DiabCare 2013: A cross-sectional study of hospital based diabetes care delivery and prevention of diabetes related complications in Malaysia

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ABSTRACT

Aims: The aim of the study was to re-evaluate the relationship between hospital based diabetes care delivery and prevention of complications.

Methods: DiabCare is an observational, non-interventional, cross-sectional study of hospital-based outpatient diabetes care.

Results: A total of 1668 patients participated in the study: mean age 57.8 ± 11.0 years, duration of diabetes 13.0 ± 8.6 years, and duration of insulin treatment 5.6 ± 5.5 years. Mean weight was 74.3 ± 16.6 kg (BMI 29.1 ± 5.8 kg/m2). The majority of patients were female (53.6%) and the largest ethnic group was Malay (51.3%), followed by Indian (21.9%) and Chinese (20.1%). The percentage of patients with HbA1c < 6.5% (< 42 mmol/mol) and < 7.0% (< 53 mmol/mol) was 12.2% and 23.8%, respectively (mean HbA1c 8.52 ± 2.01% [70 ± 22 mmol/mol]). The proportion of patients using insulin was 65% at a total daily dose of 60 ± 37 IU. One or more episodes of hypoglycaemia were reported by 39% (n=658) of patients within the previous three months. The risk of any hypoglycaemia was associated with the use of insulin (odds ratio [OR 3.26, 95% CI 2.59–4.09]), and total daily insulin dose (OR 1.04, 95% CI 1.01–1.07 per 10 IU increase). Mean HbA1c had not changed significantly between DiabCare cohorts 2008 and 2013 (p=0.08).

Conclusions: Despite evidence of improving processes of diabetes care, glycaemic control and the prevalence of many diabetes related complications were unchanged.

KEY WORDS:
Type 2 diabetes mellitus; hospital care; prevention; diabetes complications; hypoglycaemia

INTRODUCTION

Diabetes is one of the three major non-communicable diseases in the Asia Pacific region.[1] Malaysia has one of the highest and most rapidly increasing prevalence of diabetes in the Western Pacific region, with a national prevalence of 16.6% in 2014.[2] This compares adversely with a worldwide diabetes prevalence of 8.3%. Rates of urbanisation, lifestyle Westernisation and a demographic shift toward an aging population are some of the reasons why diabetes is becoming a major challenge for developing Asian countries.[3] Strategies aimed at preventing long-term diabetes complications can have a substantial impact on a developing, but fragile, economy.[3] Diabetes-related end-stage renal failure alone has been estimated to result in a decade of lost life-years, and a disproportionate increase in healthcare expenditure.[4] The escalating burden of non-communicable diseases has major implications for healthcare services that remain oriented towards the care of acute illnesses and maternal and child health.[5]

DiabCare is a series of cross-sectional observational studies, with the most recent being DiabCare 2013. These studies used an evidence-based approach to evaluate diabetes management, control, complications, and psychosocial aspects of living with type 2 diabetes, and to monitor the effects of social and economic change. In Malaysia, the results of successive DiabCare audits have facilitated diabetes healthcare policy decision-making.[6-9] Specific examples include the successive revision of the Malaysian Clinical Practice Guidelines for Type 2 Diabetes Mellitus, introduction of a national Diabetes Nurse Educator training programme, establishment of dedicated diabetes clinics, and standardised procedures for follow-up of diabetes patients.[10,11] However, many patients with diabetes still attend general medical clinics, often without structured diabetes management plans.[12] Gaps between national guidance and clinical practice, particularly in terms of deficiencies in lifestyle interventions and screening for complications have been highlighted.[12, 13]

The present study (DiabCare 2013) aims to describe the status of hospital-based outpatient diabetes care in Malaysia, and re-evaluate the relationship between diabetes duration, long-term complications, treatment and prevention in this patient population.

MATERIALS AND METHODS

Subjects

The present study used an observational, non-interventional, cross-sectional study design (clinicaltrial.gov registration

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number: NCT01934673). Participants were patients with type 2 diabetes recruited from 19 centres between September and November 2013. All participating centres were tertiary care government or public hospitals with more than 100 diabetes patient visits per month.

Study Procedures

The study was approved by an independent ethics committee, and co-ordinated by a national steering committee comprising eight members. All aspects of the study were conducted in accordance with the Declaration of Helsinki and the Guidelines for Good Pharmacoepidemiology Practice (GPP). Informed consent was obtained from all participating patients. Screening, enrolment, cross-sectional data collection, and all other study procedures were performed and supervised by DiabCare study investigators or their co-investigators, during a single study specific visit. To ensure adherence to the study protocol, one steering committee member was present during the visit. No assistance was provided by staff working at participating centres. Information collected for this study was kept confidential. Appropriate measures such as encryption were enforced to protect patient identity. Records containing patients' sensitive data were kept with the investigators according to local regulations pertaining to personal data protection.

