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COHORT PROFILE

Cohort Profile: The Fremantle Diabetes Study

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Why was the cohort set up?

When the Fremantle Diabetes Study (FDS) Phase I was conceived in 1991 by its chief investigator (T.M.E.D.), there were few published longitudinal community-based diabetes natural history studies. Population studies such as Framingham[1] in the United States and Busselton[2] in Australia contained relatively small subgroups from which limited additional diabetes-specific information was collected. The United Kingdom Prospective Diabetes Study (UKPDS) had recruited more than 5000 newly diagnosed type 2 subjects aged 25–65 years but the sample, although relatively large, was not community based. The diagnosis of diabetes was based on a low fasting plasma glucose concentration (>6 mmol/l), and the study was interventional with outcomes presented in 1998.[3] There were also Australia-specific aspects of diabetes that had not been characterized in detail, especially the disproportionately large number of patients from a migrant (especially Southern European) background[4] and the important question of diabetes in indigenous groups.[5]

The aim of FDS Phase I was, therefore, to identify from all potential sources, and collect detailed prospective data from, known diabetic patients in a stable multi-ethnic urban Australian population to examine clinically relevant aspects of diabetes including clinical management, metabolic control, complications and cost. Based on the amount of available seeding funding from the Raine Foundation, University of Western Australia (WA) and respecting a reasonable patient time commitment and throughput, it was decided to attempt to recruit all consenting patients from the Fremantle Hospital (FH) primary catchment area, a postcode-defined population of approximately 120 000 living in and around the port of Fremantle in Western Australia. A 3-year registration period between 1993 and 1996 was followed by yearly reviews of the FDS Phase I cohort until 2001 (a minimum follow-up of 5 years) by which time more than half of the patients had died or withdrawn, although acquisition of hospitalizations, cancer registrations and deaths through the WA Data Linkage System (WADLS)[6] has continued since.

During and after the active data collection in Phase I, the results of a number of studies were published that provided important data relating to diabetes epidemiology and management. The Australian Diabetes, Obesity, and Lifestyle (AusDiab) Study[7] showed that the prevalence of diabetes had increased at the rate of 0.15%/year in males and 0.18%/year in females in individuals aged $\geqslant$25 years during the 19 years since the first Australian estimate from the Busselton survey in 1981.[2] The incidence of type 1 diabetes in Australia was also increasing.[8] A contributor to this increased prevalence was the lowering of the threshold fasting plasma glucose for diagnosis of diabetes from 7.8 mmol/l to 7.0 mmol/l by the World Health Organization in 1999.[9]

In relation to management, results of the Diabetes Control and Complications Trial (DCCT) in type 1 diabetes were first presented in 1993 and confirmed the benefits of tight glycaemic control in the prevention of microvascular disease.[10] Parallel findings for type 2 diabetes from the UKPDS followed in 1998[3,11] but the UKPDS also highlighted the vascular benefits of intensive management of hypertension.[12] Other landmark non-glycaemic intervention trials, such as the Heart Outcomes Prevention Evaluation (HOPE and MICRO-HOPE),[13] the Heart Protection Study[14] and the Fenofibrate Intervention and Event Lowering in Diabetes Study[15] provided further evidence of the benefits of individual intensive vascular risk factor management in type 2 diabetes. The Steno-2 Study extended these findings in a multifactorial intervention that reduced both micro- and macrovascular disease.[16] In addition, the 33% 2-year mortality rate in conventionally treated diabetic patients after myocardial infarction in the Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction (DIGAMI) Study carried out in the early 1990s[17] had fallen to 19% in similar patients in the more recent DIGAMI-2 Study[18] in the presence of increased

use of aspirin, β-blockers, ACEI and especially statin therapy. These studies were likely to have influenced changes in management of Australian diabetic patients during and after the active data collection in Phase I.

Although findings from Phase I had contributed to an understanding of the natural history of diabetes, the changes in diabetes epidemiology and management justified a Phase II that duplicated and extended data collection. Funding for this new study was obtained from the National Health and Medical Research Council of Australia and it started in the first part of 2008, some 15 years after the first patient was recruited to Phase I. The Phase II baseline cohort was recruited over a 3-year period from the same catchment area using similar methods of ascertainment as Phase I. Longitudinal follow-up data collection is continuing at present.

