representative of diabetes and cognition in older age groups. Results from other studies suggest diabetes control, evidenced by HbA1c levels, is associated with cognition in older age groups.<sup>33</sup> Due to small numbers in the older age group, we could not examine the effect of diabetes control in these older ages. Our study also had limited information about medication prescribing and no information about adherence. Year of diagnosis with diabetes was only available in a handful of cases. Duration of diabetes is important, as time with the disease increases risk of cognitive impairment.<sup>6</sup> The small sample size reduced our confidence in regression modelling with interaction terms for multiple age groups. While aggregating participants into three age groups improved this modelling, it prevented examining differences between the younger age groups. This study also did not differentiate by diabetes into Type 1 and 2 Diabetes and GDM. However, given that T2DM is particularly prevalent in this population,<sup>16</sup> it is likely this accounted for most of the diabetes cases.

# 5 | CONCLUSIONS

In a global context where diabetes remains an important risk factor for cognitive decline, our findings suggest that early and subtle decrements in working memory may be a potential complication of diabetes among Indigenous Australians living in the Torres Strait. In this population, which has elevated dementia rates linked to chronic disease, our results highlight the need for more preventative health resourcing. Our results suggest that early identification of younger people with diabetes, targeted education and supported glycaemic control could be important for protecting cognitive health.

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#### CONFLICT OF INTEREST

P.M. is a full-time employee of CogState Ltd. CogState Ltd. provided the CogState tasks reported in this study. The remaining authors declare no conflicts of interest.

#### AUTHOR CONTRIBUTIONS

Fintan Thompson: Data curation (Lead); Formal analysis (Lead); Investigation (Supporting); Methodology (Equal); Writing-original draft (lead); Writing-review & editing (lead). Linton R. Harriss: Investigation (equal); Methodology (equal); Project administration (equal); Writing-original draft (supporting); Writing-review & editing (supporting). Sarah Russell: Formal analysis (supporting); Writingoriginal draft (supporting); Writing-review & editing (supporting). Sean Taylor: Conceptualization (equal); Investigation (equal); Methodology (equal); Project administration (equal); Writingoriginal draft (supporting). Lucette A. Cysique: Formal analysis (supporting); Methodology (supporting); Resources (supporting); Software (supporting); Writing-original draft (supporting). Edward Strivens: Writing-original draft (supporting); Writing-review & editing (supporting). Paul Maruff: Methodology (supporting); Resources (supporting); Software (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). Robyn McDermott: Conceptualization (lead); Funding acquisition (lead); Investigation (lead); Methodology (lead); Project administration (lead); Resources (supporting); Writing-original draft (supporting); Writing-review & editing (supporting).

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are not publicly available due to privacy or ethical restrictions. The data are available on request from the corresponding author. Additional institutional approvals, such as ethics approval, would be required to enable sharing of these data.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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