Participants were screened by the DiabCare study team to confirm their eligibility. Inclusion criteria were: ≥18 years of age; a clinical diagnosis of type 2 diabetes, pharmacological or non-pharmacological diabetes treatment for ≥2 years; last visit to the centre within the previous three to six months; and willingness to provide informed consent. Patients were excluded if they had previously participated in the study, were deemed to be unable to comply with the requirements of the study protocol, or if they had a confirmed or suspected pregnancy. Patients were enrolled consecutively and recruitment continued until the target number of patients was reached. Patients were treated according to routine clinical practice, at the discretion of the treating physician.

Relevant data were collected from the medical records of eligible patients and recorded in standardised case record forms (CRFs). Data were collected by patient interview during enrolment and from medical records. Data collected from the medical records included patient demographics, clinical history, complications, eye and foot examinations, diabetes management, and most recent laboratory investigations (within the past one year). Patients were asked to complete three questionnaires: the EuroQol-5 Domain (EQ-5D) health questionnaire; a treatment adherence questionnaire; and a hypoglycaemia questionnaire. Questionnaires were administered by interview with the responsible investigator or their deputy. Venous or capillary blood samples were obtained from all patients for glycated haemoglobin A1c (HbA1c) assessment by a central laboratory, according to National Glycohaemoglobin Standardisation Programme (NGSP) guidelines, as described elsewhere.[14] All CRF data were entered into a database by double data entry. Data were validated and any discrepancies were followed up until all queries were resolved.

The primary endpoint was defined as the proportion of patients having HbA1c less than 7% (53 mmol/mol), as measured by the central laboratory, upon study entry. Secondary endpoints included: duration of diabetes, duration and type of treatment, other measures of glycaemic control (fasting plasma glucose (FPG) and post-prandial glucose (PPG)), lipid control (total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and fasting triglycerides), presence of diabetes-related complications or known risk factors (dyslipidaemia and hypertension), hypoglycaemia, treatment adherence, and quality of life.

DiabCare 2008 cohort

In order to evaluate trends over time, the DiabCare 2013 cohort has been compared with the historic Malaysian DiabCare 2008 cohort. The DiabCare 2008 study was conducted from 6th April 2009 to 30th December 2009, and included subjects recruited from the same centres participating in the present study. The methodology for both studies was identical, but for the addition of the EQ-5D and hypoglycaemia questionnaires. Results of the DiabCare 2008 cohort have been published previously.[8]

Statistical analysis

The prevalence of cardiovascular disease (CVD) was used as the basis for sample size calculation. Assuming a CVD prevalence of 2.5%, a sample of 1667 patients was needed to determine the prevalence of the most infrequent diabetes complications with 90% power and a 30% margin of error.

The full analysis set (FAS) included all patients with at least one data point, and was used for all analyses. No standardisation or transformation of locally recorded laboratory values was performed. Missing data were not replaced. The number of missing patients is reported in the tables. The level of significance was set at $p = 0.05$.

Continuous variables were summarised using descriptive statistics: mean ± standard deviation (SD), median (range), and number missing. Categorical variables were presented as number and percentages (%). Unless otherwise specified, percentages were calculated from the proportion of patients with non-missing values.

The influence of potential predictor variables on outcome variables (any diabetes complications) were evaluated by analysis of covariance (ANCOVA) for continuous variables, and by logistic regression for categorical variables. Multivariate analyses included all candidate predictor variables. Candidate variables were retained in the model using a backward stepwise model procedure (criteria for retention in the model $p < 0.05$).

Unless otherwise specified, comparisons of continuous data between DiabCare 2013 and 2008 cohorts were made using Student's t-test for normally distributed data and the Mann-Whitney test for non-normally distributed data. Comparisons of categorical data between the two cohorts were made using the Chi square test. As the two cohorts were non-randomised, the statistical significance of these comparisons should be interpreted with caution.

RESULTS

Demographics

In total, 1668 patients participated in the present study (Table I). The mean age of onset of type 2 diabetes was 44 ± 11 years. The majority of patients were female (54.6%) and most patients had a family history of diabetes (71.5%). The largest ethnic group was Malay (51.3%) followed by Chinese and Indian in similar proportions (20.1% and 21.9%, respectively).