Who is in the cohort?

The samples for Phases I and II have been drawn from the same geographical area. From Australian Bureau of Statistics data,[19] there were 120 000 people in the postcode-defined catchment area at the start of Phase I in 1993 and 153 000 in 2008 at the start of Phase II. In addition to a 28% increase in the population during the 15 years between Phases I and II, the demography and ethnic mix have changed. For example, the percentage born in Southern Europe has fallen from 7.4% to 2.5% and the mean age has increased with those aged $\geqslant 50$ years comprising 30.7% compared with 25.6% in 1993.

In Phase I, diabetic patients residing in the study catchment area were identified from FH clinic and inpatient lists, local physician referrals, allied health facilities, pharmacies, opticians, advertising in local media and word of mouth. Of 2258 potential subjects identified during registration between 1993 and 1996, 1426 (63%) were recruited.[20,21] This compares favourably with the AusDiab Study, which recruited 41% of randomly selected households and obtained biomedical data from 56% of identified individuals within them.[7] A range of baseline and outcome data was also collected from the 832 patients who were identified but not recruited to provide an objective assessment of the representative nature of the sample. Eligible patients who declined participation were a mean of 1.4 years older than participants, but their country of birth, sex distribution and the distributions of diabetes types and treatment modalities were similar.[20,21]

For Phase II, recruitment strategies were the same as those used in Phase I except that third-party mail-outs of potentially eligible patients were arranged through the Australian National Diabetes Services Scheme and National Diabetes Register. A consort diagram that summarizes recruitment is shown in Figure 1. There were 4952 diabetic patients identified between 2008 and 2011, including 796 original Phase I surviving participants of whom 168 had moved out of the study area but from whom long-term follow-up data were being sought. A total of 1732 (35.0%) subjects were recruited to Phase II (including 64 non-resident Phase I subjects), a lower rate than Phase I but still higher than AusDiab.[7] Exclusion of the out-of-area participants left 4784 identified and residing within the study area with 1668 (34.9%) of these recruited.

As in Phase I, data are being collected to characterize as many non-recruited patients as possible from all possible sources (Table 1). Phase II non-recruited subjects were a mean of 1.2 years younger than participants at the start of recruitment but their sex distribution was similar with just over 50% males. Available preliminary data for other variables including ethnicity do not show marked differences.

How often have they been followed up?

In Phase I, baseline and subsequent annual assessments were performed until death, withdrawal, relocation out of the study area or the close-out of individual patient data collection in 2001 (Table 2). The WADLS was established in 1995 to connect all available health and related information for the WA population.[6] The FDS has been linked with the WADLS since 2001 and continues to receive regular data updates. The latest regular update was in early 2011, providing up to 17 years of follow-up of our Phase I cohort. Data collections linked by WADLS include core datasets comprising the Hospital Morbidity Data Collection (HMDC; since 1970), Emergency Department Data Collection (since 2002), Western Australian Cancer Registry (since 1982) and the Death Register (since 1969). Linkage has also been possible with Silver Chain[22] (one of the largest providers of community and health services to the WA community) and St John Ambulance[23] (the main ambulance provider in Western Australia) in collaboration with their respective data custodians but facilitated by the WADLS. The Metropolitan Cemeteries Board[24] database and individual hospital case notes have also complemented and validated linkage data.

