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Research: Care Delivery

A multicentre demonstration project to evaluate the effectiveness and acceptability of the web-based Joint Asia Diabetes Evaluation (JADE) programme with or without nurse support in Chinese patients with Type 2 diabetes

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Abstract

Aims To test the hypothesis that delivery of integrated care augmented by a web-based disease management programme and nurse coordinator would improve treatment target attainment and health-related behaviour.

Methods The web-based Joint Asia Diabetes Evaluation (JADE) and Diabetes Monitoring Database (DIAMOND) portals contain identical built-in protocols to integrate structured assessment, risk stratification, personalized reporting and decision support. The JADE portal contains an additional module to facilitate structured follow-up visits. Between January 2009 and September 2010, 3586 Chinese patients with Type 2 diabetes from six sites in China were randomized to DIAMOND (n = 1728) or JADE, plus nurse-coordinated follow-up visits (n = 1858) with comprehensive assessments at baseline and 12 months. The primary outcome was proportion of patients achieving ≥ 2 treatment targets (HbA_{1c} < 53 mmol/mol (7%), blood pressure < 130/80 mmHg and LDL cholesterol < 2.6 mmol/l).

Results Of 3586 participants enrolled (mean age 57 years, 54% men, median disease duration 5 years), 2559 returned for repeat assessment after a median (interquartile range) follow-up of 12.5 (4.6) months. The proportion of participants attaining ≥ 2 treatment targets increased in both groups (JADE 40.6 to 50.0%; DIAMOND 38.2 to 50.8%) and there were similar absolute reductions in HbA_{1c} [DIAMOND −8 mmol/mol vs JADE −7 mmol/mol (−0.69 vs −0.62%)] and LDL cholesterol (DIAMOND −0.32 mmol/l vs JADE −0.28 mmol/l), with no between-group difference. The JADE group was more likely to self-monitor blood glucose (50.5 vs 44.2%; P = 0.005) and had fewer defaulters (25.6 vs 32.0%; P < 0.001).

Conclusions Integrated care augmented by information technology improved cardiometabolic control, with additional nurse contacts reducing the default rate and enhancing self-care. (Clinical trials registry no.: NCT01274364)

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Introduction

Achieving and maintaining recommended treatment targets decreases the risk of diabetes-related vascular complications, mortality and associated healthcare costs [1–4]. In the UK

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What's new?

- The value of quality improvement programmes in the management of chronic conditions has been established in a number of prospective studies and meta-analyses.
- The effect of the Joint Asia Diabetes Evaluation (JADE) programme, an information technology-augmented integrated care model, on diabetes-related outcomes has been demonstrated in several studies within developed healthcare systems.
- This study represents one of the few quality improvement initiatives undertaken in a developing country and is the first to answer the question of whether initiatives such as JADE are effective in enhancing quality of care in underfunded healthcare systems.
- Given the increasing demand for healthcare resources in developing countries, quality improvement has the potential to improve chronic care without substantial additional costs.

Prospective Diabetes Study, an 11-mmol/mol (1%) reduction in mean HbA_{1c} led to 21% fewer deaths, 14% fewer myocardial infarctions and a 37% decrease in microvascular complications [5]. Despite collective accord, there are major treatment gaps attributable to suboptimum self-care, poor adherence to treatment and clinical inertia, resulting in low rates of treatment target attainment in both developed and developing regions [6,7].

These barriers are amplified by systemic factors, especially in developing countries. In China, for example, the majority of chronic care occurs in an in-patient setting with most clinical assessments and treatment covered or reimbursed; however, in a primary or ambulatory care setting, many laboratory tests and chronic medications require co-payments or are not reimbursed. Electronic medical systems exist but are largely fragmented, resulting in duplication or overlapping of consultations, investigations and medications. Despite an initiative to promote primary care by establishing community-based clinics, many patients prefer going to hospitals for specialist care, with long waiting times and short contact intervals. Patients typically return every 1–2 months, mainly to collect medications, often without pre-booking, assessment or education, and with high default rates [8,9].

One area of focus is the lack of structure for documenting risk factors and complications, as well as the arbitrary nature of risk stratification and patient follow-up. In the USA, the Institute of Medicine recommended the following strategies to improve chronic care: redesign care processes based on best practices, use information technology to manage clinical data with decision support, transfer knowledge and skills to team members to coordinate care and use performance and outcome measures for quality control [10]. In a meta-analysis of strategies for quality improvement, promotion of self-care and team change were associated with a 4-mmol/mol (0.37%) mean reduction in HbA_{1c}, along with improvements in LDL cholesterol and blood pressure (BP) [11].

Since 1995, the Chinese University of Hong Kong (CUHK) Diabetes Care and Research Team has re-designed workflows and trained nurses to assess patients and deliver protocol-based care. By changing workflows and through task delegation, we were able to improve medication adherence, with attainment of multiple targets and reduced risks of cardiovascular-renal complications [12,13]. Based on these prototypes, we designed the web-based Joint Asia Diabetes Evaluation (JADE) portal, consisting of two modules. The comprehensive assessment (CA) module comprises templates for periodic assessment, risk stratification, personalized reporting and automated decision support. The follow-up module includes templates for documentation of modifiable risk factors, hypoglycaemia and key events to track clinical progress and reinforce adherence [14]. A separate portal with a CA module identical to that of JADE, was also created to help doctors establish a diabetes monitoring database (DIAMOND) as a first step towards a comprehensive quality improvement programme. In this demonstration project, we examined the effectiveness of delivering integrated care in China with or without nurse-coordinated follow-up visits using the JADE and DIAMOND portals, respectively, on cardiometabolic control and health behaviours, including default rates.

Patients and methods

The study assessed a 1-year multicentre randomized non-blinded quality improvement programme. Between January 2009 and September 2010, patients with Type 2 diabetes aged ≥ 18 years were recruited from six tertiary hospitals in China. Exclusion criteria included Type 1 diabetes, life-threatening conditions, reduced life expectancy or inability to understand the scope of the study. The study was approved by the New Territories East Cluster Clinical Research Ethics Committee and local institutional ethics boards at each participating site. All participants provided written informed consent.