There were significant differences between the DiabCare 2013 and DiabCare 2008 cross-sectional cohorts (Table I). Compared with the 2008 cohort, patients in the 2013 cohort were significantly heavier ($p < 0.001$), had a higher BMI ($p < 0.001$), and larger waist circumference ($p < 0.001$). Greater proportions of the 2013 cohort had a positive family history of diabetes ($p < 0.001$). Although age and duration of oral antidiabetic (OAD) medication was not significantly different between the two cohorts, the duration of diabetes was longer in the 2013 cohort ($p < 0.001$). The mean interval from onset of diabetes to OAD therapy was longer in the 2013 cohort ($p = 0.005$), and the mean interval between commencing OAD therapy and commencing insulin therapy was shorter in the 2013 cohort ($p < 0.001$). Educational status was significantly different between 2013 and 2008 cohorts, with a shift toward higher education in the latter cohort. There were a greater proportion of patients in the 2013 cohort with private health insurance or the financial means to personally cover health costs, compared with the 2008 cohort. Health expenses categories were not mutually exclusive.

Metabolic Control

In the present study, mean HbA1c was 8.52 ± 2.01% (70 ± 22 mmol/mol), and the majority of patients (73.0%) had HbA1c measurements > 7% (> 53 mmol/mol) (Table II). Mean FPG was 8.68 ± 5.19 mmol/L with 27.6% of patients meeting target FPG values ≤ 6 mmol/L. PPG measurements were only available in 28% of patients. Mean PPG was 10.86 ± 5.33 mmol/L with 29.9% of patients with PPG measurements meeting target PPG values < 10 mmol/L. The proportion of patients with dyslipidaemia (defined as LDL cholesterol > 2.6 mmol/L and Fasting Triglycerides > 1.7 mmol/L and HDL Cholesterol < 1.09 mmol/L for men or HDL Cholesterol < 1.29 for women) was 79.8% at the time of the study, irrespective of treatment with lipid lowering agents. The proportion of patients with hypertension (defined as a blood pressure > 130/80 mmHg) was 68.0%, irrespective of treatment with antihypertensive medication. Mean serum creatinine was 104.9 ± 83.0 umol/L. HbA1c and serum creatinine increased with longer duration of diabetes (both $p < 0.001$).

Mean HbA1c, and the proportion of patients reaching target HbA1c values between ≤ 6.5 and < 8.5% (< 48 and < 69 mmol/mol) were not significantly different in the 2013 and 2008 cohorts. The mean FPG was significantly higher in the 2013 cohort than in the 2008 cohort, but the proportion of patients reaching FPG targets (≤ 6 mmol/L and ≤ 7.22 mmol/L) were not significantly different. Conversely, the mean PPG was significantly lower in the 2013 cohort relative to the 2008 cohort. HDL cholesterol and fasting triglycerides were significantly higher in the 2013 cohort, but the proportion of patients with evidence of dyslipidaemia at the time of assessment was not significantly different between the two cohorts ($p = 0.450$). Systolic blood pressure was higher in the 2013 cohort, as was the proportion of patients with evidence of hypertension at the time of assessment. Serum creatinine was not recorded in the 2008 cohort.

Diabetes-related Complications

The cumulative proportions of complications are shown in Figure 1. With the exception of left ventricular hypertrophy, stroke or transient ischaemic attack, end stage renal failure and dialysis, the risk of all other assessed complications was significantly associated with duration of diabetes. Overall, the most frequently reported complications were peripheral neuropathy (41.0%) and cataract (31.5%). The most frequently reported complication in men was erectile dysfunction (42.9%). Of patients with angina or myocardial infarction, 42.8% had a history of a revascularisation procedure.

The most frequently reported cardiovascular complications in both the 2013 and 2008 cohorts were angina (15.7% and 18.4% respectively, $p = 0.04$) and myocardial infarction (10.9% and 12.1% respectively, $p = 0.277$). The proportion of patients with a history of revascularisation procedures was lower in the 2013 cohort than in the 2008 cohort (10.3% and 13.0% respectively, $p = 0.01$). The proportions of patients with end-stage renal disease or dialysis were not significantly different between the two cohorts (1.5% and 1.0%, $p = 0.247$). In addition, no significant differences were found comparing the frequencies of eye and foot complications between the two cohorts.