At the beginning of Phase II recruitment in mid-February 2008, 603 (42.3%) of the original Phase I cohort had died and 27 were lost to follow-up (18 had definitely/probably moved overseas or interstate, whereas the whereabouts of 9 was unknown). By the end of Phase II recruitment at end-June 2011, a further 124 had died, 106 of whom were unable to be recruited to Phase II out of the remaining 406 Phase I patients (Table 2). In summary, $<2\%$ of the original cohort is no longer providing data for analyses. Table 1 compares the characteristics of Phase I

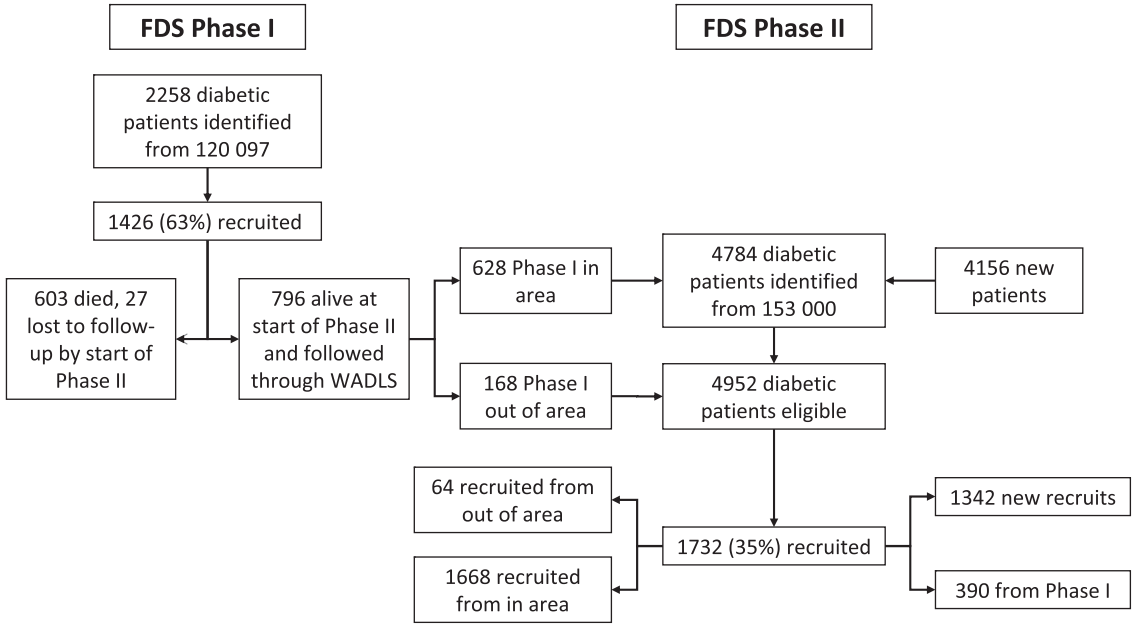

Figure 1 Consort diagram showing patient recruitment for both phases of the FDS

participants who (i) were recruited to Phase II, (ii) were alive at the start of Phase II recruitment and had not been lost to follow-up but who were not recruited and (iii) either died before Phase II started or were lost to follow-up before Phase I.

In Phase II, baseline and subsequent biennial detailed assessments will be performed until death or withdrawal, but questionnaires are being sent out every second year to gather data, including those relating to changes in management and the development of complications and co-morbidities, to complement full in-person data collection. In contrast to Phase I, relocation out of the study area will not be a criterion for cessation of active data collection. As the recruitment period for Phase II only recently closed, there has been insufficient time for an assessment of attrition in this cohort.

What has been measured?

The data collected at baseline and at each subsequent visit (annually for Phase I and biennially for Phase II) are summarized in Table 3.

Modified questionnaires are sent out to Phase II participants in intervening years based on the self-reported data collected in person.

In both phases, patients have attended after a >10-h overnight fast with venous blood and spot morning urine specimens collected, and serum and plasma prepared from centrifuged blood. Routine care analytes are assayed the same day in a single nationally accredited biochemistry laboratory. Either the same assay methodology has been used for both Phases or calibration equations are applied when assays change.

