BMJ Open

The prevalence and incidence of diabetes among Aboriginal people in remote communities of the Northern Territory, Australia: a retrospective, longitudinal data-linkage study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-059716
Article Type:	Original research
Date Submitted by the Author:	29-Nov-2021
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Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH

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Abstract

Objectives: To assess the prevalence and incidence of diabetes among Aboriginal peoples in remote communities of the Northern Territory (NT), Australia.

Design: Retrospective cohort analysis of linked clinical and administrative dataset from 1st July 2012 to 30th June 2019.

Setting: All remote health centres using the NT Government Primary Care Information System (n=51).

Participants: All Aboriginal clients residing in remote communities serviced by these health centres (N=21 267).

Primary outcome measures: Diabetes diagnoses were established using hospital and primary care coding, biochemistry and prescription data.

Results: Diabetes prevalence across all ages increased from 14.4% (95% CI: 13.9-14.9%) to 17.0% (95% CI: 16.5-17.5%) over seven years. Among adults (≥20 years), the 2018/19 diabetes prevalence was 28.6% (95% CI: 27.8-29.4%), being higher in Central Australia (39.5%, 95% CI: 37.8-41.1%) compared to the Top End region (24.2%, 95% CI: 23.3-25.1%, p<0.001). Between 2016/17 and 2018/19, diabetes incidence across all ages was 7.9 per 1000 person-years (95% CI: 7.3-8.7 per 1000 person-years). The adult incidence of diabetes was 12.6 per 1000 person-years (95% CI: 11.5-13.8 per 1000 person-years).

Conclusions: The burden of diabetes in the remote Aboriginal population of the NT is among the highest in the world. Strengthened systems of care and public health prevention strategies, developed in partnership with Aboriginal communities, are needed.

Strengths and limitations of this study

- This study describes the burden of diabetes among Aboriginal peoples in the Northern Territory, Australia, who represent some of the world's longest surviving cultures but experience substantial health and social inequality compared to the broader Australian population.
- The large sample size and use of detailed, individual-level data with a robust data-linkage methodology provide reliable epidemiological estimates in a context where traditional observational studies are immensely challenging, not least due to the population being dispersed over such a vast geographic area.
- The retrospective approach relies on existing clinical data, so the prevalence and incidence of diabetes may be underestimated due to incomplete screening.
- Our findings are unlikely to be generalisable to Aboriginal peoples living in urban centres or in other regions of Australia.

Introduction

Diabetes is a major cause of morbidity and premature mortality worldwide. Prevalence rates of type 2 diabetes and obesity have increased in recent decades due to factors such as globalisation and urbanisation, which are accompanied by sedentary behaviour and energy-dense diets.[1,2] Accompanying these factors, there is growing interest in the role of epigenetic mechanisms and the intrauterine environment as drivers of intergenerational diabetes and obesity risk.[2] The increasing prevalence of diabetes is also contributed to by ageing of populations and improved survival with the condition.[1-3]

Indigenous populations are disproportionately affected by diabetes and associated complications.[4] Social determinants of health are likely key contributors.[4] In Australia, diabetes was the third leading cause of death for Aboriginal and Torres Strait Islander peoples in 2019.[5] The 2018-19 National Aboriginal and Torres Strait Islander Health Survey estimated a diabetes prevalence of 8% among all ages, being higher (12%) in remote areas.[6] These self-reported data are an underestimation. There is also geographic variability, with prevalence rates up to 33% previously reported in specific communities.[7]

The Northern Territory (NT) of Australia spans a vast area of 1.35 million km^2 (more than twice the area of France) with a population density of just 0.2 people/km^2.[8] Over 30% of the population identify as Aboriginal people, 77% of whom live in remote or very remote areas.[8] Some areas of the NT were less impacted by colonisation until the mid-20th century and there remains great strength and diversity of culture, with more than 100 Aboriginal languages still spoken.[9] The NT is commonly considered in two broad regions, the Top End and Central Australia. In 2005, the prevalence of diabetes among Aboriginal people was estimated at 16% in Central Australia and 7.7% in the Top End.[10] More recent accurate estimates of the diabetes burden are lacking.

In this context, we examined trends in diabetes prevalence, contemporary diabetes incidence rates, and the demographic and clinical characteristics of people with diabetes among Aboriginal peoples in remote communities across the NT.

Methods

Study population

The study included all Aboriginal clients, who were recorded as being local residents, of all remote health centres using the NT Health Primary Care Information System. This electronic medical record system is used in 51 out of 84 remote health services in the NT (approximate locations shown in Fig. 1). As the clinics are sole service providers in these communities, almost all the local population are clients. To have been included, an individual must have had an interaction with a clinic since 1st July 2007. Births and deaths are updated monthly by relevant government agencies. Additionally, client lists are updated every six months in collaboration with local community members to account for population mobility. Aboriginal ethnicity is self-identified in NT Health records. A 2011 validation study showed 98% concordance between Aboriginal identification in health records and findings from interviews.[11]

Study design

A retrospective cohort analysis of linked clinical and administrative data from 1st July 2012 to 30th June 2019 was performed.

Data sources

Deidentified data were from the NT Health Primary Care Information System (PCIS) and the Hospital Inpatient Activity dataset. Individual level records were deterministically linked using a unique identifier, the Hospital Reference Number (HRN), which is used across all NT Health services. The HRN has been reliably used for deterministic linkage in previous studies.[12] Implementation of PCIS commenced in 2004 and was completed by 2010. Data for this study included demographics, community 'resident' or 'visitor' status, International Classification of Primary Care (ICPC) coded diagnoses, medication prescriptions, biochemistry results and date of death. The Hospital Inpatient Activity dataset provided International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM) codes for principal and secondary diagnoses for inpatient admissions to the NT's six public hospitals during the study period and date of death from discharge coding.

Outcome definitions

Individuals meeting any of the following criteria were considered to have diabetes: (i) coding for diabetes in primary care (ICPC) or hospital (ICD-10-AM) data, (ii) prescription of a diabetes medication according to Anatomical Therapeutic Chemical (ATC) classification code A10 other than metformin, and/or (iii) biochemical evidence of diabetes on at least two occasions. Details of ICPC and ICD-10-AM inclusions are in Supplementary Table 1. Our case ascertainment was informed by a manual validation study of individual patient records (details in Appendix). Biochemical criteria included haemoglobin A1c (HbA1c) ≥6.5% (≥48 mmol/mol), fasting plasma glucose ≥7.0 mmol/L, 2-hour plasma glucose ≥11.1 mmol/L, and/or random capillary or plasma glucose ≥11.1 mmol/L. In order to avoid inclusion of gestational diabetes mellitus (GDM), data were excluded for nine months prior and three months following a diagnosis code for GDM in either the primary care or hospital datasets. Type 1 and "other" diabetes were identified using ICD-10-AM and ICPC coding. People with diabetes, not identified as type 1 or "other", were presumed to have type 2. If a person was assigned conflicting codes relating to diabetes type (n=39), their clinical records were manually reviewed and

diabetes type adjudicated based on documentation by their treating clinicians and relevant investigations.

Statistical methods

Descriptive statistics were calculated for the total study population, people with prevalent diabetes and people with incident diabetes. Annual diabetes prevalence (%) was calculated for the total population for each financial year (1st July to 30th June) between 2012/13 and 2018/19. Current prevalence (2018/19) was stratified by sex and decade of age and also calculated for adults, defined as ≥20 years old for consistency with the International Diabetes Federation Diabetes Atlas.[13] Trends in prevalence over time were assessed using negative binomial regression. Subgroup analyses of the Top End and Central Australia regions were performed for 2018/19 due to known demographic and epidemiological differences between these populations.[10,14] Comparisons between regions were performed using the Pearson chi-square test, nonparametric equality-of-medians test and unpaired t-test as appropriate.

Due to smaller numbers, diabetes incidence was assessed in aggregate over a three-year period (2016/17 to 2018/19). Trends in incidence over time were not assessed. A diagnosis was considered incident when a person was first recorded as meeting the study criteria for diabetes and that person had records available within the preceding five years with no evidence of diabetes.

All analyses were performed in Stata (Version SE16.1, StataCorp, Texas).

Patient and Public Involvement

Interpretation and reporting of the study findings involved Aboriginal people living in the NT, including two of the authorship group and a third contributor, who requested to remain anonymous. Wider dissemination and communication of the research findings back to Aboriginal communities in

the NT and the development of future translational work to address the public health concerns raised in this study will be guided by the Aboriginal and Torres Strait Islander Advisory Group of the Diabetes across the Lifecourse: Northern Australia Partnership.

Ethics

The study was approved by the Human Research Ethics Committee of Northern Territory Department of Health and Menzies School of Health Research (Ref: 2016-2675).

Results

Over seven years, 21 267 Aboriginal people from 51 remote communities across the NT were included. Median age at baseline was 22 (9-39) years, 10 902 (51.3%) were women, 15 035 (70.7%) were from the Top End and 1059 (5.0%) died during the study period. In the 2012/13 financial year, 14.4% (95% CI: 13.9%-14.9%, n/N=2749/19 042) of people had diabetes. By 2018/19 this prevalence had increased to 17.0% (95% CI: 16.5%-17.5%, n/N=3477/20 429). Figure 2 depicts the 18% increase in prevalence over the study period (annual increase 2.5%, 95% CI: 1.9%-3.1%, p<0.001). In 2018/19, the prevalence among adults was 28.6% (95% CI: 27.8%-29.4%, n/N=3414/11 939). Figure 3 shows that diabetes prevalence was higher with increasing age, except in the oldest age-group (≥70 years), and that there were more women than men with diabetes in all age-groups.