Diabetes Management

Most patients in the 2013 cohort had undergone urinalysis (97.8%), fundal examination (93.3%) and foot examination (97.1%); and all three examinations had been performed in more than 90% of patients within the last 12 months, in accordance with national guidelines. As defined by the protocol inclusion criteria, all patients were receiving a pharmacological or herbal treatment for diabetes at the time of assessment. The most commonly used treatments were metformin (78.6%), insulin (65.0%), sulphonylureas (35.0%), and DPP4 inhibitors (10.3%) (Table III). The majority of patients in the 2013 cohort were still using human insulin (71.2%, total mean dose 58.4 ± 35.1 IU/d) compared with analogue insulin (28.8%, total mean dose 65.1 ± 41.3 IU/d) preparations. In the subgroup of patients using insulin, the most commonly used oral therapies were Metformin (72.9%), sulphonylureas (16.9%), and DPP4 inhibitors (8.1%).

There were significant differences in oral therapy preferences comparing the 2013 and 2008 cohorts (Table III). The largest relative change in the pattern of OAD prescribing was the increase in DPP4 inhibitors from 2008 (1.5%) to 2013 (10.3%). The proportion of patients using insulin also increased from 54% in 2008 to 65% in 2013 ($p < 0.001$). With the exception of the use of premixed human insulin, the use of all other types of human and analogue insulin was significantly increased in the 2013 cohort relative to the 2008 cohort. The total daily insulin dose in the 2013 cohort was also higher than the 2008 cohort (60 ± 37 IU and 51 ± 32 IU respectively, $p < 0.001$). The proportion of patients using analogue insulin had increased from 10% in 2008 to 19% in 2013 ($p < 0.001$).

Table I: Patient demography

	DiabCare 2013 Cohort	DiabCare 2008 Cohort	p-value
N	**1668**	**1549**	
Patient characteristics			
Age (years)	57.8 ± 11.0 59.0 (68.0)	57.5 ± 10.9 58.0 (73.0)	0.363*
Missing (n)	13	26	
Duration of diabetes (years)	13.0 ± 8.6 11.0 (54.0)	11.5 ± 7.9 10.0 (44.0)	<0.001*
Missing (n)	1	57	
Duration of OAD treatment (years)	11.3 ± 7.7 10.0 (48.0)	11.0 ± 8.3 9.0 (57.0)	0.125*
Missing (n)	28	194	
Duration of insulin treatment (years)	5.6 ± 5.5 4.0 (46.0)	4.1 ± 4.4 2.8 (29.9)	0.013*
Missing (n)	259	879	
Interval between onset of diabetes and commencing OAD therapy (years)	1.8 ± 4.6 0.0 (46.0)	0.8 ± 2.3 0.0 (21.8)	0.005*
Missing (n)	29	232	
Interval between onset of diabetes and commencing insulin therapy (years)	9.6 ± 7.5 8.0 (55.0)	10.8 ± 7.5 10.0 (35.0)	<0.001*
Missing (n)	260	908	
Interval between commencing OAD therapy and commencing insulin therapy (years)	8.9 ± 7.0 7.5 (46.0)	10.5 ± 7.9 9.5 (56.0)	<0.001*
Missing (n)	383	961	
Male gender (%)	774 (46.4)	708 (45.7)	0.695
Weight (kg)	74.3 ± 16.6 72.0 (129.6)	72.3 ± 29.6 70.0 (164.0)	<0.001*
Missing (n)	10	300	
BMI (kg/m^2)	29.1 ± 5.8 28.4 (55.7)	27.8 ± 4.5 27.4 (21.7)	<0.001*
Missing (n)	25	705	
Waist circumference (cm)	97.8 ± 13.1 97.0 (103)	93.9 + 17.1 95.0 (150)	<0.001*
Missing (n)	62	905	
Educational status (n, %)			0.003
LCTRW#	102 (6.1)	123 (8.1)	
5 years	334 (20.1)	359 (23.0)	
10 years	868 (52.2)	741 (48.6)	
Graduate	292 (17.5)	263 (17.2)	
Postgraduate	68 (4.1)	40 (2.6)	
Risk Factors (n, %)			
Family History	1192 (75.9)	1057 (70.2)	<0.001
Current smoking	148 (8.9)	140 (9.2)	0.539
Health Expenses (n, %)			
Government/Community	1478 (88.6)	1344 (86.8)	0.111
Self	309 (18.5)	193 (12.5)	<0.001
Insurance	46 (2.8)	2 (0.1)	<0.001
Ethnic groups (n, %)			
Malay	856 (51.3)	855 (55.2)	
Chinese	335 (20.1)	334 (21.6)	
Indian	366 (21.9)	308 (19.9)	
Others	111 (6.7)	47 (3.0)	

All continuous data are presented as mean ± standard deviation and median (range).
LCTRW: Limited Capability To Read & Write
*Mann-Whitney test.