What has it found? Key findings and publications

There have been over 60 peer-reviewed publications reporting Phase I data (see (http://www.medpharm.uwa.edu.au/research/fremantle_diabetes_study). The broad research themes covered by Phase I have been the following:

(i) Epidemiology: these reports have ranged from the identification of a low prevalence of latent autoimmune diabetes of adults (LADA) in a multi-ethnic setting[21] and a poor outcome in type 2 indigenous patients[48] to an assessment of the nature of type 2 diabetes in young[49] and elderly[20] Australians. Phase I also showed that people from Southern European migrant stock have a high prevalence of diabetes and progress more rapidly to insulin therapy than other ethnic groups[50] but do not die at a younger age as a result.[51]

(ii) Clinical management: contributions in this area have ranged from data suggesting that fibrates are protective against peripheral neuropathy,[52] that elderly males with type 2 diabetes would benefit from low-dose aspirin in a primary prevention setting[53] and that renin–angiotensin system blocking drugs have equivalent effect on albuminuria in community-based patients to those reported in clinical trials,[54] to the development of an Australian diabetes cardiovascular risk calculator[55] and a diabetes-specific hand-held medical record.[56] Our data have questioned the value of self-monitoring of blood glucose (SMBG) in non-insulin-treated

Table 1 Comparison of characteristics of diabetic residents recruited to and not recruited to FDS Phase II, including those who also participated in Phase I (data as at April 2012)

Variable	New recruits to Phase II	New non-recruits to Phase II	*P*-value[#]	Phase II recruits from Phase I	Phase II non-recruits from Phase I	Phase I recruits deceased/lost to follow-up before Phase II	*P*-value[#]
N	1342	2814		390	406	630	
Age[a] (years)	60.4 ± 13.8	59.3 ± 17.7	0.029	68.4 ± 11.9	72.5 ± 13.2***	82.3 ± 11.0***,###	<0.001
Sex (male) (%)	51.9	53.0	0.53	52.6	39.7***	54.3###	<0.001
Ethnic background[b] (%)							
Anglo-Celt	53.2	63.4		64.9	62.8	64.3	0.66
Southern European	11.1	15.4		16.9	20.0	17.5	
Other European	6.9	7.6		8.2	6.9	9.2	
Asian	4.1	4.7		4.1	3.7	2.1	
Indigenous	8.0	4.9		1.0	1.2	1.6	
Mixed/other	16.8	4.0		4.9	5.4	5.4	
Not fluent in English (%)	8.8	–		12.1	13.8	16.4	0.16
Educated beyond primary level (%)	89.2	–		82.9	73.9**	71.2***	<0.001
Diabetes type[c] (1/2/other; %)	6.6/91.4/2.0	4.3/93.3/2.4		12.8/86.9/0.3	9.1/90.6/0.2	6.0/93.5/0.5**	0.003
Diabetes duration[a,d] (years)	6.0 (2.0–12.0)	–		16.6 (14.3–20.3)[e]	17.2 (14.6–21.5)[e]	19.4 (15.7–26.4)[e],***, ###	<0.001
Deceased during Phase II recruitment [*n* (%)]	34 (2.5)	296 (10.5)	<0.001	18 (4.6)	106 (26.1)	NA	<0.001

[a]Ethnic background for 2496 newly identified diabetic patients who were not recruited to Phase II was based on the country of patient's birth only, compared with self-selection, country of the patient's birth, country of father's/mother's birth and language spoken at home in Phase I.
[b]Age and duration of diabetes were as at 18 Feb 2008 (start of Phase II).
[c]Data are for 1459 new non-recruits to Phase II.
[d]Projected for those who died before Phase II started.
[e]Data are median and (inter-quartile range).
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (Phase II recruits as reference), #$P < 0.05$, ##$P < 0.01$, ###$P < 0.001$ (Phase II non-recruits as reference). Pairwise comparisons (other than for variables with incomplete data) unadjusted for multiple comparisons.

patients with type 2 diabetes[57] and have contributed to the development of the International Diabetes Federation SMBG guidelines.[58]

(iii) Acute and chronic complications: in relation to acute complications, Phase I data have shown that, in parallel with large-scale glycaemic intervention studies,[59] severe hypoglycaemia is paradoxically associated with a higher HbA_{1c} in type 2 diabetes,[60] whereas metformin-associated lactic acidosis is rare.[61] Regarding chronic complications, we found that diabetes protects against abdominal aortic aneurysms[62] but that peripheral arterial disease (PAD) has an ominous prognosis in type 2 diabetes.[63] The presence of carotid bruit, an easily detectable sign, proved to be a strong predictor of stroke among type 2 patients,[64] whereas serum HDL cholesterol was the strongest modifiable predictor of first stroke in type 1 subjects.[65] Analyses have also confirmed that silent myocardial infarction is common in diabetes but that the prognosis in such patients is better than in those with symptomatic presentations.[66]