In 2018/19, diabetes was more prevalent in Central Australia than the Top End across all ages (23.0% vs. 14.5%, p<0.001) and among adults (39.5% vs. 24.2%, p<0.001). Characteristics of all people with diabetes in 2018/19 are presented in Table 1. Among these, 2115 (60.8%) were women, 669 (19.2%) were prescribed insulin and 567 (16.3%) had HbA1c ≥10% (≥86 mmol/mol). In Central Australia, a

greater proportion of people had an HbA1c ≥10% (≥86 mmol/mol) and rates of insulin prescribing were higher than in the Top End (both p<0.001).

Between July 2016 and June 2019, there were 483 new cases of diabetes. The incidence rate in the total population was 7.9 (95% CI: 7.3-8.7) per 1000 person-years. Age-specific incidence rates are presented in Figure 4. Median age at diabetes diagnosis was 38 (IQR 29-49) years. The peak incidence was among 50-59 year-olds (16.4 [95% CI: 15.9-16.9] per 1000 person-years), with similarly high rates among 30-39 and 40-49 year-olds. Among adults, the incidence rate was 12.6 (95% CI: 11.5-13.8) per 1000 person-years. Of all people with incident diabetes, 287 (59.4%) were female, 328 (67.9%) lived in the Top End and 481 (99.6%) had type 2 diabetes.

Discussion

The burden of diabetes among Aboriginal people in remote communities of the NT, Australia, is immense and growing. Despite the relatively young age of this population, which includes children, we report a current diabetes prevalence of 17%. The findings are particularly concerning when restricted to adults (29% affected). The prevalence was greatest in Central Australia, where 40% of adults now have diabetes. Age of onset was relatively young with high incidence rates observed between 30-59 years of age. Of people with diabetes who had an HbA1c level checked in 2018/19, more than one in five had an HbA1c ≥10% (≥86 mmol/mol). This combination of young age of onset and severe chronic hyperglycaemia is likely to be accompanied by a high burden of diabetes complications and premature mortality.[15,16]

The epidemic of diabetes among Aboriginal people in the remote NT has occurred in recent history and has continued to grow in the last few decades. In 1997, the prevalence of diabetes in Aboriginal

adults from 15 remote communities was estimated at 15%.[17] Using similar data sources to our study (also including children), the prevalence of diabetes in 2005 was estimated at 16% in Central Australia and 7.7% in the Top End.[10] We report rates of 23% in Central Australia and 15% in the Top End. Thus, in less than 15 years, there has been substantial growth in the diabetes burden. The adult prevalence among Aboriginal people in Central Australia is among the highest ever reported, being similar to what was famously reported among the Pima Indian population of Arizona in the 1970s (42% among those aged ≥25 years) and higher than the current top country-wide prevalence, which is in the Marshall Islands (31% among those aged ≥20 years).[13,18] These comparisons are made for illustrative purposes only given the differences in study methodologies and lack of age standardisation to a common reference population.

We found that diabetes was more common with increasing age, except over 70 years, where prevalence dropped considerably. In Western populations, diabetes prevalence consistently increases with age.[19] However, studies in the NT Aboriginal population from the 1990s and early 2000s found that diabetes prevalence peaked in middle age (45-54 years) and then decreased among older age-groups.[20] This was likely due to a combination of a 'healthy survivor' effect and the timing of lifestyle changes relating to colonisation. Another contributing factor could be that, despite the importance of connection to country, as a last resort, older people with chronic conditions are more likely to move to urban centres with better access to services, leaving a relatively healthier older population in remote communities. Now, two decades later, the age at which this phenomenon is observed is proportionately higher. This likely reflects improvements in life expectancy for people with chronic conditions and a greater length of time since these communities underwent rapid social and environmental transitions.

The higher prevalence of diabetes observed among women compared to men in all age groups is noteworthy. This difference has been observed in Aboriginal Australians previously and also in other

Indigenous populations in North America.[7,18,21,22] It contrasts with the national Australian population and most populations internationally, in which the prevalence of known diabetes is greater among men.[1,13,19] The disparity observed among Aboriginal women in Australia has been shown to relate to obesity.[7,23] However, further research is needed to understand the mechanisms underlying this disparity in metabolic health between Aboriginal women and men. One postulated mechanism is a sex-specific difference in the impact of maternal glycaemia on the developing fetus and thus diabetes risk in that next generation. The effect of fetal hyperinsulinism on both birthweight and postnatal growth appears to differ between girls and boys.[24,25] It has been hypothesised that fetal hyperinsulinism may lead to a degree of persistent insulin resistance that is more pronounced in girls.[25] Nevertheless, it is likely that numerous biological and sociocultural factors are contributing to the higher prevalence of diabetes among women than men. Differences in physical activity may be partly responsible, especially among younger age groups.[23] Additionally, uptake of screening may contribute to some of the observed difference, with national data showing that women are more likely than men to undertake a routine health check specifically funded for Aboriginal and Torres Strait Islander people.[26]

Few studies have examined diabetes incidence in Aboriginal communities in Australia. The first available estimate is from two remote Central Australia communities, published in 1999. Diabetes incidence among people aged ≥15 years was 20.3 per 1000 person-years.[27] Our current observed adult incidence rate across remote NT communities was lower (12.6 per 1000 person-years). This incidence rate is also lower than that observed in an Aboriginal cohort in Queensland between 1999-2007.[28] Each of these studies involved geographically and culturally distinct populations and employed different methodologies. Furthermore, the estimates are not age and sex-standardised.

While there may have been some improvement in diabetes incidence in the last two decades, the observed rates remain high. Australian data from the National Diabetes Services Scheme (NDSS)

show that the national type 2 diabetes incidence rate in 2014 was 2.4 per 1000 person-years.[29] These NDSS data may underestimate the true incidence due to unregistered cases. Nevertheless, it has been estimated that 87% of people with diabetes are NDSS-registered.[30] Compared to these data from the multiethnic national population of Australia, the age-specific incidence rate in our study cohort was 26-times greater at 20-29 years, 12-times greater at 30-39 years and 5-times greater at 40-49 years (DJ Magliano, personal communication).

Our study again confirms the high rates of metabolic disease that accompany rapid transitions in lifestyle among previously lean and physically active populations. Such epidemiological transitions have particularly impacted Indigenous peoples with similar histories of European colonisation.[4,31] The underlying determinants are not well delineated but are likely multifactorial and compound each other. A degree of heightened genetic susceptibility is hypothesised but not well proven.[32] Growing evidence suggests epigenetic mechanisms also have a role, with factors such as intrauterine exposure to hyperglycaemia or maternal undernutrition impacting long-term phenotypic expression in the offspring.[33] Such alterations in gene expression may also be passed on to subsequent generations.[34] The NT Aboriginal population continues to experience elevated rates of low birthweight and pre-term birth.[35] At the same time, rates of diabetes in pregnancy and high birthweight are increasing.[35] These early-life risk factors may be contributing to the ongoing diabetes epidemic.

The higher burden of diabetes observed in Central Australia compared to the Top End is consistent with previous studies.[10] There are numerous distinct Aboriginal people groups across the NT, with great diversity in culture, environment and socioeconomic factors. An early study from the 1980s found that Aboriginal people from desert communities had greater hyperinsulinemia than coastal communities.[36] The authors predicted that this could indicate a future greater burden of diabetes in these people groups as the duration of urbanisation increased.[36]

Underlying these biological hypotheses, the most important contributors to this epidemic are likely to be social and environmental factors. Aboriginal people in the NT experience socioeconomic disadvantage across numerous domains, including income, employment, education and housing.[37] These factors explain a large portion of the inequity in health outcomes relative to non-Aboriginal people.[37] These challenges are more pronounced in remote areas, where overcrowded, inadequate housing and food insecurity are major issues.[38] Healthy food items are expensive in remote stores, with survey data suggesting more than a third of daily energy intake is from discretionary food and drinks.[38] Previous evidence suggests that some of the health disparities between Central Australia and Top End communities relate to differences in social and environmental factors.[14]

Strengths of our study include the use of detailed, individual-level data and the large sample size. The use of a client population raises the question of whether the study cohort represents the true population of these remote communities. As discussed in the methods, the client databases of these sole-provider remote health services include almost all the local Aboriginal population. The study is inherently limited by the retrospective design. Our diabetes estimates are reliant on known diagnoses and it is likely the population is incompletely screened, which would contribute to an underestimation of both prevalence and incidence. There may also be some bias regarding the demographics of people who are more likely to participate in screening. Unfortunately, we were unable to assess time trends in diabetes incidence due to limited numbers and the potential unreliability of differentiating incident and prevalent cases in the early years of the PCIS electronic medical record system. Our findings are unlikely to be generalisable to Aboriginal peoples living in urban centres or in other regions of Australia.

Conclusion

The burden of diabetes among Aboriginal people in remote communities of the NT is among the highest reported of any population globally despite the population being relatively young. Many factors associated with increasing prevalence of diabetes are beyond individual control, and thus strengthened systems of care and public health prevention strategies, developed and implemented in partnership with Aboriginal communities, are needed. These strategies should be holistic, considering emotional, spiritual and mental wellbeing, as well as physical health. The enormity of the diabetes burden necessitates population-wide prevention strategies, including cross-sectoral collaboration to address the social determinants of health.