Table II: Percentage of patients reaching clinical targets

	DiabCare 2013 Cohort	DiabCare 2008 Cohort	p-value
Glycaemic Control			
Central Laboratory Measured HbA1c (n)	1667	1495	
HbA1c (%)	8.52 ± 2.01	8.66 ± 2.09	0.081*
	8.10 (14.30)	8.30 (11.40)	
Missing (n)	0	54	
HbA1c (mmol/mol)	70 ± 22	71 ± 23	
HbA1c Quantile (n, %)			
< 6.5% (<42 mmol/mol)	203 (12.2)	176 (11.8)	0.726
≤ 6.5% (<48 mmol/mol)	242 (14.5)	200 (13.4)	0.356
< 7.0% (<53 mmol/mol)	396 (23.8)	341 (22.8)	0.530
< 7.5% (<58 mmol/mol)	617 (37.0)	525 (35.1)	0.268
< 8.0% (<64 mmol/mol)	793 (47.6)	658 (44.0)	0.045
< 8.5% (<69 mmol/mol)	950 (57.0)	809 (54.1)	0.104
Plasma Glucose			
FPG (mmol/L)	8.68 ± 5.19	7.98 ± 2.92	<0.020*
	7.40 (82.20)	7.30 (13.90)	
Missing (n)	133	336	
FPG Target (n, %)			
≤ 6 mmol/L	423 (27.6)	369 (30.4)	0.102
≤ 7.22 mmol/L	723 (47.1)	599 (49.4)	0.241
PPG (mmol/L)	10.86 ± 5.33	12.96 ± 4.82	<0.001*
	10.00 (77.70)	12.40 (22.40)	
Missing (n)	1195	1349	
PPG Target (n, %)			
≤ 8 mmol/L	141 (29.9)	33 (16.5)	<0.001
< 10 mmol/L	229 (48.5)	60 (30.0)	<0.001
Lipids			
Total Cholesterol (mmol/L)	4.71 ± 2.44	4.33 ± 2.11	0.031*
	4.50 (64.70)	4.40 (43.60)	
Missing (n)	38	80	
Total Cholesterol ≤ 5.2 mmol/l (n, %)	1208 (75.2)	1105 (75.2)	0.496
HDL Cholesterol (mmol/L)	1.25 ± 0.51	1.13 ± 0.70	<0.001*
	1.20 (10.20)	1.10 (11.00)	
Missing (n)	93	102	
HDL Cholesterol ≥ 1.0 mmol/l (n, %)	1276 (81.1)	1023 (70.7)	<0.001
LDL Cholesterol (mmol/L)	2.62 ± 1.01	2.69 ± 0.98	0.015*
	2.50 (10.70)	2.50 (8.50)	
Missing (n)	100	109	
LDL Cholesterol ≤ 2.6 mmol/l (n, %)	900 (57.4)	794 (55.1)	0.205
Fasting Triglycerides (mmol/L)	1.76 ± 1.09	1.65 ± 1.22	0.004*
	1.50 (13.70)	1.50 (10.70)	
Missing (n)	51	86	
Fasting Triglycerides ≤ 2.2 mmol/l (n, %)	1290 (79.8)	1156 (79.0)	0.578
Dyslipidaemia[a]	150 (10.5)	150 (9.7)	0.450
Blood pressure			
Systolic (mmHg)	140 ± 20	137± 20	<0.001*
	139 (143)	135 (170)	
Missing (n)	22	60	
Diastolic (mmHg)	79 ± 12	79 ± 12	0.628*
	80 (162)	80 (180)	
Missing (n)	22	64	
Hypertensionb	1118 (68.0)	883 (59.3)	<0.001

All continuous data are presented as mean ± standard deviation and median (range).

a Dyslipidaemia defined as LDL Cholesterol > 2.6 mmol/L and Fasting Triglycerides > 1.7 mmol/L and HDL Cholesterol < 1.09 mmol/L (male) or HDL Cholesterol < 1.29 (female).

b Hypertension defined as blood pressure > 130/80 mmHg.

*Mann-Whitney test.