(iv) Unconventional complications: Phase I provided some of the first data linking diabetes and, in particular, poor glycaemic control to lung damage[67] and added to the data implicating type 1 diabetes as a risk factor for osteoporosis.[68] Diabetic patients with PAD are particularly susceptible to cognitive decline and dementia,[69] whereas a history of cerebrovascular disease is a strong predictor of depression in type 2 patients.[70] Diabetes is a risk factor for hepatobiliary disease

Table 2 Longitudinal demographic data of FDS Phase I participants and reasons for loss to follow-up

Annual review,[a] *n* (%)	Phase 1 baseline 1426 (100)	1 1131 (79.3)	2 956 (67.0)	3 828 (58.1)	4 694 (48.7)	5 579 (40.6)	6 410 (28.8)	7 225 (15.8)	8 35 (2.5)	Phase 2 baseline 390 (27.3)
Follow-up time (years)	0	1.1 (1.0–1.2)	2.1 (2.0–2.4)	3.2 (3.0–3.5)	4.2 (4.1–4.5)	5.3 (5.1–5.6)	6.3 (6.2–6.6)	7.3 (7.2–7.5)	8.2 (8.0–8.3)	14.7 (14.0–15.4)
Age (years)	62.1 ± 13.3	63.3 ± 12.3	64.1 ± 11.9	64.9 ± 11.6	65.8 ± 11.2	66.5 ± 10.9	67.2 ± 10.1	69.5 ± 9.0	74.8 ± 5.7	69.7 ± 11.8
Gender (male) (%)	49.6	51.1	51.9	52.8	53.6	55.1	54.1	52.4	54.3	52.6
Diabetes type (1/2/other) (%)	8.9/90.7/0.4	8.1/91.5/0.4	8.1/91.5/0.4	8.2/91.5/0.2	7.9/91.8/0.3	7.9/91.7/0.3	6.6/92.9/0.5	4.9/94.7/0.4	2.9/97.1/0	13.3/86.4/0.3[b]
Diabetes duration (years)	4.0 (1.0–10.0)	5.1 (2.1–11.0)	6.1 (3.1–11.1)	7.1 (4.2–11.8)	8.0 (5.2–12.4)	9.0 (6.3–13.2)	9.8 (7.4–13.7)	11.2 (8.3–14.8)	12.4 (9.7–17.9)	17.9 (15.6–21.7)
Marital status (currently married/*de facto* relationship) (%)	64.7	65.8	66.4	64.1	66.2	63.8	66.4	67.9	73.5	55.4
English ability (non-fluent) (%)	14.5	14.1	13.1	12.7	12.5	12.1	10.2	8.0	0	14.1
Educational attainment (⩽ primary schooling) (%)	24.8	24.5	22.8	23.0	22.5	21.6	19.7	19.1	22.9	19.3
Ethnic background (%)										
Anglo-Celt	64.0	65.2	65.3	65.7	67.3	68.6	70.2	76.0	80.0	64.9[c]
Southern European	18.0	17.6	17.3	17.4	17.1	16.6	15.6	14.2	11.4	16.9
Other European	8.3	8.0	7.8	8.1	8.6	8.5	7.8	5.3	5.7	8.2
Asian	3.1	3.4	3.7	3.3	3.0	2.8	2.7	1.3	0	4.1
Mixed/other	5.3	5.0	5.2	5.0	3.7	3.5	3.4	3.1	2.9	4.9
Indigenous	1.3	0.9	0.7	0.6	0.1	0.2	0.2	0	0	1.0
Reasons for loss to follow-up (*n*)										
Death[a] [165 (11.6%)]		45	30	21	20	24	11	11	3	603 + 106
Moved out of area [124 (8.7%)]		69	23	13	10	4	5	0	0	2[d]
Withdrew [421 (29.5%)]		143	99	68	70	31	8	2	0	205
Unknown[e] [84 (5.9%)]		38	6	6	9	10	12	3	0	n/a
Study closed[f] [632 (44.3%)]		17	20	25	46	133	169	187	35	n/a
										Other[g]:120
Total (1426)		312	178	133	155	202	205	203	38	