A total of 3586 eligible patients were randomized in a 1:1 ratio to DIAMOND (CA only) or JADE (CA plus nurse-coordinated structured follow-up). At each centre, randomization was performed using computer-generated codes kept in sealed, opaque envelopes, numbered 1 to 600 prefixed by the study site. Personnel at the site not participating in the study opened the envelope and informed consenting participants of their group assignment.

Each centre was given a grant to support an additional CUHK project team-trained nurse to perform the CA, guided by the JADE/DIAMOND portals and supervised by a physician. Both doctors and nurses received training on the use of the portals to perform a structured patient evaluation,

Table 1 Baseline characteristics of all randomized Chinese patients with type 2 diabetes

	n	DIAMOND		JADE	*P*
Number randomized		1728		1858	
Demographics					
Mean ± SD age, years	1728	56.8 ± 11.7	1858	56.1 ± 11.6	0.096
Gender: men, *n* (%)	1728	941 (54.5)	1858	1011 (54.4)	0.98
Median (IQR) disease duration, years	1705	5.0 (1.0, 10.0)	1809	5.0 (1.0, 10.0)	0.725
Education, *n* (%)	1724		1849		0.001
< 6 years		168 (9.7)		132 (7.1)	
6–11 years		415 (24.0)		424 (22.8)	
> 11 years		1140 (66.0)		1291 (69.5)	
Unemployed, *n* (%)	1724	1103 (64.0)	1850	1153 (62.3)	0.306
Tobacco use, *n* (%)	1712		1827		0.998
Never		1123 (65.6)		1202 (65.8)	
Former		206 (12.0)		208 (11.4)	
Current		383 (22.4)		417 (22.8)	
Alcohol use, *n* (%)	1718		1830		0.773
Never		1187 (69.1)		1269 (69.3)	
Physical activity ≥ 3 times/week, *n* (%)	1717	867 (50.5)	1849	991 (53.6)	0.064
SMBG ≥ weekly, *n* (%)	1576	677 (43.0)	1713	780 (45.5)	0.137
Adherence to balanced diet, *n* (%)	1719	1091 (63.5)	1852	1205 (65.1)	0.156
Median (IQR) follow-up, months	1728	12.5 (5.28)	1858	12.5 (3.98)	0.449
Complications and comorbidities, *n* (%)					
Retinopathy	1681	228 (13.6)	1808	241 (13.3)	0.84
Sensory neuropathy	1722	143 (8.3)	1852	113 (6.1)	0.011
Chronic kidney disease, *n* (%)	1646	37 (2.2)	1789	37 (2.1)	0.717
All heart events including heart failure, *n* (%)	1726	164 (9.5)	1845	155 (8.4)	0.221
Stroke, *n* (%)	1720	54 (3.1)	1850	42 (2.3)	0.109
Peripheral vascular disease, *n* (%)	1556	164 (10.5)	1688	122 (7.3)	0.001
Risk categories, *n* (%)					0.483
Low: 1/2	1727	220 (12.7)	1855	251 (13.5)	
High: 3/4	1727	1507 (87.3)	1855	1604 (86.5)	
Treatments, *n* (%)					
Lifestyle modification only	1728	385 (22.3)	1858	388 (20.9)	0.309
On oral antidiabetic drug	1728	1214 (70.3)	1858	1321 (71.1)	0.579
Insulin	1728	452 (26.2)	1858	512 (27.6)	0.345
Any BP drugs	1728	390 (22.6)	1858	420 (22.6)	0.98
Angiotensin-converting enzyme inhibitors	1728	33 (1.9)	1858	34 (1.8)	0.86
Angiotensin II receptor type 1 receptor blocker	1728	207 (12.0)	1858	220 (11.8)	0.898
Statins	1728	544 (31.5)	1858	597 (32.1)	0.676
Risk factor control					
Mean ± SD body weight, kg	1715	69.52 ± 12.67	1845	69.57 ± 12.62	0.911
Mean ± SD waist circumference, cm					
Women	682	87.15 ± 9.97	713	85.96 ± 10.19	0.028
Men	800	91.46 ± 9.68	815	91.81 ± 9.48	0.47
Mean ± SD BMI (kg/m^2)	1715	25.32 ± 3.62	1845	25.18 ± 3.58	0.246
Mean ± SD diastolic BP (mmHg)	1694	78.4 ± 10.4	1824	78.8 ± 11.0	0.243
Mean ± SD systolic BP (mmHg)	1694	125.8 ± 15.8	1824	125.0 ± 15.7	0.131
Mean ± SD total cholesterol, mmol/l	1653	4.95 ± 1.31	1785	4.91 ± 1.16	0.47
Mean ± SD HDL cholesterol, mmol/l					
Women	751	1.26 ± 0.31	799	1.29 ± 0.34	0.06
Men	891	1.1 ± 0.28	960	1.12 ± 0.27	0.108
Mean ± SD LDL cholesterol, mmol/l	1644	2.94 ± 0.89	1768	2.92 ± 0.88	0.446
Mean ± SD haemoglobin, g/dl	1446	14.49 ± 7.44	2545	14.31 ± 5.77	0.443
Mean ± SD HbA_{1c}, % (mmol/mol)	1648	7.91 (53) ± 2.08 (15)	1788	7.78 (59) ± 1.95 (15)	0.057
Median (IQR) triglyceride, mmol/l	1654	1.54 (1.14)	1788	1.48 (1.22)	0.005
Median (IQR) urine albumin to creatinine ratio, mg/mmol	1506	1.20 (2.75)	1606	1.25 (2.85)	0.059
Mean ± SD estimated GFR, ml/min/1.73 m^2	1646	122.2 ± 38.74	1789	122.63 ± 41.88	0.754
Obesity, *n* (%)	1539	1081 (70.2)	1607	1114 (69.3)	0.575
Dyslipidaemia, *n* (%)	1669	1551 (92.9)	1810	1668 (92.2)	0.385
Hypertension, *n* (%)	1707	1275 (74.7)	1835	1392 (75.9)	0.421
Macroalbuminuria, *n* (%)	1506	75 (5.0)	1606	89 (5.5)	0.64
Microalbuminuria, *n* (%)	1506	330 (21.9)	1606	385 (24.0)	0.322
Frequency of hypoglycaemic episodes ≥ once/month, *n* (%)	1713	178 (10.4)	1847	185 (10.0)	0.712
Attainment of treatment targets, *n* (%)					
HbA_{1c} < 7.0% (53 mmol/mol)	1648	692 (42.0)	1788	811 (45.4)	0.047