Contributors: MJLH led the analysis planning, interpretation of findings and drafting of the manuscript. HF and LJMB contributed equally as senior authors, supervising all aspects of the study, including conception of the study, ethics application, study design, study conduct, analysis planning, interpretation of findings and manuscript preparation . YZ, SG, PB and ELMB contributed to study conception, study design, analysis planning, interpretation of findings and critically revised the manuscript. YZ additionally provided statistical expertise and undertook the data analysis. DB (a Jawoyn woman and health policymaker), AR (a Gubbi Gubbi woman and Senior Remote Medical Practitioner in Central Australia) and EE (Endocrinologist in Central Australia) contributed to interpretation of data and critically revised the work for important intellectual content. All authors approved the final version and agreed to be accountable for the work. YZ is the guarantor for the analyses.

Acknowledgements: We gratefully acknowledge the contribution of an Aboriginal community member from the Central Australia region of the NT, who revised the manuscript and requested to remain anonymous. We acknowledge NT Health for access to the datasets used and thank professionals from NT Health hospitals and remote primary healthcare who contributed to these datasets in their day-to-day work.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors. MJLH is supported by National Health and Medical Research Council (NHMRC) postgraduate scholarship (No. 1169091), Diabetes Australia and the Australian Academy of Science. LJMB is supported by NHMRC Investigator Grant (No. 1194698).

Data availability statement: The Northern Territory Department of Health is the owner of the data used for this study. Reasonable requests for access to the deidentified study dataset would be considered after required approvals from the data custodians are in place.

Competing interests: MJLH has received honoraria for lectures and consultancies from AstraZeneca, Eli Lilly and Novo Nordisk. All other authors have no interests to declare.

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Table 1. Characteristics of Aboriginal people with prevalent diabetes in 2018/19 in the NT, with comparison by region

	Total NT (n=3477)	Central Australia (n=1382)	Top End (n=2095)	*P* value (CA vs TE)
Age, years	49 (39-58)	48 (37-58)	49 (40-58)	0.003
Female	2115 (61)	834 (60)	1281 (61)	0.637
Diabetes type				0.269
Type 2	3429 (98.6)	1368 (98.9)	2061 (98.4)	
Type 1	34 (1.0)	9 (0.7)	25 (1.2)	
Other	14 (0.4)	5 (0.5)	9 (0.4)	
Treatment				
No GLT	1627 (47)	542 (39)	1085 (52)	<0.001
Non-insulin GLT	1181 (34)	508 (37)	673 (32)	0.005
Combined GLT (with insulin)	610 (18)	307 (22)	303 (15)	<0.001
Insulin alone	59 (1.7)	25 (1.8)	34 (1.6)	0.678
Mean HbA1c*	7.9 (±2.2)	8.4 (±0.07)	7.7 (±0.05)	<0.001
HbA1c category*				<0.001
<7.0% (<53 mmol/mol)	1216 (35)	375 (27)	641 (40)	
7.0-7.9% (53-63 mmol/mol)	415 (12)	159 (12)	256 (12)	
8.0-9.9% (64-85 mmol/mol)	540 (16)	228 (17)	312 (15)	
≥10% (≥86 mmol/mol)	567 (16)	281 (20)	286 (14)	
No result	739 (21)	339 (25)	400 (19)	

Data are n (%), median (IQR) or mean (±SE). CA = Central Australia, TE = Top End, GLT = glucose lowering therapy, HbA1c = haemoglobin A1c. *The single most recent HbA1c result for each individual within the 2018/19 year was included. Individuals with no HbA1c in that 12 month period were excluded from calculation of means and reported in the "no result" category.

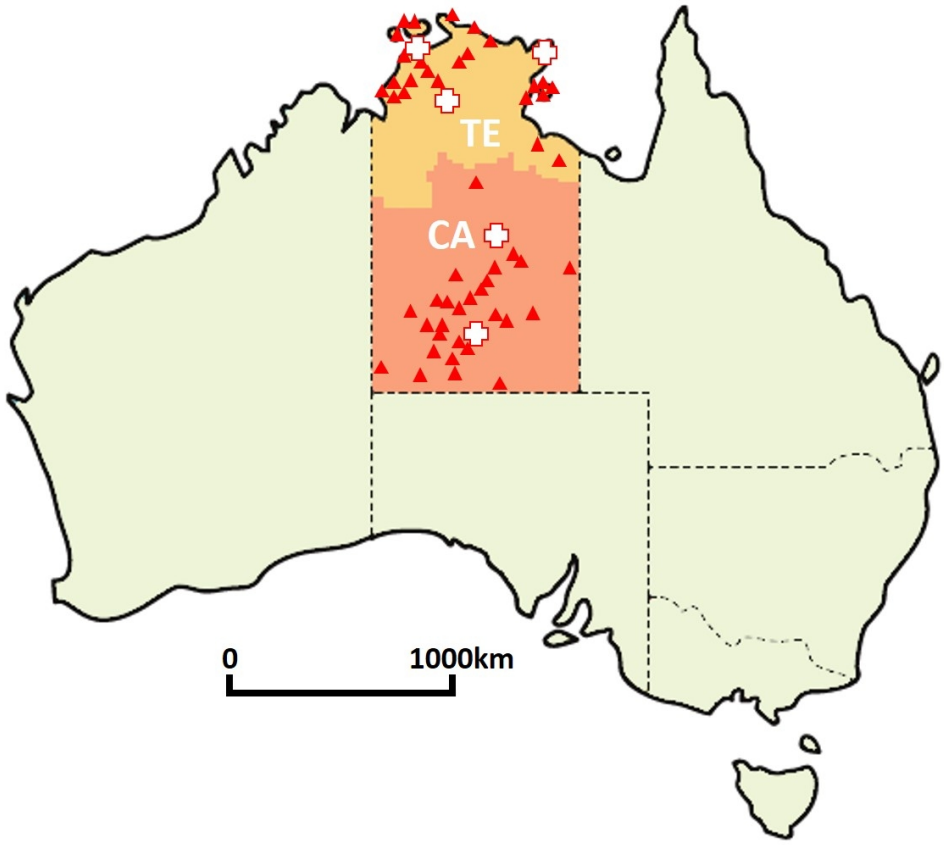
Figure Legends

Figure 1. Map of the Top End (TE) and Central Australia (CA) regions of the Northern Territory, Australia, showing the 51 remote clinics (triangles) and 6 hospitals (crosses) contributing data to this study. Nb. There are two hospitals in the location at the top left (North West) of the Top End. Distances and locations are approximate.

Figure 2. Trend in crude diabetes prevalence among Aboriginal people (all ages) in remote NT communities over seven years. Error bars are 95% confidence intervals.

Figure 3. Age and sex-specific diabetes prevalence in 2018/19 among Aboriginal people in remote NT communities. Error bars are 95% confidence intervals.

Figure 4. Age-specific diabetes incidence rates between 2016/17 and 2018/19 among Aboriginal people in remote NT communities. Error bars are 95% confidence intervals.



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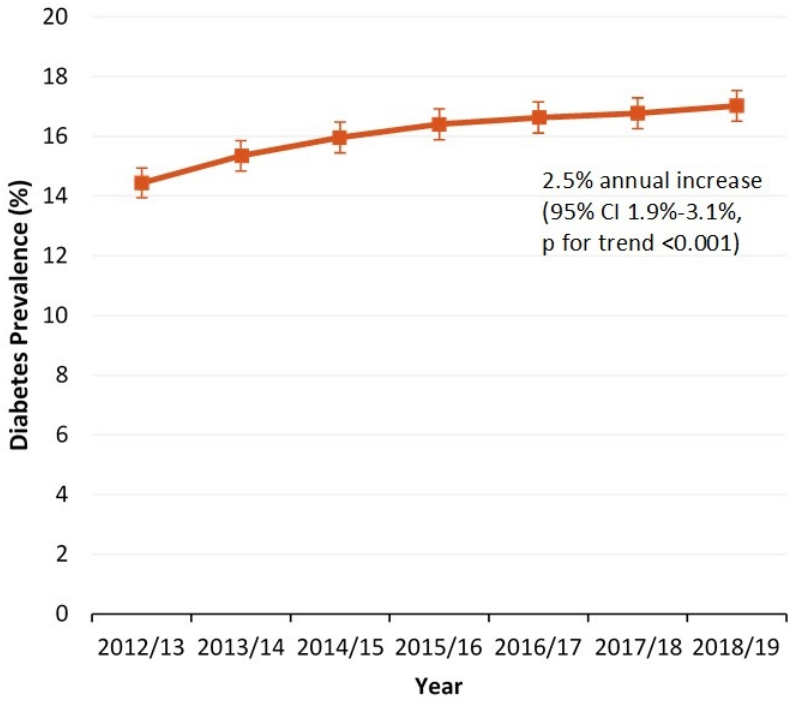

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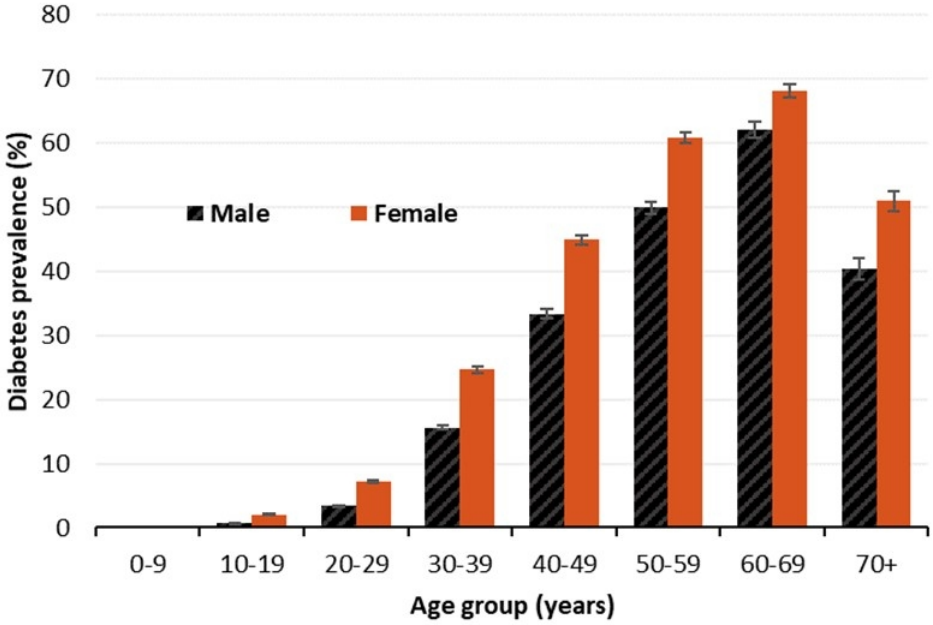