[a]There were 317 (22.2%) deaths by 1 November, 2001 (end Phase I active follow-up); 603 (42.3%) before Phase II baseline assessments started on 18 February, 2008 and 727 (51.0%) before Phase II baseline assessments closed; deaths counted in each year if they occurred within 1.5 years of the last assessment.
[b]In Phase II, categorization of type of diabetes was not constrained with respect to age at diagnosis but, for comparison purposes, the Phase I classification is presented.
[c]In Phase II, grandparent country of birth (COB) was ascertained in addition to participant and parents' COB leading to an increase in category 5 (mixed). For comparison purposes, the Phase I classification is presented.
[d]Moved overseas during Phase I.
[e]⩾1.5 years from last visit to last Phase I assessment date (1 November 2001).
[f]<1.5 years from last visit to 1 November 2001.
[g]Other = no response/return to sender/not on electoral roll ($n = 115$), poor health ($n = 5$).

Table 3 Data collection in FDS Phases I and II

Questionnaires	
	(1) Demographic details
	(2) Diabetes-related information
	(3) Current lifestyle measures—in Phase II, this includes specific validated questionnaires relating to diet[25,26] and physical activity[27,28]
	(4) Availability of, and access to, care
	(5) Knowledge of diabetes—including a validated knowledge test in both Phases[29]
	(6) General medical information —including, in Phase II, a family history of diseases[30] and Berlin sleep[31] questionnaires
	(7) Current health status—ascertained by General Health Questionnaire[32] in Phase I and by multiple validated instruments[33–36] in Phase II
	(8) Cognitive function, mood and activities of daily living and others if indicated clinically—this can include, for Phase II, the mini-mental state examination and other validated instruments[37–39]
	(9) Costs of diabetes—determined from self-reported health service usage and linkage to WADLS and associated databases[40–42]
Clinical examination	
	(1) Anthropometric measures—including, in Phase II, body fat by bioimpedance[43]
	(2) Cardiovascular status—including autonomic function testing,[44] auscultation for carotid bruits, Doppler studies for determination of ankle:brachial index and resting 12-lead electrocardiography
	(3) Respiratory assessment—including spirometry
	(4) Neurological assessment—data relevant to the Michigan Neuropathy Screening Instrument clinical score[45]
	(5) Ophthalmic assessment—including fundus photography in Phase II
	(6) Skin autofluorescence—in Phase II only[46]
	(7) Pulse wave velocity—in a randomly selected sample of 50% of Phase II patients[47]
	(8) Overnight home-based sleep studies—in a subset of Phase II patients with Berlin scores that are either low risk or high risk for obstructive sleep apnoea
Laboratory tests	
	(1) Serum glucose, glycated haemoglobin, serum urea, creatinine and electrolytes, serum cholesterol, triglycerides, HDL-cholesterol and non-HDL-cholesterol, serum uric acid, liver function tests, urine albumin and creatinine
	(2) Glutamic acid decarboxylase antibodies at baseline (Phase I)[21]
	(3) Full blood count (Phase II)
	(4) Extraction and storage of DNA
	(5) Aliquots of remaining serum, plasma, urine and whole blood stored at −80°C for further specialized analyses when required

and associated mortality,[71] but the contribution of fatty liver appears to have been overestimated.

(v) Health-economic implications: Phase I data have shown that the costs of diabetes in Australia could quadruple over the next 40 years if current trends continue,[72] with a substantial contribution from medications to treat non-glycaemic cardiovascular risk factors.[40] However, even moderate weight loss ($\geqslant$5% of initial body weight) confers important cost savings.[41]

Phase I spawned the Fremantle Diabetes and Cognition Study, which has produced a range of data, including evidence that community-living older diabetic subjects have high rates of cognitive impairment, deficits in physical function and depressive symptomatology.[73]

What are the main strengths and weaknesses?