Table 1 (*Continued*)

	n	DIAMOND		JADE	*P*
BP < 130/80 (mmHg)	1694	662 (39.1)	1824	710 (38.9)	0.926
LDL cholesterol < 2.6 (mmol/l)	1644	600 (36.5)	1768	644 (36.4)	0.966
At least one target	1595	1211 (75.9)	1716	1300 (75.8)	0.911
At least two targets	1595	555 (34.8)	1716	624 (36.4)	0.347
All three targets	1595	105 (6.6)	1716	136 (7.9)	0.137
Quality of life					
Mean ± SD EQ-VAS	1715	83.01 ± 12.10	1830	82.83 ± 12.35	0.721
Mean ± SD EQ-5D index	1708	0.91 ± 0.13	1817	0.91 ± 0.14	0.995

BP, blood pressure; DIAMOND, DIAbetes MONitoring Database; IQR, interquartile range; JADE, Joint Asia Diabetes Evaluation; SMBG, self-monitoring of blood glucose; VAS, visual analogue scale.

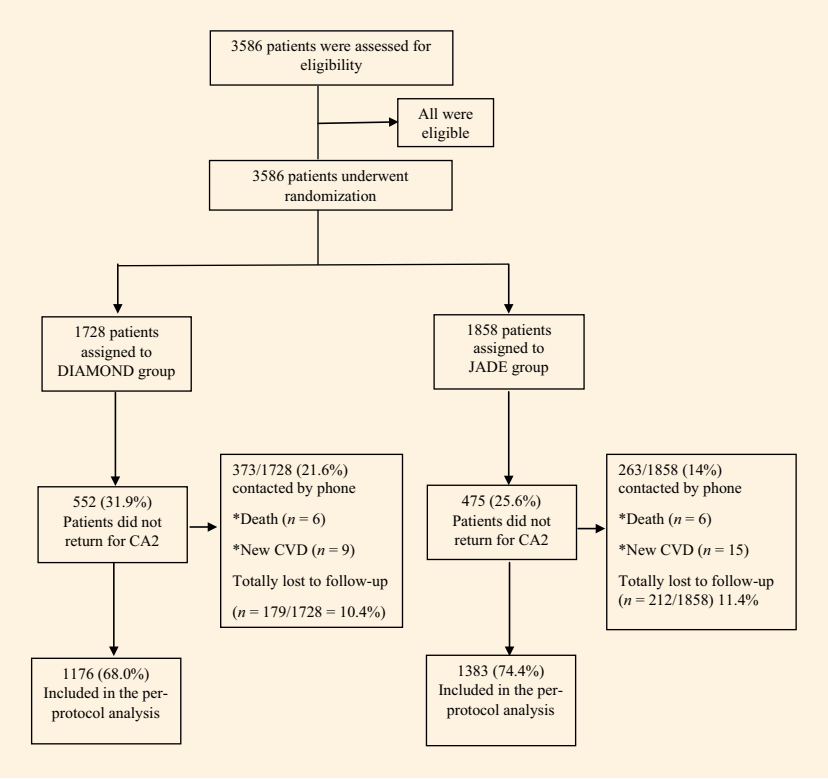

FIGURE 1 Randomization and disposition of patients included in the intend to treat and per protocol analyses.

document care processes and communicate results of clinical and laboratory assessments to participants. For participants randomized to JADE, the additional nurse was trained to use the follow-up module to manage follow-up appointments and facilitate ongoing patient support between clinic visits, while the DIAMOND group received usual care. Details of the JADE programme have been published and are included in Appendix S1 [15]. The CA report consists of 5-year probabilities for coronary heart disease, heart failure, stroke and end-stage renal disease, estimated using validated risk equations [16–19]. Patients were classified into one of four risk categories based on risk scores derived from risk equations, presence or absence of cardiovascular-renal disease, and an ensemble of metabolic risk factors. Each risk category corresponded to a recommended care level that determined frequency of structured follow-up visits and intensity of care [14].

Automated reports provided to patients and physicians contained trend lines of attained versus recommended metabolic targets, 5-year probabilities of major events, and risk categories. The physician report included triggered reminders on treatment intensification, while the patient report included practice tips to promote lifestyle changes, treatment adherence and self-monitoring, in the local language. Both participants and referring doctors in the DIAMOND group received their respective reports followed

by usual care. Participants assigned to JADE were recommended to receive 2–4 h of diabetes education and at least two additional contacts by the nurse coordinator (telephone or face-to-face visits). Facilitated by the follow-up module, nurses were asked to reinforce treatment and lifestyle adherence, encourage self-monitoring of blood glucose (SMBG) and remind them about structured follow-up appointments that included documentation of laboratory measurements, body weight, blood pressure, hypoglycaemia, self-care and other major events in the JADE portal. The nurse coordinator issued a follow-up report, discussed cardiometabolic control and clarified concerns regarding therapy. Participants in the lower risk categories (l or 2, with few risk factors/complications) were recommended to have structured follow-up visits every 4–6 months and those in higher risk categories (3 or 4, with multiple risk factors and/or complications) every 2–3 months. At the end of 12 months, all participants underwent repeat CA, and non-returnees were contacted by telephone to ascertain health status.

The primary outcome was the proportion of participants attaining ≥ 2 treatment targets (HbA_{1c} < 53 mmol/mol (7%), BP < 130/80 mmHg, LDL cholesterol < 2.6 mmol/l) after 12 months. Other outcomes included default rates, change in quality-of-life measures, frequency of hypoglycaemia, adherence to lifestyle modification/self-care activities, and new onset of physician-documented diabetes-related endpoints. Events were recorded using standard forms, with predefined diagnosis accompanied by a narrative, albeit not adjudicated. Power calculation and statistical analyses applied are available in Appendix S2.

Results

Between January 2009 and September 2010, 3586 eligible participants, representing ~65% of all subjects considered [mean age 56.5 ± 11.6 years, 54.4% men, median (interquartile range) disease duration of 5 (1–10) years, mean HbA_{1c} 62 ± 22 mmol/mol (7.85 ± 2.02%)] were recruited from patients already receiving treatment at the clinics. The primary reasons for declining were testing costs and recurring travel to study site. A total of 1728 participants were assigned to DIAMOND and 1858 to JADE, with both groups having similar characteristics at baseline (Table 1).