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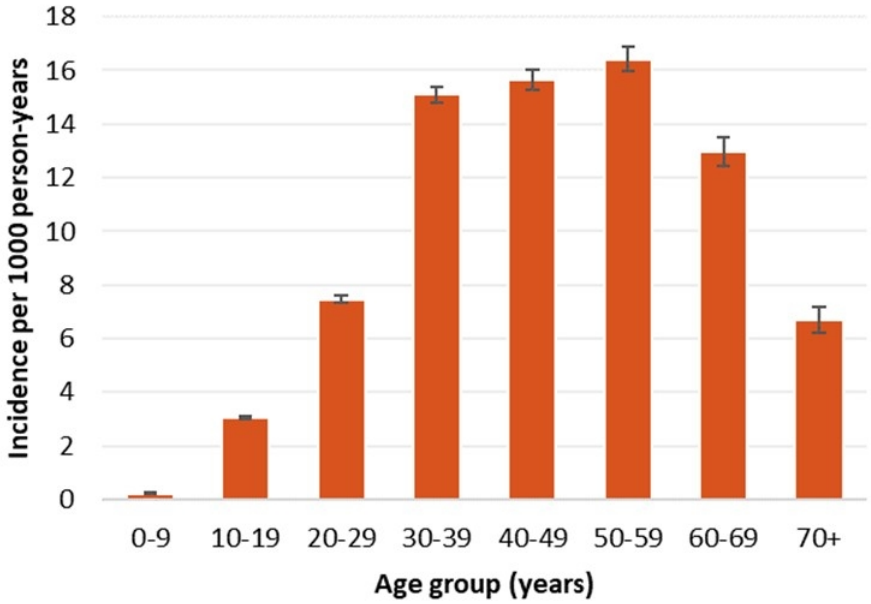

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APPENDIX

Supplementary Table 1. ICPC and ICD-10-AM diagnostic codes used in diabetes case definitions

	ICPC	ICD-10-AM
Any diabetes	T89* T90*	E10*-E14* O24.0-O24.3 O24.5 O24.9
Type 1 diabetes	T89002	E10* O24.0
Other diabetes	T90017	E13*
Gestational diabetes	W85*	O24.4

** indicates truncation. ICPC: International Classification of Primary Care; ICD-10-AM: International Classification of Diseases, Tenth Revision, Australian Modification.*

Validation study results

Manual review of individual electronic health records was undertaken to inform our study definition of diabetes. Three specific potential issues were targeted including: (i) whether or not prescription of metformin indicates a diagnosis of diabetes, (ii) whether cases of gestational diabetes mellitus (GDM) were adequately excluded, and (iii) the accuracy of determination of diabetes type, especially in young-onset diabetes. This work was undertaken by a single research assistant with a clinical background under the supervision of an endocrinologist, who personally reviewed all records where there was any doubt about the patient's diabetes diagnosis.

Metformin prescription was removed from the study definition of diabetes following manual review of a sample (n=62) of people prescribed metformin but with no other glucose-lowering medication, no coding for a diabetes diagnosis and no biochemical data to support a diabetes diagnosis. Of these people, 52 (81%) did not have diabetes. The most common indication for metformin in this subgroup was diabetes prevention in high-risk individuals (including pre-diabetes, evidence of insulin resistance and antipsychotic use), followed by GDM and polycystic ovarian syndrome.

To avoid including diagnoses of GDM, we excluded all medication and biochemistry data in the nine months preceding and three months following the allocation of a GDM diagnostic code in either the primary care or hospital datasets. In order to assess this approach, we investigated the health records of a random sample of women (n=40) of childbearing age (born between 1st July 1968 and 1st July 1998) who had been defined as having diabetes. Once metformin had been removed from the study definition of diabetes, 39 (98%) of these women were confirmed as having established diabetes. Therefore, we deemed that the approach to excluding GDM was adequate.

With regard to determining diabetes type, we were concerned about two non-specific ICPC codes (T89001 – "Insulin dependent" and T89003 – "Juvenile onset") intended to report type 1 diabetes in the ICPC classification system. Insulin is frequently used for type 2 diabetes and there is a high burden of youth-onset type 2 diabetes among Aboriginal people in the Northern Territory. In a random sample (n=28), only 4 (14%) of people coded as T89001 had type 1 diabetes, therefore we did not include this code in our type 1 diabetes definition. Only two people were assigned the

T89003 code. One of these had type 2 diabetes, the other had pre-diabetes. This code was also removed from the type 1 diabetes definition.

To further assess the accuracy of identification of diabetes type in young people, we took a random sample (n=40) of people with diabetes born on or after 1st July 1988. Only one of these people had type 1 diabetes and it had been coded appropriately in the study dataset.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6 (+appendix)
Bias	9	Describe any efforts to address potential sources of bias	5,13
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	19
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	19
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8,9
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8,9
		(*b*) Report category boundaries when continuous variables were categorized	19
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence and incidence of diabetes among Aboriginal people in remote communities of the Northern Territory, Australia: a retrospective, longitudinal data-linkage study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-059716.R1
Article Type:	Original research
Date Submitted by the Author:	07-Mar-2022
Complete List of Authors:	Hare, Matthew; Charles Darwin University, Menzies School of Health Research; Royal Darwin Hospital, Department of Endocrinology Zhao, Yuejen; NT Health, Population and Digital Health Guthridge, Steven; Charles Darwin University, Menzies School of Health Research Burgess, Paul; NT Health, Population and Digital Health; Top End Region, NT Health, Primary Health Care Division Barr, Elizabeth L. M.; Charles Darwin University, Menzies School of Health Research; Baker Heart and Diabetes Institute, Clinical Diabetes and Epidemiology Ellis, Elna; Alice Springs Hospital, Department of Medicine Butler, Deborah; NT Health Rosser, Amy; Central Australia Region, NT Health, Primary Health Care Division Falhammar, Henrik; Karolinska Institutet, Department of Molecular Medicine and Surgery; Karolinska University Hospital, Department of Endocrinology Maple-Brown, Louise; Charles Darwin University, Menzies School of Health Research; Royal Darwin Hospital, Department of Endocrinology
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology, Global health, Public health
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY, PUBLIC HEALTH

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Prevalence and incidence of diabetes among Aboriginal people in remote communities of the Northern Territory, Australia: a retrospective, longitudinal data-linkage study

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Abstract

Objectives: To assess the prevalence and incidence of diabetes among Aboriginal peoples in remote communities of the Northern Territory (NT), Australia.

Design: Retrospective cohort analysis of linked clinical and administrative datasets from 1st July 2012 to 30th June 2019.

Setting: Remote health centres using the NT Government Primary Care Information System (51 out of a total of 84 remote health centres in the NT).

Participants: All Aboriginal clients residing in remote communities serviced by these health centres (N=21 267).

Primary outcome measures: Diabetes diagnoses were established using hospital and primary care coding, biochemistry and prescription data.

Results: Diabetes prevalence across all ages increased from 14.4% (95% CI: 13.9-14.9%) to 17.0% (95% CI: 16.5-17.5%) over seven years. Among adults (≥20 years), the 2018/19 diabetes prevalence was 28.6% (95% CI: 27.8-29.4%), being higher in Central Australia (39.5%, 95% CI: 37.8-41.1%) compared to the Top End region (24.2%, 95% CI: 23.3-25.1%, p<0.001). fBetween 2016/17 and 2018/19, diabetes incidence across all ages was 7.9 per 1000 person-years (95% CI: 7.3-8.7 per 1000 person-years). The adult incidence of diabetes was 12.6 per 1000 person-years (95% CI: 11.5-13.8 per 1000 person-years).

Conclusions: The burden of diabetes in the remote Aboriginal population of the NT is among the highest in the world. Strengthened systems of care and public health prevention strategies, developed in partnership with Aboriginal communities, are needed.

Strengths and limitations of this study

- This study describes the burden of diabetes among Aboriginal peoples in the Northern Territory, Australia, who represent some of the world's longest surviving cultures but experience substantial health and social inequality compared to the broader Australian population.
- The large sample size and use of detailed, individual-level data with a robust data-linkage methodology provide reliable epidemiological estimates in a context where traditional observational studies are immensely challenging, not least due to the population being dispersed over such a vast geographic area.
- The retrospective approach relies on existing clinical data, so the prevalence and incidence of diabetes may be underestimated due to incomplete screening.
- Our findings are unlikely to be generalisable to Aboriginal peoples living in urban centres.