The strengths of both Phases of the FDS are the inclusive and generally representative nature of the cohorts, the range and detail of data collection and linkage to well-established morbidity and mortality databases in Western Australia and, in future, Australia as a whole. The design and implementation of the FDS means that specific questions regarding

the natural history of diabetes, its impact on the individual and its costs can be addressed with relative rigour. The main weakness was the proportion of patients who were not recruited or who withdrew despite repeated attempts to contact them and, if this was successful, to arrange assessments at a convenient time. The lower recruitment rate in Phase II vs Phase I reflected, in part, the institution of government-funded diabetes care plans through primary care in 1999[74] that ensured availability of free or subsidized regular metabolic and complications screening. The FDS assessment was considered by some potential recruits and previous participants as a duplication of this service.

Specific limitations of Phase I, which arose partly because of the time when it was designed, have been addressed in Phase II, including (i) employment of an Aboriginal health worker to facilitate recruitment and follow-up of indigenous patients (112 recruited to Phase II compared with only 20 in Phase I), (ii) third-party mail-outs through national diabetes-related organizations that helped quantify the number of people in the catchment area with diabetes as well as facilitating recruitment, (iii) pre-appointment posting of questionnaires to be completed in advance and thus reduce the time commitment (between 2 and 3.5 h if data were collected), (iv) institution of home assessments for patients unable to attend FH and (v) availability of out-of-hours assessment timeslots for young, working patients.

The choices of sample size and range of data to be collected in a study such as FDS are restrained by financial and logistic considerations. Relatively subtle but clinically important effects of diabetes on outcomes may be missed if the sample size is too small. However, attrition from natural causes and patient withdrawal, such as that which occurred in Phase I, should be factored in to sample size selection. Patient recruitment and retention depend on time commitment, which can be reduced if processes are in place allowing patients to progress through varied assessments and procedures efficiently. Employing dedicated personnel to engage special groups (such as those from an indigenous background) is strongly recommended, as evidenced by an increase in Aboriginal participants from 1.3% of the cohort in Phase I to 6.5% in Phase II.

FDS data are observational and subject to inherent limitations. An example of this is when intervention effects are estimated. Nonetheless, there is little evidence that such estimates in well-conducted observational studies are consistently larger than, or qualitatively different from, those obtained in randomized controlled trials (RCTs).[75] RCTs remain the gold standard evidence base for management of complex conditions such as diabetes, but observational studies can be useful or complementary where RCTs have incomplete coverage or are difficult. Examples include recruitment of the elderly or those with multiple complications and when effects may be maximal over a long period of follow-up.

Can I get hold of the data? Where can I find out more?

The data are held in a secure, confidential database, which can only be accessed by members of the FDS team. The data custodian is the FDS biostatistician (W.A.D.) who, with the chief investigator (T.M.E.D.), is the main point of contact. The FDS has a dedicated website (http://www.medpharm.uwa.edu.au/research/fremantle_diabetes_study).
Researchers with similar data who might want to share ideas or suggest collaborative projects should contact T.M.E.D. or W.A.D.

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Conflict of interest: None declared.

KEY MESSAGES

Among a range of outcomes, the FDS has found the following:

- Relative to the majority Anglo-Celt ethnic group, patients of Southern European migrant stock have a high prevalence of type 2 diabetes and progress more rapidly to insulin therapy, and Australian Aborigines with diabetes have worse glycaemic control and a poor prognosis.

- Fibrates are protective against peripheral neuropathy, and elderly males with type 2 diabetes benefit from low-dose aspirin in a primary prevention setting.
- Diabetes protects against abdominal aortic aneurysms but peripheral vascular disease has an ominous prognosis in type 2 diabetes.
- Diabetes and, in particular, poor glycaemic control contribute to lung damage, whereas peripheral vascular disease and cerebrovascular disease are associated with dementia and depression, respectively, in type 2 patients.
- The costs of diabetes in Australia are likely to quadruple over the next 40 years.

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