Between March 2011 and December 2013, after a median (interquartile range) follow-up of 12.5 (4.6) months, 2559 out of 3586 randomized participants (71.4%) returned for the second CA (CA2), with documentation of clinical and biochemical data and event rates. A total of 1027 participants (28.6%) did not return for CA2, but 636 of those were contacted by telephone for ascertainment of health status, while 371 (10.3%) were lost to follow-up with no vitality ascertainment. In all, 24 participants had a cardiovascular event and 12 died. A final total of 2559 participants were included in the per-protocol analysis (Fig. 1).

In the JADE group, 191 participants were in risk category 1–2, with the remaining 1192 in risk category 3–4. The mean frequencies of nurse-coordinated follow-up visits in risk categories 1–4 were 1.2, 1.8, 1.9 and 2.4 times per year, respectively. Follow-up frequency for patients in DIAMOND was not captured because the DIAMOND portal was not designed to capture follow-up frequency.

Compared with baseline, the proportion of participants attaining ≥ 2 treatment targets (DIAMOND 38.2 to 50.8%, $P < 0.01$; JADE 40.6 to 50.0%, $P < 0.01$); HbA_{1c} < 53 mmol/mol (7%) (DIAMOND 45.8 to 61.1%, $P < 0.01$, JADE 49.0 to 58.5%, $P < 0.01$) and LDL cholesterol < 2.6 mmol/l (DIAMOND 36.4 to 52.9%, $P < 0.01$;

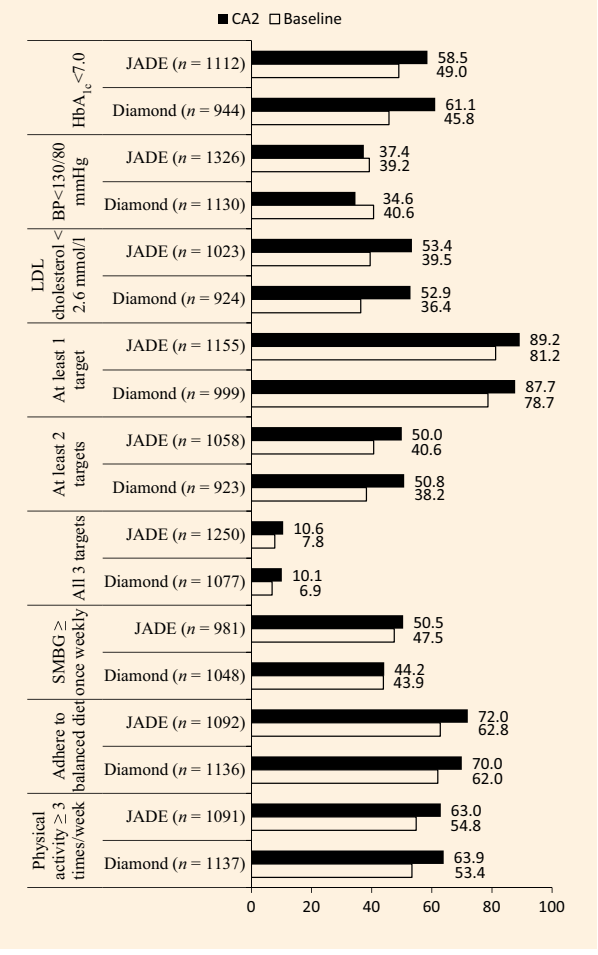

FIGURE 2 Proportions of patients in the Diabetes Monitoring Database (DIAMOND) and Joint Asia Diabetes Evaluation (JADE) groups attaining treatment targets at repeat assessment after 1 year of follow-up. Between-group comparisons adjusted for trial centre, age, gender, disease duration and baseline value. All *P*-values for within-group comparison (CA2 vs baseline) were $P < 0.01$ except that of JADE on blood pressure (BP) < 130/80 mmHg ($P = 0.239$). No significant difference for changes in target achievement between groups. Only patients with paired data for baseline and second comprehensive assessment (CA2) are included in analysis. SMBG, self-monitoring of blood glucose.

JADE 39.5 to 53.4%, $P < 0.01$) increased similarly, with no between-group difference (Fig. 2). The absolute change in HbA_{1c} [DIAMOND −8 mmol/mol, JADE −7 mmol/mol (DIAMOND −0.69%, JADE −0.62%); $P = 0.473$] and LDL cholesterol (DIAMOND −0.32 mmol/l, JADE −0.28 mmol/l; $P = 0.286$) was similar in each group (Table 2). The proportion of participants with BP < 130 mmHg fell in the DIAMOND group but remained unchanged in the JADE group (DIAMOND 40.6 to 34.6%, $P < 0.01$; JADE 39.2 to 37.4%, $P = 0.239$) with no between-group difference (Fig. 2). More patients had a reduction in systolic BP of ≥ 10 mmHg (DIAMOND 18.4 vs JADE 22.2%; $P = 0.052$) and in diastolic BP of ≥ 5 mmHg (DIAMOND: 26.6% vs JADE: 33.5%, $P = 0.018$) in the JADE than the DIAMOND group (Table 2).

Both groups reported improved adherence to self-care behaviours ($P < 0.01$ compared with baseline) with more patients in the JADE group performing SMBG at study end (50.5 vs 44.2%, $P = 0.005$; Fig. 1). In the DIAMOND group, 16 of 205 participants (7.8%) and 21 of 199 (10.6%) in the JADE group stopped smoking, with no between-group difference (Table 2).

At study end, more participants in the JADE group initiated oral antidiabetic drug treatment (DIAMOND 19.1% vs JADE 25.1%; $P = 0.041$). New use of antihypertensive/lipid-lowering drugs was significantly different from baseline but similar in both groups. The proportion of participants reporting hypoglycaemic episodes at least monthly fell similarly in both groups (DIAMOND 11.9 to 6.7%, $P < 0.001$; JADE 10.8 to 7.3%, $P = 0.002$). Scores on the EuroQol health status index, the EQ-5D (visual analogue scale), tended to improve in the JADE group and declined in the DIAMOND group, with no between-group difference.