Table III: Pharmacological diabetes treatments

	DiabCare 2013 Cohort	DiabCare 2008 Cohort	p-value
Diabetes Treatment (n, %)			
Metformin	1311 (78.6)	1144 (73.9)	0.001
Sulphonylurea	584 (35.0)	703 (45.4)	<0.001
Thiazolidinedione	11 (0.7)	77 (5.0)	<0.001
Glucosidase Inhibitor	76 (4.6)	146 (9.4)	<0.001
Glinide	5 (0.3)	10 (0.6)	0.151
DPP4 Inhibitor	172 (10.3)	23 1.5)	<0.001
GLP-1 Analogue	11 (0.7)	4 (0.3)	0.095
Herbal/Traditional Medicine	8 (0.5)	6 (0.4)	0.690
Insulin	1085 (65.0)	831 (53.6)	<0.001
Insulin Types (n, %)			
NPH	375 (22.5)	230 (14.8)	<0.001
Basal Analogue	167 (10.0)	85 (5.5)	<0.001
Premixed Human Insulin	369 (22.1)	363 (23.4)	0.375
Premix Insulin Analogue	131 (7.9)	54 (3.5)	<0.001
Human Soluble Insulin	322 (19.3)	142 (9.2)	<0.001
Rapid Acting Analogue	83 (5.0)	32 (2.1)	<0.001
Insulin Delivery (n, %)			
Pen Device	1066 (97.7)	n.a.	
Vial/Syringe	3 (0.0)	n.a.	
Insulin Regimens (n, %)			
Basal + OAD	189 (11.3)	185 (11.9)	0.593
Premix OD	9 (0.5)	5 (0.3)	0.350
Premix BD	425 (25.5)	360 (23.2)	0.137
Premix TID	46 (2.8)	12 (0.8)	<0.001
Basal-Bolus	344 (20.6)	164 (10.6)	<0.001
Total Daily Insulin Dose (IU/d)			
All Regimens	60.3 ± 37.1 54.0 (226.0)	50.9 ± 32.3 48.0 (229.0)	<0.001*
Basal + OAD	21.6 ± 22.6 14.0 (182.0)	17.1 ± 14.5 14.0 (163.0)	0.059*
Premix OD	24.3 ± 11.6 20.0 (36.0)	18.6 ± 6.1 19.0 (16.0)	0.328
Premix BD	55.0 ± 23.2 52.0 (126.0)	55.1 ± 22.0 54.0 (108.0)	0.568*
Premix TID	92.1 ± 33.3 96.0 (146.0)	78.2 ± 33.9 75.0 (122.0)	0.204
Basal-Bolus	84.8 ± 37.0 82.0 (208.0)	76.5 ± 33.8 71.0 (211.0)	0.012*

All continuous data are presented as mean ± standard deviation and median (range). *Mann-Whitney test.
n.a. – not available.

Hypoglycaemia

Results of the hypoglycaemia questionnaire are shown in Table IV. In total, 658 (39%) patients reported one or more symptomatic episodes consistent with hypoglycaemia within the last three months, irrespective of the duration of diabetes. However, severe hypoglycaemia was rare (1.6 ± 1.6 events in 41 patients in the last three months). The proportion of patients experiencing mild, severe and nocturnal hypoglycaemia increased per year duration of diabetes (mild: odds ratio [OR] 1.05, 95% confidence interval [CI] 1.04–1.06; severe: OR, 1.07, 95% CI 1.04–1.10; and nocturnal: OR 1.05, 95% CI 1.04–1.08). However, there were no significant associations between the frequency of hypoglycaemia and duration of diabetes. The only diabetes-specific treatment significantly associated with the reporting of any hypoglycaemia was the use of insulin (OR 3.26, 95% CI 2.59–4.09). In the subgroup of patients using insulin, there was no significant association between insulin regimen and reporting of any hypoglycaemia, only the total daily dose (OR 1.04, 95% CI 1.01–1.07) per 10 IU increase.

Symptomatic episodes consistent with hypoglycaemia also prompted changes in self-care behaviour in the majority of patients. The majority of patients (70%) checked blood glucose after experiencing hypoglycaemia symptoms, and 25% of patients attended hospital following probable or confirmed hypoglycaemia at some time. In response to hypoglycaemia, snacking and skipping or reducing insulin doses was reported in 57% and 20% of patients respectively; and 23% reported more frequent blood glucose measurement in the days following hypoglycaemia symptoms.

The hypoglycaemia questionnaire was new to DiabCare 2013, so no comparisons with the 2008 cohort were possible.