Introduction

Diabetes is a major cause of morbidity and premature mortality worldwide. Prevalence rates of type 2 diabetes and obesity have increased in recent decades due to factors such as globalisation and urbanisation, which are accompanied by sedentary behaviour and energy-dense diets.[1,2] Accompanying these factors, there is growing interest in the role of epigenetic mechanisms and the intrauterine environment as drivers of intergenerational diabetes and obesity risk.[2] The increasing prevalence of diabetes is also contributed to by ageing of populations and improved survival with the condition.[1-3]

Unlike type 1 diabetes, which is caused by insulin deficiency due to autoimmune-mediated pancreatic beta-cell failure, type 2 diabetes is characterised by insulin resistance and a degree of beta-cell dysfunction.[4] Indigenous populations are disproportionately affected by type 2 diabetes and associated complications.[5] Social determinants of health are likely key contributors.[5] In Australia, diabetes was the third leading cause of death for Aboriginal and Torres Strait Islander peoples in 2019.[6] The 2018-19 National Aboriginal and Torres Strait Islander Health Survey estimated a diabetes prevalence of 8% among all ages, being higher (12%) in remote areas.[7] These self-reported data are an underestimation. There is also geographic variability, with prevalence rates up to 33% previously reported in specific communities.[8]

The Northern Territory (NT) of Australia spans a vast area of 1.35 million km^2 (more than twice the area of France) with a population density of just 0.2 people/km^2.[9] Over 30% of the population identify as Aboriginal people, 77% of whom live in remote or very remote areas.[9] Some areas of the NT were less impacted by colonisation until the mid-20th century and there remains great strength and diversity of culture, with more than 100 Aboriginal languages still spoken.[10] The NT is commonly considered in two broad regions, the Top End and Central Australia. In 2005, the prevalence of

diabetes among Aboriginal people was estimated at 16% in Central Australia and 7.7% in the Top End.[11] More recent accurate estimates of the diabetes burden are lacking.

In this context, we examined trends in diabetes prevalence, contemporary diabetes incidence rates, and the demographic and clinical characteristics of people with diabetes among Aboriginal peoples in remote communities across the NT.

Methods

Study population

The study included all Aboriginal clients, who were recorded as being local residents, of all remote health centres using the NT Health Primary Care Information System. This electronic medical record system is used in 51 out of 84 remote health services in the NT (approximate locations shown in Fig. 1). Each of these health services are in locations defined as either remote or very remote according to the Australian Statistical Geography Standard.[12] These remoteness classifications are based on relative accessibility to services in urban centres according to road distance measurements. As the clinics are sole service providers in these communities, almost all the local population are clients. To have been included, an individual must have had an interaction with a clinic since 1st July 2007. Births and deaths are updated monthly by relevant government agencies. Additionally, client lists are updated every six months in collaboration with local community members to account for population mobility. Aboriginal ethnicity is self-identified in NT Health records. A 2011 validation study showed 98% concordance between Aboriginal identification in health records and findings from interviews.[13]

Study design

A retrospective cohort analysis of linked clinical and administrative data from 1st July 2012 to 30th June 2019 was performed.

Data sources

Deidentified data were from the NT Health Primary Care Information System (PCIS) and the Hospital Inpatient Activity dataset. Individual level records were deterministically linked using a unique identifier, the Hospital Reference Number (HRN), which is used across all NT Health services. The HRN and other personal identifiers are routinely stored in a centralised Client Master Index, which connects to and synchronises across various NT Health information systems, including both PCIS and the Hospital Inpatient Activity dataset. The Client Master Index is subject to continual audit and review and is deemed reliable for deterministic linkage in research.[13,14] Implementation of PCIS commenced in 2004 and was completed by 2010. Data for this study included demographics, community 'resident' or 'visitor' status, International Classification of Primary Care (ICPC) coded diagnoses, medication prescriptions, biochemistry results and date of death. The Hospital Inpatient Activity dataset provided International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM) codes for principal and secondary diagnoses for inpatient admissions to the NT's six public hospitals during the study period and date of death from discharge coding.

Outcome definitions

Individuals meeting any of the following criteria were considered to have diabetes: (i) coding for diabetes in primary care (ICPC) or hospital (ICD-10-AM) data, (ii) prescription of a diabetes medication according to Anatomical Therapeutic Chemical (ATC) classification code A10 other than metformin, and/or (iii) biochemical evidence of diabetes on at least two occasions. Details of ICPC and ICD-10-AM inclusions are in Supplementary Table 1. Metformin was excluded from the diabetes definition as it is commonly used for other indications, including polycystic ovarian syndrome and "pre-diabetes". Our case ascertainment was informed by a manual validation study of individual

patient records (details in Appendix). Biochemical criteria included haemoglobin A1c (HbA1c) ≥6.5% (≥48 mmol/mol), fasting plasma glucose ≥7.0 mmol/L, 2-hour plasma glucose ≥11.1 mmol/L, and/or random capillary or plasma glucose ≥11.1 mmol/L.[15] In order to avoid inclusion of gestational diabetes mellitus (GDM), data were excluded for nine months prior and three months following a diagnosis code for GDM in either the primary care or hospital datasets. Type 1 and "other" diabetes were identified using ICD-10-AM and ICPC coding. People with diabetes, not identified as type 1 or "other", were presumed to have type 2. If a person was assigned conflicting codes relating to diabetes type (n=39), their clinical records were manually reviewed and diabetes type adjudicated based on documentation by their treating clinicians and relevant investigations.

Statistical analysis

Descriptive statistics were calculated for the total study population, people with prevalent diabetes and people with incident diabetes. Annual diabetes prevalence (%) was calculated for the total population for each financial year (1st July to 30th June) between 2012/13 and 2018/19, with 95% confidence intervals calculated using: $\hat{p} \pm 1.96\sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$. Current prevalence (2018/19) was stratified by sex and decade of age and also calculated for adults, defined as ≥20 years old for consistency with the International Diabetes Federation Diabetes Atlas.[16] Trends in prevalence over time were assessed using negative binomial regression. Subgroup analyses of the Top End and Central Australia regions were performed for 2018/19 due to known demographic and epidemiological differences between these populations.[11,17] Comparisons between regions were performed using the Pearson chi-square test, nonparametric equality-of-medians test and unpaired t-test as appropriate.

Due to smaller numbers, diabetes incidence was assessed in aggregate over a three-year period (2016/17 to 2018/19). Trends in incidence over time were not assessed. A diagnosis was considered incident when a person was first recorded as meeting the study criteria for diabetes and that person had records available within the preceding five years with no evidence of diabetes.

All analyses were performed in Stata (Version SE16.1, StataCorp, Texas).

Patient and public involvement

Interpretation and reporting of the study findings involved Aboriginal people living in the NT, including two of the authorship group and a third contributor, who requested to remain anonymous. Wider dissemination and communication of the research findings back to Aboriginal communities in the NT and the development of future translational work to address the public health concerns raised in this study will be guided by the Aboriginal and Torres Strait Islander Advisory Group of the Diabetes across the Lifecourse: Northern Australia Partnership.

Ethics

The study was approved by the Human Research Ethics Committee of Northern Territory Department of Health and Menzies School of Health Research (Ref: 2016-2675).

Results

Over seven years, 21 267 Aboriginal people from 51 remote communities across the NT were included. Median age at baseline was 22 (IQR 9-39) years, 10 902 (51.3%) were women, 15 035 (70.7%) were from the Top End and 1059 (5.0%) died during the study period. In the 2012/13 financial year, 14.4% (95% CI: 13.9%-14.9%, n/N=2749/19 042) of people had diabetes. By 2018/19 this prevalence had increased to 17.0% (95% CI: 16.5%-17.5%, n/N=3477/20 429), with 98.6% (n/N=3429/3477) of diagnoses classified as type 2 diabetes. Figure 2 depicts the 18% increase in prevalence over the study period (annual increase 2.5%, 95% CI: 1.9%-3.1%, p<0.001). In 2018/19, the prevalence among adults was 28.6% (95% CI: 27.8%-29.4%, n/N=3414/11 939). Figure 3 shows

that diabetes prevalence was higher with increasing age, except in the oldest age-group (≥70 years), and that there were more women than men with diabetes in all age-groups.

In 2018/19, diabetes was more prevalent across all ages in Central Australia (23.0%, 95% CI: 22.0%-24.1%) than the Top End (14.5%, 95% CI: 13.9%-15.1%, p<0.001). When restricted to adults, the prevalence was 39.5% (95% CI: 37.9%-41.1%) in Central Australia compared to 24.2% (95% CI: 23.3%-25.1%) in the Top End (p<0.001). Characteristics of all people with diabetes in 2018/19 are presented in Table 1. Among these, 2115 (60.8%) were women, 669 (19.2%) were prescribed insulin and 567 (16.3%) had HbA1c ≥10% (≥86 mmol/mol). In Central Australia, a greater proportion of people had an HbA1c ≥10% (≥86 mmol/mol) and rates of insulin prescribing were higher than in the Top End (both p<0.001).

Between July 2016 and June 2019, there were 483 new cases of diabetes. The incidence rate in the total population was 7.9 (95% CI: 7.3-8.7) per 1000 person-years. Age-specific incidence rates are presented in Figure 4. Median age at diabetes diagnosis was 38 (IQR 29-49) years. The peak incidence was among 50-59 year-olds (16.4 [95% CI: 15.9-16.9] per 1000 person-years), with similarly high rates among 30-39 and 40-49 year-olds. Among adults, the incidence rate was 12.6 (95% CI: 11.5-13.8) per 1000 person-years. Of all people with incident diabetes, 287 (59.4%) were female, 328 (67.9%) lived in the Top End and 481 (99.6%) had type 2 diabetes.