Table 2 Mean changes for HbA_{1c}, blood pressure, lipids and quality of life measures as well as changes in medications and self-care behaviour in the DIAMOND and JADE groups who underwent comprehensive assessments at baseline and after 12 months

Month 12: baseline visit	Valid number	DIAMOND (95% CI)	Valid number	JADE (95% CI)	Crude *P* value	Adjusted *P* value*
Metabolic control						
Median (IQR) HbA_{1c}, mmol/mol	944	−8 (−9, −7)	1112	−7 (−8, −6)	0.372	0.473
Median (IQR) HbA_{1c}, %	944	−0.69 (−0.81, −0.57)	1112	−0.62 (−0.73, −0.50)	0.372	0.473
Median (IQR) SBP, mmHg	1130	2.43 (1.49, 3.37)	1326	1.64 (0.77, 2.50)	0.221	0.091
Median (IQR) DBP, mmHg	1130	0.25 (−0.37, 0.86)	1326	−1.03 (−1.65, −0.41)	0.004	0.057
Median (IQR) LDL cholesterol, mmol/l	924	−0.32 (−0.38, −0.27)	1023	−0.28 (−0.34, −0.23)	0.335	0.286
Median (IQR) body weight, kg	1148	−0.13 (−0.48, 0.22)	1353	−0.02 (−0.29, 0.25)	0.612	0.482
HbA_{1c} reduction ≥ 0.5%, *n* (%)	944	400 (42.4)	1112	420 (37.8)	0.034	0.223
Systolic BP reduction ≥ 10 mmHg, *n* (%)	1130	208 (18.4)	1326	294 (22.2)	0.021	0.052
Diastolic BP reduction ≥ 5 mmHg, *n* (%)	1130	301 (26.6)	1326	444 (33.5)	< 0.001	0.018
LDL cholesterol reduction ≥ 30%, *n* (%)	924	193 (20.9)	1023	206 (20.1)	0.682	0.511
Body weight reduction ≥ 3%, *n* (%)	1148	232 (20.2)	1353	259 (19.1)	0.503	0.344
Smoking cessation, *n* (%)	205	16 (7.8)	199	21 (10.6)	0.346	0.759
Add on medication†, *n* (%)						
Insulin		50/885 (5.6)		71/1027 (6.9)	0.295	0.175
Oral antidiabetic drug		67/350 (19.1)		96/383 (25.1)	0.199	0.041
BP-lowering drugs		63/894 (7.1)		55/1072 (5.1)	0.098	0.126
Lipid-regulating drugs		106/793 (13.4)		110/899 (12.2)	0.337	0.586
Quality of life						
Median (IQR) EQ-5D index	1039	0.028 (0.018, 0.038)	992	0.037 (0.027, 0.047)	0.192	0.146
Median (IQR) EQ-VAS	1001	−0.80 (−1.52, −0.086)	967	0.66 (−0.12, 1.44)	0.005	0.478

BP, blood pressure; DIAMOND, DIAbetes MONitoring Database; IQR, interquartile range; JADE, Joint Asia Diabetes Evaluation.
*Adjusted for age, gender, disease duration, baseline value and trial centre.
†New users/non users at baseline.

Table 3 New onset of diabetes-related endpoints in JADE and DIAMOND study groups

	n	DIAMOND, *n* (%)	*n*	JADE, *n* (%)
All patients with vitality status	1549		1646	
Self-reported new cardiovascular event (coronary heart disease or stroke)		30 (1.9)		42 (2.5)
Returnees	1176	21 (1.8)	1383	27 (2.0)
Non-returnees	373	9 (2.4)	263	15 (5.7)
Death		6 (0.3)		6 (0.18)
Returnees for repeat assessment	1176		1383	
New chronic kidney disease: 50% loss of estimated GFR	900	16 (1.8)	1026	12 (1.2)
New appearance of sensory neuropathy in patients without sensory neuropathy at baseline	1072	49 (4.6)	1048	52 (5.0)
Remission of sensory neuropathy in patients with sensory neuropathy at baseline	96	70 (72.9)	75	53 (70.7)
Worsening or new appearance of diabetic retinopathy	992	28 (2.8)	869	37 (4.3)
Improvement of diabetic retinopathy in patients with diabetic retinopathy at baseline	59	59 (100)	45	41 (91.1)
Improved visual acuity in at least one eye	563	164 (29.1)	657	228 (34.7)
Deteriorated visual acuity in at least one eye	570	216 (37.9)	658	239 (36.3)

DIAMOND, DIAbetes MONitoring Database; JADE, Joint Asia Diabetes Evaluation.
Worsening /improvement of diabetic retinopathy is defined as advancement or stabilization in the grading by ophthalmologist (pre-proliferative, proliferative, advanced).
n includes returnees and a subset of defaulters who could be reached for health status assessment at study end.

Amongst returnees for CA2, the rate of incident diabetes-related complications including, chronic kidney disease, sensory neuropathy, foot ulcer, loss of visual acuity or advanced eye disease, were similar between groups (Table 3).

There were fewer defaulters in the JADE group than in the DIAMOND group (25.6 vs 32.0%; $P < 0.001$). At baseline, defaulters were younger (55.8 vs 56.7 years; $P = 0.036$), were more likely to have a positive smoking history (35.2 vs 33.9%; $P = 0.002$), were less well educated (> 11 years' education, 61.40 vs 70.70%; $P = 0.017$), and had worse cardiometabolic risk profile and higher rates of chronic kidney disease (3.20 vs 1.70%; $P = 0.007$) and macroalbuminuria (8.10 vs 4.20%; $P < 0.001$), despite similar disease duration. Although defaulters were more likely to be treated with insulin (30.70 vs 25.30%; $P = 0.001$) and lipid-lowering drugs (38.20 vs 33.90%; $P = 0.016$), they were less likely to adhere to regular physical exercise (46.10 vs 54.50%; $P < 0.001$) and achieve HbA_{1c} target (37.20 vs 46.40%; $P < 0.001$) or ≥ 2 treatment targets (30.60 vs 37.40%; $P < 0.001$; Table 4).