Table IV: Hypoglycaemia questionnaire

		2012 Cohort
Hypoglycaemia symptoms in the last 3 months		
Mild 'hypo' - Sweating, dizziness, trembling, tingling in the hands, feet or lips, hunger, blurred vision, difficulty in concentrating, palpitations and occasional headache	N (%)	614 (37.1)
	Number of episodes	3.5 ± 4.1
		2 (44)
Moderate 'hypo' - Odd behaviour such as rudeness or laughter (appearing drunk when you are not), bad temper or moodiness, aggressive behaviour, confusion.	N (%)	106 (6.6)
	Number of episodes	2.3 ± 1.8
		2 (10)
Severe 'hypo' - Unconsciousness or help from someone else.	N (%)	41 (2.6)
	Number of episodes	1.6 ± 1.6
		1 (10)
Nocturnal 'hypo' - Symptoms between bedtime and breakfast.	N (%)	260 (16.3)
Number of episodes	3.3 ± 4.0	2 (36)
Did you check your blood glucose on these occasions?*		
Always	N (%)	256 (41.4)
Sometimes	N (%)	175 (28.3)
Never	N (%)	187 (30.3)
Did you visit hospital on these occasions?*		
Always	N (%)	47 (7.5)
Sometimes	N (%)	112 (17.9)
Never	N (%)	468 (74.6)
Following an episode, did you*		
Start snacking in between meals to avoid hypo?	N (%)	425 (57.2)
Skip or reduce your insulin or tablet dose?	N (%)	149 (20.1)
Measure blood glucose frequently for the next few days?	N (%)	169 (22.7)
Are you worried about the 'low blood sugar' (Hypo's)		
Yes	N (%)	768 (46.0)
No	N (%)	815 (48.9)

All continuous data are presented as mean ± standard deviation and median (range).
* Only for patients reporting hypoglycaemia (percentage of all patients reporting hypoglycaemia)

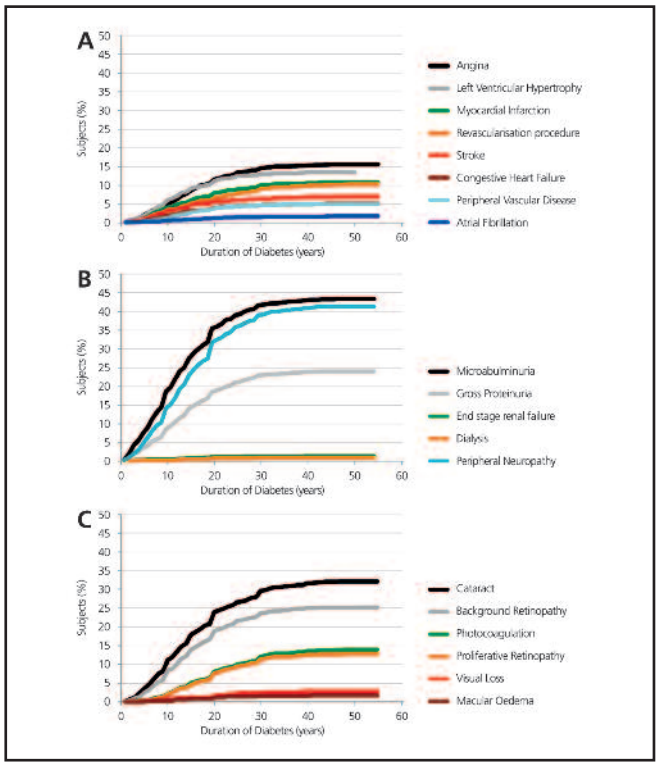

Fig. 1: Cumulative proportion with diabetes related complications involving (A) cardiovascular system, (B) kidney, and (C) eye.

DISCUSSION

DiabCare is an established study design, which has been instrumental in guiding Malaysian national health care policy. This fifth iteration of DiabCare (2013) is timely, allowing the status of diabetes care to be re-evaluated five years after implementation of the Malaysian National Diabetes Care Guidelines, which recommended treatments and metabolic targets aimed at reducing the risk of macro- and micro-vascular complications. A national insulin educational programme, designed to guide healthcare professionals in the effective use of insulin, had also been implemented over the same period.

In 2010, Malaysia was reported to have the tenth highest prevalence of diabetes worldwide, with diabetes management accounting for 16% of the national healthcare budget.[15] The high prevalence of type 2 diabetes in Malaysia is attributed to increasing affluence, higher caloric diets and a decline in physical activity.[1] The demographic differences between 2013 and 2008 cohorts appear to fit with these previously reported trends in increasing affluence (as represented by the shift towards higher education and away from reliance on government hospitals to cover health expenses), higher caloric diets and a decline in physical activity (leading to increases in weight, BMI and waist circumference).