Discussion

The burden of type 2 diabetes among Aboriginal people in remote communities of the NT, Australia, is immense and growing. Despite the relatively young age of this population, which includes children, we report a current diabetes prevalence of 17%, of which 99% is classified as type 2

diabetes. The findings are particularly concerning when restricted to adults (29% affected). The prevalence was greatest in Central Australia, where 40% of adults now have diabetes. Age of onset was relatively young with high incidence rates observed between 30-59 years of age. Of people with diabetes who had an HbA1c level checked in 2018/19, more than one in five had an HbA1c ≥10% (≥86 mmol/mol). This combination of young age of onset and severe chronic hyperglycaemia is likely to be accompanied by a high burden of diabetes complications and premature mortality.[18,19] Of additional concern is the high proportion of people meeting criteria for diabetes who were not prescribed glucose-lowering therapy (47%) despite the mean HbA1c being 7.9% (63 mmol/mol). This suggests a significant gap between established treatment recommendations and real-world implementation into practice.

The epidemic of type 2 diabetes among Aboriginal people in the remote NT has occurred in recent history and has continued to grow in the last few decades. In 1997, the prevalence of diabetes in Aboriginal adults from 15 remote communities was estimated at 15%.[20] Using similar data sources to our study (also including children), the prevalence of diabetes in 2005 was estimated at 16% in Central Australia and 7.7% in the Top End.[11] We report rates of 23% in Central Australia and 15% in the Top End. Thus, in less than 15 years, there has been substantial growth in the diabetes burden. The adult prevalence among Aboriginal people in Central Australia is among the highest ever reported, being similar to what was famously reported among the Pima Indian population of Arizona in the 1970s (42% among those aged ≥25 years) and higher than the current top country-wide prevalence, which is in the Marshall Islands (31% among those aged ≥20 years).[16,21] These comparisons are made for illustrative purposes only given the differences in study methodologies and lack of age standardisation to a common reference population.

There are limited published data examining temporal trends in diabetes epidemiology among Aboriginal people in Australia. An early study conducted in a single community in Central Australia, showed that the prevalence of diabetes increased from 11.6% in 1987 to 20.7% in 1995.[22] More

recent studies from Western Australia and the NT have examined diabetes prevalence trends during pregnancy, showing substantial growth in the number of Aboriginal women with type 2 diabetes diagnosed prior to pregnancy.[23,24] In addition, the incidence of diabetes among Aboriginal and Torres Strait Islander children (aged under 16 years) in Western Australia increased considerably between 2000 and 2019.[25] Our findings add to this existing literature, showing an 18% increase in diabetes prevalence over seven years. Numerous factors, not assesed in our study, may have contributed to the observed change, such as increasing incidence, improved survival and greater uptake of screening.

We found that diabetes was more common with increasing age, except over 70 years, where prevalence dropped considerably. In Western populations, diabetes prevalence consistently increases with age.[26] However, studies in the NT Aboriginal population from the 1990s and early 2000s found that diabetes prevalence peaked in middle age (45-54 years) and then decreased among older age-groups.[27] This was likely due to a combination of a 'healthy survivor' effect and the timing of lifestyle changes relating to colonisation. Another contributing factor could be that, despite the importance of connection to country, as a last resort, older people with chronic conditions are more likely to move to urban centres with better access to services, leaving a relatively healthier older population in remote communities. Now, two decades later, the age at which this phenomenon is observed is proportionately higher. This likely reflects improvements in life expectancy for people with chronic conditions and a greater length of time since these communities underwent rapid social and environmental transitions.

The higher prevalence of diabetes observed among women compared to men in all age groups is noteworthy. This difference has been observed in Aboriginal Australians previously and also in other Indigenous populations in North America.[8,21,28,29] It contrasts with the national Australian population and most populations internationally, in which the prevalence of known diabetes is greater among

men.[1,16,26] The disparity observed among Aboriginal women in Australia has been shown to relate to obesity.[8,22] However, further research is needed to understand the mechanisms underlying this disparity in metabolic health between Aboriginal women and men. One postulated mechanism is a sex-specific difference in the impact of maternal glycaemia on the developing fetus and thus diabetes risk in that next generation. The effect of fetal hyperinsulinism on both birthweight and postnatal growth appears to differ between girls and boys.[30,31] It has been hypothesised that fetal hyperinsulinism may lead to a degree of persistent insulin resistance that is more pronounced in girls.[31] Nevertheless, it is likely that numerous biological and sociocultural factors are contributing to the higher prevalence of diabetes among women than men. Differences in physical activity may be partly responsible, especially among younger age groups.[22] Additionally, uptake of screening may contribute to some of the observed difference, with national data showing that women are more likely than men to undertake a routine health check specifically funded for Aboriginal and Torres Strait Islander people.[32] Routine screening for diabetes during pregnancy and following a pregnancy complicated by gestational diabetes may also have an impact.

Few studies have examined diabetes incidence in Aboriginal communities in Australia. The first available estimate is from two remote Central Australia communities, published in 1999. Diabetes incidence among people aged ≥15 years was 20.3 per 1000 person-years.[33] Our current observed adult incidence rate across remote NT communities was lower (12.6 per 1000 person-years). This incidence rate is also lower than that observed in an Aboriginal cohort in Queensland between 1999-2007.[34] Each of these studies involved geographically and culturally distinct populations and employed different methodologies. Furthermore, the estimates are not age and sex-standardised.

While there may have been some improvement in diabetes incidence in the last two decades, the observed rates remain high. Australian data from the National Diabetes Services Scheme (NDSS) show that the national type 2 diabetes incidence rate in 2014 was 2.4 per 1000 person-years.[35]

These NDSS data may underestimate the true incidence due to unregistered cases. Nevertheless, it has been estimated that 87% of people with diabetes are NDSS-registered.[36] Compared to these data from the multiethnic national population of Australia, the age-specific incidence rate in our study cohort was 26-times greater at 20-29 years, 12-times greater at 30-39 years and 5-times greater at 40-49 years (DJ Magliano, personal communication). Establishing the contemporary diabetes incidence rate in our study context is important for the future evaluation of public health strategies aimed at preventing diabetes.

Our study again confirms the high rates of metabolic disease that accompany rapid transitions in lifestyle among previously lean and physically active populations. Such epidemiological transitions have particularly impacted Indigenous peoples with similar histories of European colonisation.[5,37] The underlying determinants are not well delineated but are likely multifactorial and compound each other. A degree of heightened genetic susceptibility is hypothesised but not well proven.[38] Growing evidence suggests epigenetic mechanisms also have a role, with factors such as intrauterine exposure to hyperglycaemia or maternal undernutrition impacting long-term phenotypic expression in the offspring.[39] Such alterations in gene expression may also be passed on to subsequent generations.[40] The NT Aboriginal population continues to experience elevated rates of low birthweight and pre-term birth.[24] At the same time, rates of diabetes in pregnancy and high birthweight are increasing.[24] These early-life risk factors may be contributing to the ongoing diabetes epidemic.

The higher burden of diabetes observed in Central Australia compared to the Top End is consistent with previous studies.[11] There are numerous distinct Aboriginal people groups across the NT, with great diversity in culture, environment and socioeconomic factors. An early study from the 1980s found that Aboriginal people from desert communities had greater hyperinsulinemia than coastal

communities.[41] The authors predicted that this could indicate a future greater burden of diabetes in these people groups as the duration of urbanisation increased.[41]

Underlying these biological hypotheses, the most important contributors to this epidemic are likely to be social and environmental factors. Aboriginal people in the NT experience socioeconomic disadvantage across numerous domains, including income, employment, education and housing.[42] These factors explain a large portion of the inequity in health outcomes relative to non-Aboriginal people.[42] These challenges are more pronounced in remote areas, where overcrowded, inadequate housing and food insecurity are major issues.[43] Healthy food items are expensive in remote stores, with survey data suggesting more than a third of daily energy intake is from discretionary food and drinks.[43] Previous evidence suggests that some of the health disparities between Central Australia and Top End communities relate to differences in social and environmental factors.[17]

Strengths of our study include the use of detailed, individual-level data and the large sample size. The use of a client population raises the question of whether the study cohort represents the true population of these remote communities. As discussed in the methods, the client databases of these sole-provider remote health services include almost all the local Aboriginal population. The study is inherently limited by the retrospective design. Our diabetes estimates are reliant on known diagnoses and it is likely the population is incompletely screened, which would contribute to an underestimation of both prevalence and incidence. There may also be some bias regarding the demographics of people who are more likely to participate in screening. Significant heterogeneity exists between Aboriginal communities across the NT. The inclusion of data in our study from most, but not all, remote communities in the region could have introduced some bias and limit the generalisability. Furthermore, our findings may not be generalisable to Aboriginal peoples living in urban centres due to the unique environments and population characteristics of remote Aboriginal communities. Unfortunately, we were unable to assess time trends in diabetes incidence due to

limited numbers and the potential unreliability of differentiating incident and prevalent cases in the early years of the PCIS electronic medical record system.

Conclusion

The burden of type 2 diabetes among Aboriginal people in remote communities of the NT is among the highest reported of any population globally despite the population being relatively young. Many factors associated with increasing prevalence of diabetes are beyond individual control, and thus strengthened systems of care and public health prevention strategies, developed and implemented in partnership with Aboriginal communities, are needed. These strategies should be holistic, considering emotional, spiritual and mental wellbeing, as well as physical health. The enormity of the diabetes burden necessitates population-wide prevention strategies, including cross-sectoral collaboration to address the social determinants of health.