Discussion

In this 12-month randomized quality improvement programme in Chinese patients with Type 2 diabetes, we used a multi-component web-based portal to integrate care delivery focusing on workflow, task delegation and information technology. Irrespective of nurse support, both groups had improved cardiometabolic control, increased attainment of multiple treatment targets, enhanced self-care and smoking cessation. The additional contacts by nurses during the follow-up period did not further improve cardiometabolic control but reduced default rates and improved SMBG.

Given the multi-component nature of the JADE/DIAMOND programme, it was challenging to identify the specific components that drove treatment effects, although these elements are known to individually and collectively improve diabetes care [11]. In a 7-year observational study consisting of 172 patients with Type 2 diabetes without history of cardiovascular-renal complications, structured care provided by a diabetologist-nurse team reduced cardiovascular-renal disease and mortality by 50–70% compared with those attended by generalists in the medical clinic within the same institution [20]. In another study evaluating peer empowerment in participants who also received structured care through the JADE programme, HbA_{1c} was reduced by 0.3% (3 mmol/mol), with improvement in multiple targets attained and self-care [21].

The addition of nurse-coordinated follow-up visits in the JADE group did not further enhance glycaemic control or target attainment. That said, JADE participants were more likely to have stable BP control and increased SMBG and were less likely to default, suggesting that ongoing support can be translated into beneficial actions. The nurse provided was envisaged to take on a multifunctional role to promote adherence to the care protocol and reinforce patient education. Given the translational nature of this study that examined integrated care in real-world settings, we used data documented in the follow-up module of the JADE portal to assess protocol adherence. We did not rigorously enforce and strictly record compliance to protocol-recommended practice; thus, it was not possible to fully appraise intervention fidelity.

Table 4 Population characteristics at baseline for returnees versus defaulters

	Returnees	Defaulters	*P*
Total number of participants, *n* (%)	2559 (71.4)	1027 (28.6)	–
Demographics			
Mean ± SD age, years	56.70 ± 11.56	55.80 ± 11.83	0.036
Women, %	54.4	54.5	0.942
Education, %			< 0.001
< 6 years	6.7	12.7	
6–11 years	11.6	11.8	
> 11 years	70.7	61.4	
Unemployed, %	64.2	60.5	0.041
Smoking, %			0.428
Never	66.1	64.8	
Former	11.6	11.8	
Current	22.3	23.4	
Alcohol consumption, %			0.002
Never	67.8	72.8	
Former	6.4	7.5	
Occasional	16.9	11.7	
Regular	8.9	8.0	
Physical activity ≥ 3 times per week, %	54.5	46.1	< 0.001
SMBG ≥ weekly, %	45.1	42.4	0.163
Mean ± SD disease duration, years	6.43 ± 6.40	6.22 ± 6.11	0.369
Complications and comorbidities, %			
Chronic kidney disease	1.7	3.2	0.007
Coronary heart disease	9.0	8.4	0.548
Stroke	3.0	1.9	0.052
Peripheral vascular disease	9.5	7.3	0.052
Retinopathy	13.9	12.5	0.282
Sensory neuropathy	7.0	7.6	0.489
Risk categories			0.101
Low (1/2)	13.8	11.7	
High (3/4)	86.2	88.3	
Treatments, %			
Lifestyle modification only	21.2	22.3	0.487
On oral antidiabetic drug	71.4	69.0	0.163
Insulin	25.3	30.7	0.001
On lipid drugs	33.9	38.2	0.016
Statins	30.7	34.7	0.021
On BP drugs	23.2	21.0	0.154
ACE inhibitors	2.0	1.6	0.386
AT1 receptor blockers	12.3	11.0	0.279
Risk factor control			
Mean ± SD body weight, kg	69. 68 ± 12.34	69.19 ± 13.36	0.308
Mean ± SD BMI, kg/m^2	25.68 ± 3.58	25.16 ± 3.64	0.361
Mean ± SD waist circumference, cm			
Women	86.50 ± 10.11	86.68 ± 9.90	0.769
Men	91.44 ± 9.38	92.09 ± 10.04	0.214
Mean ± SD diastolic BP, mmHg	77.77 ± 9.6	77.76 ± 9.58	0.977
Mean ± SD systolic BP, mmHg	126.03 ± 15.07	126.72 ± 15.48	0.225
Mean ± SD total cholesterol, mmol/l	4.90 ± 1.18	4.99 ± 1.37	0.073
Mean ± SD HDL cholesterol, mmol/l			
Women	1.29 ± 0.32	1.26 ± 0.33	0.118
Men	1.12 ± 0.28	1.08 ± 0.27	0.001
Mean ± SD LDL cholesterol, mmol/l	2.90 ± 0.86	3.00 ± 0.94	0.005
Mean ± SD haemoglobin, g/dl	14.44 ± 6.85	14.27 ± 6.05	0.524
Mean ± SD HbA_{1c}, % (mmol/mol)	7.70 (61) ± 1.91 (14)	8.20 (66) ± 2.24 (17)	< 0.001
Median (IQR) triglyceride, mmol/l	4.80 (4.15, 5.53)	4.88 (4.19, 5.58)	0.286
Median (IQR) urine albumin to creatinine ratio, mg/mol	1.19 (0.65, 3.25)	1.35 (0.62, 4.23)	0.059
Mean ± SD estimated GFR, ml/min/1.73 m^2	120.7 ± 39.6	126.7 ± 42.1	< 0.001
Obesity, %	69.3	70.7	0.447
Dyslipidaemia, %	92.4	92.7	0.755
Hypertension, %	75.6	74.6	0.542
Macroalbuminuria, %	4.2	8.1	< 0.001
Microalbuminuria, %	22.8	23.3	0.791
Attainment of treatment targets, %			
HbA_{1c} < 7.0% (53 mmol/mol)	46.4	37.2	< 0.001
BP < 130/80 mmHg	50.0	47.1	0.154

Table 4 (*Continued*)

	Returnees	Defaulters	*P*
LDL cholesterol < 2.6 mmol/l	37.1	34.8	0.206
At least one target	72.7	70.4	0.171
At least two targets	37.4	30.6	< 0.001
All three targets	7.9	5.3	0.006
Quality of life			
Mean ± SD EQ-VAS score	83.38 ± 11.97	81.75 ± 12.80	< 0.001
Mean ± SD EQ-5D index score	0.91 ± 0.14	0.92 ± 0.14	0.156

BP, blood pressure; IQR, interquartile range; JADE, Joint Asia Diabetes Evaluation; SMBG, self-monitoring of blood glucose.