Malaysia is a multi-ethnic country comprising three main ethnic groups: Malay, Indian and Chinese. These ethnic groups may differ in their susceptibility to diabetes and

diabetes related complications, as well as in their socioeconomic status and access to healthcare.[16-18] In our study, the proportion of subjects in each of these three main ethnic groups was similar to that in the 2008 cohort and to population proportions reported elsewhere.[3] In addition, participating centres were large tertiary care hospitals situated in urban areas in different regions, and participating patients had been attending regular follow-up at these centres for at least one year. Therefore, differences in ethnicity and access to appropriate healthcare were not considered to be major confounders in our study.

Despite earlier challenges, Malaysia has experienced continued improvements in access to healthcare services, with a greater proportion of patients completing annual HbA1c measurement and assessment of complications and other metabolic risk factors than reported in earlier DiabCare studies.[14] In the present study, urinalysis had been performed in 98% of subjects, and fundal examination and foot examination had been performed in 93% and 97% of subjects, respectively. This is a marked improvement in microvascular risk assessment procedures compared with previous DiabCare and other national audits.[19] The higher proportion of patients treated with insulin in our study (65%) compared with previous DiabCare audits from 2008 (54%) and 2003 (28%), and the increased use of more intensive insulin regimens (e.g. basal-bolus), appears to indicate an improvement in initiation and intensification of insulin. These observations of changes in insulin treatment coincide with the publication of specific insulin therapy guidance and healthcare professional training in the period 2011–2013.

In recent years, we have seen a move towards more individualised HbA1c targets, and while we should continue to treat some patients aggressively, HbA1c values of < 7.0% (<53 mmol/mol) may not be suitable for specific patient groups, particularly in the presence of established cardiovascular disease and other diabetes-related comorbidities. This individualised approach to setting glycaemic targets postdates the 2009 Malaysian National Guidelines that were in place at the time the present study was performed. There was no evidence of a coordinated increase or decrease in glycaemic targets (as measured by central laboratory HbA1c values) according to the presence of cardiac complications in our study (data not shown).

Patients with type 2 diabetes are predisposed to developing hypertension and dyslipidaemia. The coexistence of these conditions is known to increase the risk of late complications such as end-stage renal failure and cardiovascular complications compared with age-matched controls with or without diabetes.[20-23] Therefore, control of hypertension and dyslipidaemia are important in preventing diabetes complications, especially macrovascular complications. In the present cohort, the high proportion of patients with measurements indicative of dyslipidaemia and hypertension, irrespective of treatment for these conditions, is cause for concern. The effects of uncontrolled hypertension and delayed disease control until after the onset of complications have been previously cited as possible reasons for the high number of complications observed in the Malaysian National Registry.[24]

Symptoms of hypoglycaemia have been reported by up to one third of patients treated with OHAs alone.[25] Although the majority of these episodes were mild, approximately 6.6% were consistent with severe hypoglycaemia. In our study, 23% of patients not treated with insulin reported hypoglycaemia in the previous three months, with only 1.2% reporting severe hypoglycaemic symptoms. Insulin use was the only diabetes therapy significantly associated with the reporting of hypoglycaemia, and this association was dose rather than regimen dependent.

The present study has several limitations. As it was a cross-sectional observational study, it was not possible to completely exclude the effect of selection bias. Although a consistent methodological approach has been used between DiabCare studies with respect to selection of participating sites, use of a site independent investigator team and data collection, selection bias and the effect of unknown confounders means that comparisons between DiabCare cohorts should be interpreted with caution. In addition, as all centres were situated in urban areas and offered specialised diabetes care services, patients attending these centres and who were eligible for enrolment in our study may not be representative of the country as a whole. Furthermore, the three-month recall period for ascertaining the rate of hypoglycaemia overlapped with the Ramadan season. Ramadan is practiced by 55% of the Malaysian population, but has not been shown to affect rates of hypoglycaemia in well-controlled patients with type 2 diabetes.[26-28]

CONCLUSION

The results of DiabCare are encouraging with respect to the progress being made on implementing processes of diabetes care, particularly with respect to screening for microvascular complications and insulin initiation and intensification. However, despite these improvements, we found no evidence of improvements in glycaemic and other metabolic parameters. In addition, the prevalence of many diabetes-related complications was unchanged. Future studies may increase our understanding of whether the failure to reduce complications is primarily due to deficiencies in diabetes management, or to an evolving patient phenotype (e.g. more obese) at greater risk of developing complications.

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Conflicts of Interest

MM and ZH have no conflicts of interest to disclose. SPC has received fees for consulting and presenting for the following companies: Novo Nordisk, Boehringer-Ingelheim, Merck Sharp and Dohme, Sanofi Aventis, Servier and Astra Zeneca.

Role of the funding source

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