Contributors: MJLH led the analysis planning, interpretation of findings and drafting of the manuscript. HF and LJMB contributed equally as senior authors, supervising all aspects of the study, including conception of the study, ethics application, study design, study conduct, analysis planning, interpretation of findings and manuscript preparation. YZ, SG, PB and ELMB contributed to study conception, study design, analysis planning, interpretation of findings and critically revised the manuscript. YZ additionally provided statistical expertise and undertook the data analysis. DB (a Jawoyn woman and health policymaker), AR (a Gubbi Gubbi woman and Senior Remote Medical Practitioner in Central Australia) and EE (Endocrinologist in Central Australia) contributed to interpretation of data and critically revised the work for important intellectual content. All authors approved the final version and agreed to be accountable for the work. YZ is the guarantor for the analyses.

Acknowledgments: We gratefully acknowledge the contribution of an Aboriginal community member from the Central Australia region of the NT, who revised the manuscript and requested to remain anonymous. We acknowledge NT Health for access to the datasets used and thank professionals from NT Health hospitals and remote primary healthcare who contributed to these datasets in their day-to-day work.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors. MJLH is supported by National Health and Medical Research Council (NHMRC) postgraduate scholarship (No. 1169091), Diabetes Australia and the Australian Academy of Science. LJMB is supported by NHMRC Investigator Grant (No. 1194698).

Data availability statement: The Northern Territory Department of Health is the owner of the data used for this study. Reasonable requests for access to the deidentified study dataset would be considered after required approvals from the data custodians are in place.

Competing interests: MJLH has received honoraria for lectures and consultancies from AstraZeneca, Eli Lilly and Novo Nordisk. All other authors have no interests to declare.

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Table 1. Characteristics of Aboriginal people with prevalent diabetes in 2018/19 in the NT, with comparison by region

	Total NT (n=3477)	Central Australia (n=1382)	Top End (n=2095)	*P* value (CA vs TE)
Age, years	49 (39-58)	48 (37-58)	49 (40-58)	0.003
Female	2115 (61)	834 (60)	1281 (61)	0.637
Diabetes type				0.269
Type 2	3429 (98.6)	1368 (98.9)	2061 (98.4)	
Type 1	34 (1.0)	9 (0.7)	25 (1.2)	
Other	14 (0.4)	5 (0.5)	9 (0.4)	
Treatment				
No GLT	1627 (47)	542 (39)	1085 (52)	<0.001
Non-insulin GLT	1181 (34)	508 (37)	673 (32)	0.005
Combined GLT (with insulin)	610 (18)	307 (22)	303 (15)	<0.001
Insulin alone	59 (1.7)	25 (1.8)	34 (1.6)	0.678
Mean HbA1c*				
(NGSP %)	7.9 (±0.04)	8.4 (±0.07)	7.7 (±0.05)	<0.001
(mmol/mol)	63 (±0.4)	68 (±0.8)	61 (±0.5)	
Median HbA1c*				<0.001
(NGSP %)	7.2 (6.1-9.4)	7.8 (6.3-10.1)	7.0 (6.0-8.9)	
(mmol/mol)	55 (43-79)	62 (45-87)	53 (42-74)	
HbA1c category*				<0.001
<7.0% (<53 mmol/mol)	1216 (35)	375 (27)	641 (40)	
7.0-7.9% (53-63 mmol/mol)	415 (12)	159 (12)	256 (12)	
8.0-9.9% (64-85 mmol/mol)	540 (16)	228 (17)	312 (15)	
≥10% (≥86 mmol/mol)	567 (16)	281 (20)	286 (14)	
No result	739 (21)	339 (25)	400 (19)	

Data are n (%), median (IQR) or mean (±SE). CA = Central Australia, TE = Top End, GLT = glucose lowering therapy, HbA1c = haemoglobin A1c. *The single most recent HbA1c result for each individual within the 2018/19 year was included. Individuals with no HbA1c in that 12 month period were excluded from calculation of means/medians and reported in the "no result" category.

Figure Legends

Figure 1. Map of the Top End (TE) and Central Australia (CA) regions of the Northern Territory, Australia, showing the 51 remote clinics (triangles) and 6 hospitals (crosses) contributing data to this study

There are two hospitals in the location at the top left (North West) of the Top End. Distances and locations are approximate.

Figure 2. Trend in crude diabetes prevalence among Aboriginal people (all ages) in remote NT communities over seven years

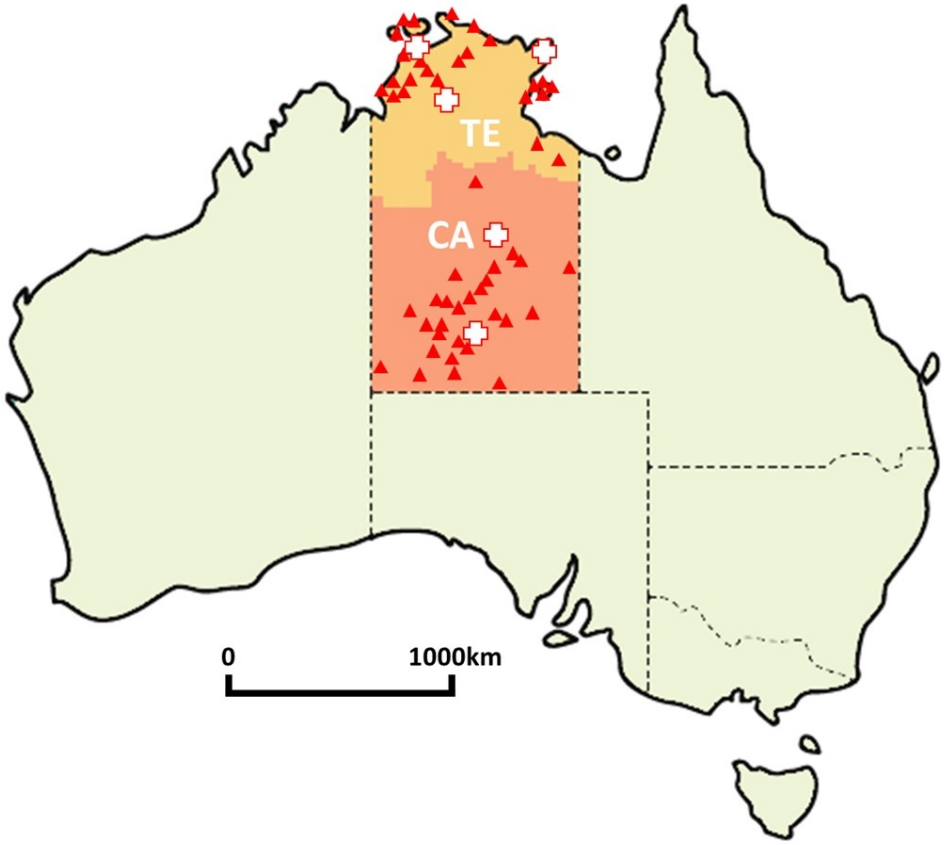
Error bars are 95% confidence intervals. Note the vast majority of prevalent diagnoses were classified as type 2 diabetes (98.6% type 2, 0.17% type 1 and 0.07% other diabetes in 2018/19).

Figure 3. Age and sex-specific diabetes prevalence in 2018/19 among Aboriginal people in remote NT communities

Error bars are 95% confidence intervals.

Figure 4. Age-specific diabetes incidence rates between 2016/17 and 2018/19 among Aboriginal people in remote NT communities

Error bars are 95% confidence intervals. Out of 483 incident diabetes diagnoses, 481 (99.6%) were recorded as type 2 diabetes.



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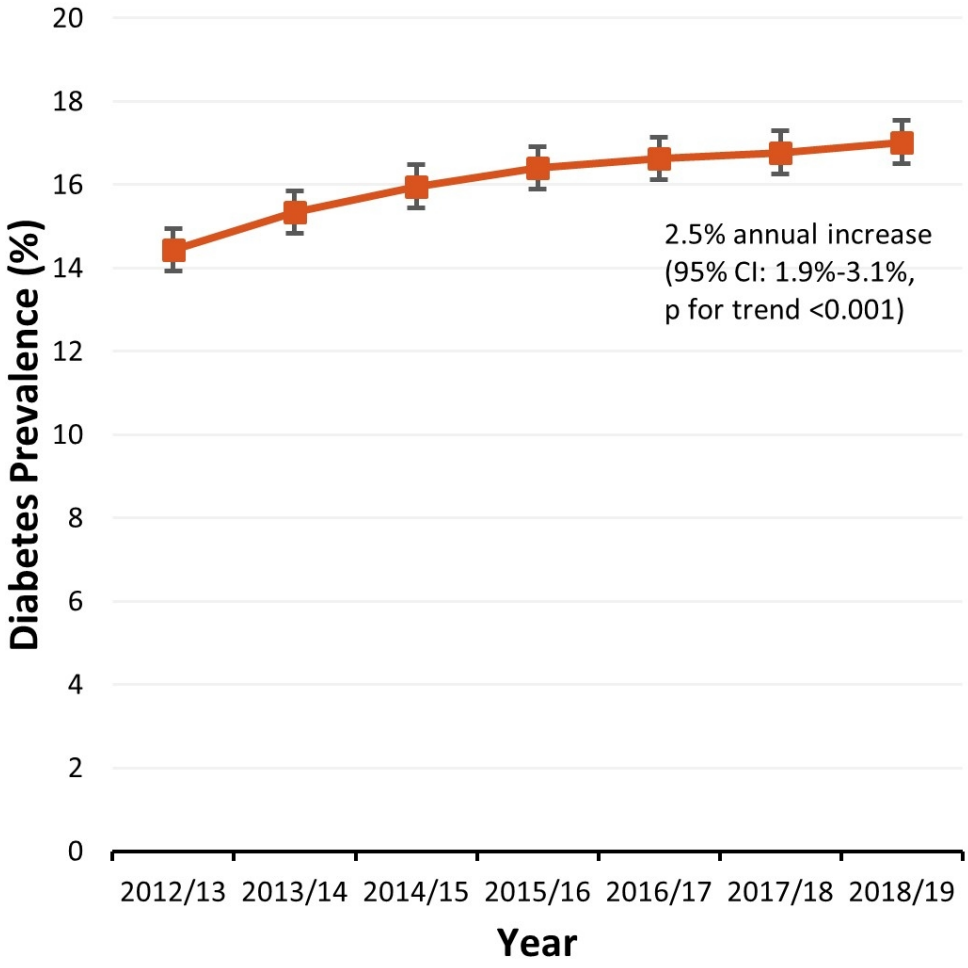