In China, delivery of chronic care is fragmented and infrastructure and capacity for team-based care are still evolving. Nurses for instance, are often tasked with simple procedures such as teaching insulin injection and SMBG or performing blood glucose tests. Furthermore, patients are less willing to engage nurses, preferring to consult directly with doctors. As such, their abilities to educate and empower patients may be less advanced compared with fully trained diabetes nurses. This may partially explain the lack of difference between the two groups. Also, the nurse coordinators in the present study received basic training in diabetes care, but, unlike case managers, were not empowered with treatment authority. In a meta-analysis, quality improvement initiatives that included case managers authorized to adjust medications without awaiting physician approval substantially improved patient care [22].

Because cultural factors are an important component in education, we examined this result in light of education programmes implemented in Chinese populations. In a 1-year prospective study in Hong Kong, a structured nurse education programme centred on cardiovascular disease risk every 3 months (mean total time 2.5 h) improved HbA_{1c}, LDL cholesterol and BP (diastolic) compared with a control group [23]. In Taiwan, the introduction of multidisciplinary care, combined with 2 h of diabetes education every 3 months for 1 year resulted in a 2-mmol/mol (0.22%) reduction in HbA_{1c}, with a nadir of 0.4% (4 mmol/mol) at 9 months, without changes in oral antidiabetic medications [24]. In the JADE group, we also recommended nurses to deliver at least 2 h of education after the CA, but in a single session rather than multiple sittings. In a meta-analysis, the benefit of patient self-care education on HbA_{1c} was most pronounced immediately after the intervention, with effects waning by 1–3 months [25]. In the Taiwanese study, subjects received initial diabetes education followed by repeated reinforcement sessions every 3 months for 1 year. The reduction in HbA_{1c} was evident at 3, 6 and 9 months but lost significance by 1 year, suggesting that physician or patient fatigue and loss of adherence may need to be addressed [24].

The fact that all participants benefitted from risk stratification with written feedback during the initial consultation might have contributed partially to a lack of separation and improvement in both groups. The proportion of participants with ≥ 2 treatment targets increased from 38.2 to 50.8% in the DIAMOND group and from 40.6 to 50.0% in the JADE group. Another reason for the lack of between-group difference was patient-structured follow-up frequency in JADE. In the low-risk category (care levels 1 and 2), the portal recommended 1–2 structured follow-up visits per year and 4–5 visits for the high-risk group (care levels 3 and 4). However, in the JADE group, the documented number of visits in the portal was 1.7 in participants at low risk and 2.0 in participants at high risk, the latter accounting for 86% of the JADE group. Given the fragmented nature of follow-up medical visits in China, we anticipated the additional nurse-coordinated visits to improve follow-up frequency. The low number of these structured visits might have nullified the expected benefits, which highlights the challenges of implementing integrated care models in countries with traditional healthcare and financing systems. Moreover, patients' perspectives need to be considered, as additional visits for a silent disease like diabetes may not be welcomed because of the extra time, tests and costs involved. By study design, there was no documentation of interval measurements between baseline and repeat CA2 in the DIAMOND group. Thus, although a variance might have existed between the two groups, the failure to fully comply a structured follow-up and education programme in the JADE group might have attenuated these differences by study end. Similar observations have been reported previously [24–26].

Despite the lack of between-group differences in cardiometabolic control, the default rate, defined *a priori*, was lower in the JADE than in the DIAMOND group. The defaulters had higher HbA_{1c} and LDL cholesterol, while concurrently were more likely to be prescribed insulin and lipid-lowering drugs. Defaulters were younger, more likely to be in paid employment and were less likely to exhibit good self-care behaviours. Patients less willing to participate in self-care behaviours become increasingly dependent on polytherapy and with chronicity, drug regimens might become more complex, which could further exacerbate non-adherence behaviours [27].

The present study has several limitations. Firstly, this was a real-world application of integrated care augmented by information technology in China, where healthcare resources are limited. All six participating sites are leading centres, although many of the recommended tests in the CA were not

reimbursed in an ambulatory setting. Unlike drug-based clinical trials, none of the participants were compensated for their participation or diagnostic/care-related expenditures. This might have led to selection of a more affluent population, although missing values for laboratory tests were found. As participating sites were selected from cosmopolitan cities, our findings cannot be extrapolated to rural populations. Secondly, while this was a randomized quality improvement programme, the treating doctors were not blinded to patient assignment and contamination was possible with participants in both the DIAMOND and JADE groups managed by the same physicians. Notwithstanding, the large sample size involving multiple centres, as well as the documentation of default rates/features known to be associated with higher mortality and treatment costs [28–30] are major strengths.

In the present study, we did not observe enhanced cardiometabolic control with the addition of a nurse coordinator to the web-based CA module, although we did observe a reduction in default rates and improved SMBG. We also verified that incorporating a quality improvement programme using an innovative care platform, such as the JADE programme, is both feasible and effective in a low-resource setting, albeit not without challenges. This prototype allowed the combining of logistics, task delegation and information technology to increase the efficiency and effectiveness of integrated care delivery with improvements in cardiometabolic control and self-care, as well as reduced clinical inertia.

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Competing interests

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References

1 Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 2003; **348**: 383–93.
2 Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008; **358**: 580–591.
3 Kong AP, Yang X, Ko GT, So WY, Chan WB, Ma RC *et al*. Effects of treatment targets on subsequent cardiovascular events in Chinese patients with type 2 diabetes. *Diabetes Care* 2007; **30**: 953–959.
4 Gaede P, Valentine WJ, Palmer AJ, Tucker DM, Lammert M, Parving HH *et al*. Cost-effectiveness of intensified versus conventional multifactorial intervention in type 2 diabetes: results and projections from the Steno-2 study. *Diabetes Care* 2008; **31**: 1510–1515.
5 Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA *et al*. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000; **321**: 405–12.
6 Ali MK, Bullard KM, Saaddine JB, Cowie CC, Imperatore G, Gregg EW. Achievement of goals in U.S. diabetes care, 1999-2010. *N Engl J Med* 2013; **368**: 1613–1624.
7 Cheng XB, Hsieh YT, Tu ST, Hsieh MC. Obesity and low target attainment rates in Chinese with type 2 diabetes. *Eur J Intern Med* 2012; **23**: e101–105.
8 Wang HH, Wang JJ, Wong SY, Wong MC, Mercer SW, Griffiths SM. The development of urban community health centres for strengthening primary care in China: A systematic literature review. *Br Med Bull* 2015; **116**: 139–154.
9 Chan JCN, Cockram CS. Organisation of diabetes care – Western Pacific Region (Hong Kong and China as examples). In: DeFronzo A, Feranninni E, Keen H, Zimmet P eds. *International textbook of diabetes mellitus*. Oxford: John, Wiley & Son, 2004.
10 Institute of Medicine. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: National Academy Press, 2001.
11 Tricco AC, Ivers NM, Grimshaw JM, Moher D, Turner L, Galipeau J *et al*. Effectiveness of quality improvement strategies on the management of diabetes: a systematic review and meta-analysis. *Lancet* 2012; **379**: 2252–2261.
12 Wu JY, Leung WY, Chang S, Lee B, Zee B, Tong PC *et al*. Effectiveness of telephone counselling by a pharmacist in reducing mortality in patients receiving polypharmacy: randomised controlled trial. *BMJ* 2006; **333**: 522.
13 Chan JCN, So WY, Yeung CY, Ko GTC, Lau IT, Tsang MW *et al*. The SURE Study: Effects of Structured versus Usual care on Renal Endpoint in Type 2 diabetes: A randomized multi-centre translational study. *Diabetes Care* 2009; **32**: 977–982.
14 Chan JCN, So WY, Ko G, Tong PCT, Yang XL, Ma RCW *et al*. The Joint Asia Diabetes Evaluation (JADE) Program: A Web-based Program to Translate Evidence to Clinical Practice in Type 2 Diabetes. *Diabet Med* 2009; **26**: 693–699.
15 Ko GT, So WY, Tong PC, Le Coguiec F, Kerr D, Lyubomirsky G *et al*. From design to implementation–the Joint Asia Diabetes Evaluation (JADE) program: a descriptive report of an electronic

web-based diabetes management program. *BMC Med Inform Decis Mak* 2010; **10**: 26.
16 Yang X, So WY, Kong AP, Ho CS, Lam CW, Stevens RJ *et al*. Development and validation of stroke risk equation for Hong Kong Chinese patients with type 2 diabetes: the Hong Kong Diabetes Registry. *Diabetes Care* 2007; **30**: 65–70.
17 Yang X, So WY, Kong AP, Ma RC, Ko GT, Ho CS *et al*. Development and validation of a total coronary heart disease risk score in type 2 diabetes mellitus. *Am J Cardiol* 2008; **101**: 596–601.
18 Yang XL, So WY, Kong AP, Ho CS, Lam CW, Ng MH *et al*. Modified end-stage renal disease risk score for Chinese type 2 diabetic patients—the Hong Kong Diabetes Registry. *Diabetologia* 2007; **50**: 1348–1350.
19 Yang X, Ma RC, So WY, Kong AP, Ko GT, Ho CS *et al*. Development and validation of a risk score for hospitalization for heart failure in patients with type 2 diabetes mellitus. *Cardiovasc Diabetol* 2008; **7**: 9.
20 So WY, Tong PC, Ko GT, Leung WY, Chow CC, Yeung VT *et al*. Effects of protocol-driven care versus usual outpatient clinic care on survival rates in patients with type 2 diabetes. *Am J Manag Care* 2003; **9**: 606–615.
21 Chan JC, Sui Y, Oldenburg B, Zhang Y, Chung HH, Goggins W *et al*. Effects of telephone-based peer support in patients with type 2 diabetes mellitus receiving integrated care: a randomized clinical trial. *JAMA Intern Med* 2014; **174**: 972–981.
22 Shojania KG, Ranji SR, McDonald KM, Grimshaw JM, Sundaram V, Rushakoff RJ *et al*. Effects of quality improvement strategies for type 2 diabetes on glycemic control: a meta-regression analysis. *JAMA* 2006; **296**: 427–440.
23 Ko GT, Li JK, Kan EC, Lo MK. Effects of a structured health education programme by a diabetic education nurse on cardiovascular risk factors in Chinese Type 2 diabetic patients: a 1-year prospective randomized study. *Diabet Med* 2004; **21**: 1274–1279.
24 Tien KJ, Hung HC, Hsiao JY, Hsu SC, Hsin SC, Shin SJ *et al*. Effectiveness of comprehensive diabetes care program in Taiwanese with type 2 diabetes. *Diabetes Res Clin Pract* 2008; **79**: 276–283.
25 Norris SL, Lau J, Smith SJ, Schmid CH, Engelgau MM. Self-management education for adults with type 2 diabetes: a meta-analysis of the effect on glycemic control. *Diabetes Care* 2002; **25**: 1159–1171.
26 Beverly EA, Fitzgerald SM, Brooks KM, Hultgren BA, Ganda OP, Munshi M *et al*. Impact of reinforcement of diabetes self-care on poorly controlled diabetes: a randomized controlled trial. *Diabetes Educ* 2013; **39**: 504–514.
27 Garcıa-Perez LE, Alvarez M, Dilla T, Gil-Guillen V, Orozco-Beltran D. Adherence to Therapies in Patients with Type 2 Diabetes. *Diabetes Ther* 2013; **4**: 175–194.
28 Currie CJ, Peyrot M, Morgan CL, Poole CD, Jenkins-Jones S, Rubin RR *et al*. The impact of treatment noncompliance on mortality in people with type 2 diabetes. *Diabetes Care* 2012; **35**: 1279–1284.
29 Asche C, LaFleur J, Conner C. A Review of Diabetes Treatment Adherence and the Association with Clinical and Economic Outcomes. *Clin Ther* 2011; **33**: 74–109.
30 Karter AJ, Parker MM, Moffet HH, Ahmed AT, Ferrara A, Liu JY *et al*. Missed appointments and poor glycemic control: an opportunity to identify high-risk diabetic patients. *Med Care* 2004; **42**: 110–115.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Clinical assessment for subjects assigned to Diabetes Monitoring Database (DIAMOND) and Joint Asia Diabetes Evaluation (JADE) groups.
Appendix S2. Power calculation and statistical analysis.