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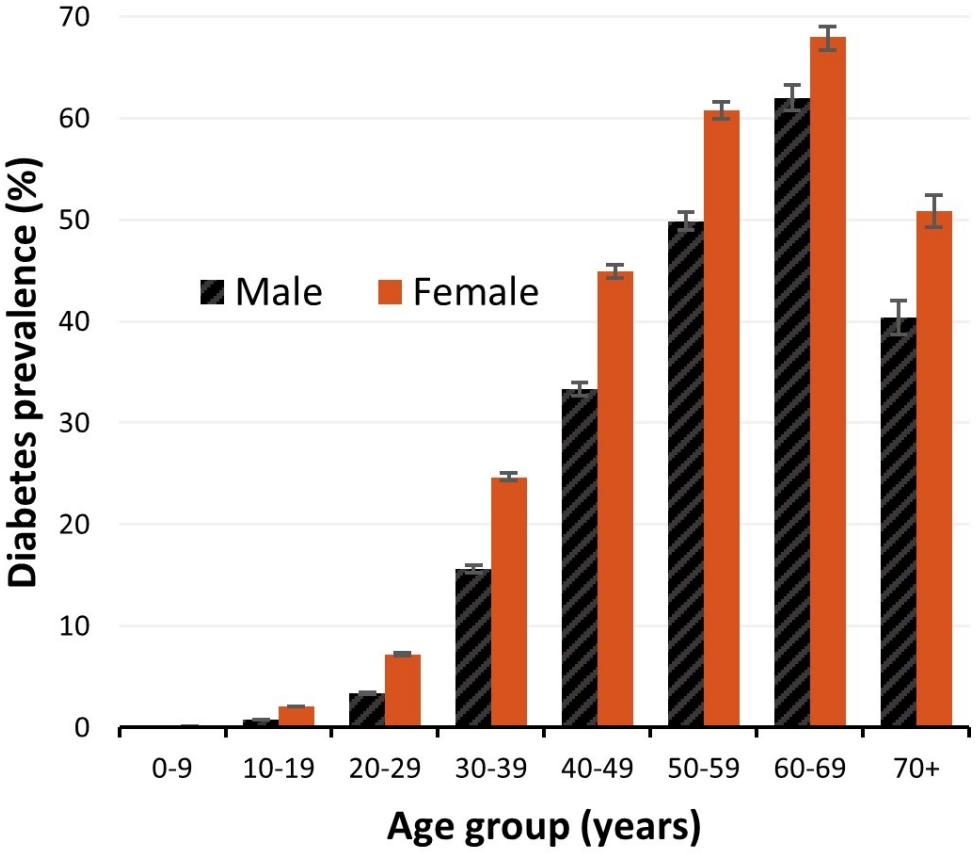

Diabetes prevalence (%)

Male	0.05	0.79	3.37	15.6	33.4	49.9	62.0	40.4
Female	0.10	2.05	7.20	24.7	44.9	60.8	68.0	50.9

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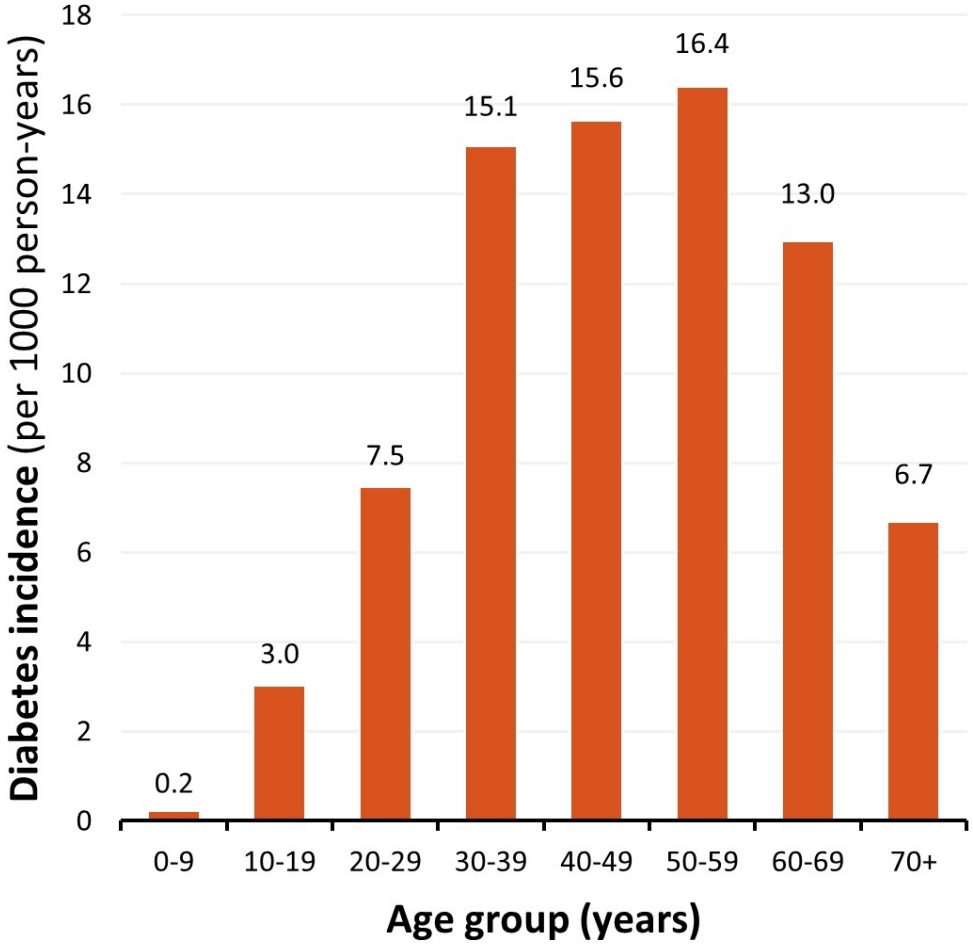

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APPENDIX

Supplementary Table 1. ICPC and ICD-10-AM diagnostic codes used in diabetes case definitions

	ICPC	ICD-10-AM
Any diabetes	T89* T90*	E10*-E14* O24.0-O24.3 O24.5 O24.9
Type 1 diabetes	T89002	E10* O24.0
Other diabetes	T90017	E13*
Gestational diabetes	W85*	O24.4

** indicates truncation. ICPC: International Classification of Primary Care; ICD-10-AM: International Classification of Diseases, Tenth Revision, Australian Modification.*

Validation study results

Manual review of individual electronic health records was undertaken to inform our study definition of diabetes. Three specific potential issues were targeted including: (i) whether or not prescription of metformin indicates a diagnosis of diabetes, (ii) whether cases of gestational diabetes mellitus (GDM) were adequately excluded, and (iii) the accuracy of determination of diabetes type, especially in young-onset diabetes. This work was undertaken by a single research assistant with a clinical background under the supervision of an endocrinologist, who personally reviewed all records where there was any doubt about the patient's diabetes diagnosis.

Metformin prescription was removed from the study definition of diabetes following manual review of a sample (n=62) of people prescribed metformin but with no other glucose-lowering medication, no coding for a diabetes diagnosis and no biochemical data to support a diabetes diagnosis. Of these people, 52 (81%) did not have diabetes. The most common indication for metformin in this subgroup was diabetes prevention in high-risk individuals (including pre-diabetes, evidence of insulin resistance and antipsychotic use), followed by GDM and polycystic ovarian syndrome.

To avoid including diagnoses of GDM, we excluded all medication and biochemistry data in the nine months preceding and three months following the allocation of a GDM diagnostic code in either the primary care or hospital datasets. In order to assess this approach, we investigated the health records of a random sample of women (n=40) of childbearing age (born between 1st July 1968 and 1st July 1998) who had been defined as having diabetes. Once metformin had been removed from the study definition of diabetes, 39 (98%) of these women were confirmed as having established diabetes. Therefore, we deemed that the approach to excluding GDM was adequate.

With regard to determining diabetes type, we were concerned about two non-specific ICPC codes (T89001 – "Insulin dependent" and T89003 – "Juvenile onset") intended to report type 1 diabetes in the ICPC classification system. Insulin is frequently used for type 2 diabetes and there is a high burden of youth-onset type 2 diabetes among Aboriginal people in the Northern Territory. In a random sample (n=28), only 4 (14%) of people coded as T89001 had type 1 diabetes, therefore we did not include this code in our type 1 diabetes definition. Only two people were assigned the

T89003 code. One of these had type 2 diabetes, the other had pre-diabetes. This code was also removed from the type 1 diabetes definition.

To further assess the accuracy of identification of diabetes type in young people, we took a random sample (n=40) of people with diabetes born on or after 1st July 1988. Only one of these people had type 1 diabetes and it had been coded appropriately in the study dataset.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6 (+appendix)
Bias	9	Describe any efforts to address potential sources of bias	5,13
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	19
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	19
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8,9
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8,9
		(*b*) Report category boundaries when continuous variables were categorized	19
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.