

BMJ Open Diabetes Shared Care Program (DSCP) and risk of infection mortality: a nationwide cohort study using administrative claims data in Taiwan

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ABSTRACT

Objective The Diabetes Shared Care Program (DSCP) is an integrated care model in Taiwan that has been proven to improve the care quality of patients with diabetes. We aimed to evaluate the efficacy of DSCP in decreasing the hospital mortality of infectious diseases.

Methods From 1 662 929 patients with type 2 diabetes newly diagnosed between 1999 and 2013, we retrieved a total of 919 patients who participated in the DSCP with the first hospitalisation for an infectious disease as the study cohort and 9190 propensity score-matched patients with type 2 diabetes who did not participate as the comparison. The efficacy of DSCP was evaluated via the following comparisons between the DSCP and non-DSCP cohorts: hospital mortality, 1-year medical cost prior to and during the hospitalisation, and complications, such as receiving mechanical ventilation and intensive care unit admission. The ratio (OR) for hospital mortality of the DSCP participants was calculated by logistical regression. Further stratification analyses were conducted to examine which group of patients with type 2 diabetes benefited the most from the DSCP during hospitalisation for infectious diseases.

Results The DSCP cohort had a lower hospital mortality rate than the non-DSCP participants (2.18% vs 4.82%, $p<0.001$). The total medical cost during the hospitalisation was lower in the DSCP cohort than in the non-DSCP cohort (NT\$72 454±30 429 vs NT\$86 385±29 350) ($p=0.006$). In the logistical regression model, the DSCP participants exhibited a significantly decreased adjusted OR for hospital mortality (adjusted OR=0.42, 95% CI 0.26 to 0.66, $p=0.0002$). The efficacy of the DSCP was much more prominent in male patients with type 2 diabetes and in patients with lower incomes.

Conclusion Participation in the DSCP was associated with a lower risk of hospital mortality for infectious diseases.

INTRODUCTION

Type 2 diabetes mellitus (DM) is an important healthcare issue in both low/middle-income countries and developed countries, with a reported prevalence of 9% in Caucasians and approximately 10%–20% among other

Strengths and limitations of this study

- This study was conducted using the nationwide claims database of 1 662 929 patients with type 2 diabetes newly diagnosed between 1999 and 2013 to evaluate the efficacy of the Diabetes Shared Care Program (DSCP) in decreasing the hospital mortality of infectious diseases.
- All the DSCP participants were enrolled for at least 1 year to evaluate the efficacy by assessing medical cost and hospital outcomes.
- Propensity score matching was conducted in this current study to reduce the selection bias between the DSCP and non-DSCP cohorts. Stratification analyses were conducted to examine which group of participants benefited the most from the DSCP.
- The limitation of this study was its observational and retrospective design, thereby making it impossible to randomly assign the DSCP enrollees.
- No laboratory data were available in this current study since this nationwide database was originally designed for expenditure claims.

races.^{1 2} In Taiwan, the prevalence of type 2DM is approximately 6%.^{1 3} Recently, the prevalence of type 2 diabetes has risen worldwide. According to National Health Interview Surveys conducted between 1999 and 2009 in the USA, there was a 9% increase in patients with diabetes.^{4 5}

Obesity, one of the most well-established risk factors of diabetes, was on the rise in Taiwan. Approximately one-fourth of adults in Taiwan were obese and therefore prone to develop type 2 diabetes.^{3 6} The numbers of patients with type 2 diabetes with comorbidities of hypertension and hyperlipidaemia also increased considerably from 10.47% in 2000 to 25.65% in 2009.^{5 7} The increasing number of patients with type 2 diabetes places a considerable burden on the healthcare system in Taiwan; the medical cost of



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the population increased from 3% to 4.5% of the total Taiwan's National Health Insurance (NHI) programme expenditures from 1986 to 2009.⁸

If left uncontrolled, type 2 diabetes would induce many detrimental complications, such as diabetic nephropathy, neuropathy, retinopathy, peripheral arterial occlusive disease and cardiovascular disease.^{1 9 10}

Infectious diseases are an important complication in patients with type 2 diabetes. A Danish cohort study demonstrated that patients with type 2 diabetes were at an increased risk for hospitalisation related to infection.¹¹ Therefore, making lifestyle modifications and receiving medical treatments after the diagnosis of type 2 diabetes is important.

In 2001, the Ministry of Health and Welfare in Taiwan initiated the Diabetes Shared Care Program (DSCP) to help patients with type 2 diabetes achieve better glycaemic control.¹ This care model emphasised the team care of the treating physicians, diabetes specialists, nurses and dietitians with the aim of improving the quality of care for patients with diabetes.⁹ Previous studies have demonstrated the improvement of cardiovascular and metabolic

outcomes in the DSCP participants of patients with type 2 diabetes.^{9 12} However, currently, no studies have investigated the influence of the DSCP on the outcomes of infection-related hospitalisation. In this study, we aimed to evaluate the efficacy of the DSCP in patients with type 2 diabetes hospitalised for infectious diseases.

METHODS

Study population

This observational, retrospective cohort study was conducted using the Longitudinal Cohort of Diabetes Patients (LHDB) data set, which was obtained from Taiwan's NHI programme. Taiwan's NHI programme is a universal health insurance system that covers nearly 99% of its residents.¹³

This study retrieved patients aged between 18 and 100 years old who were newly diagnosed with type 2 diabetes and were first hospitalised for infectious conditions. From the 1 662 929 patients with diabetes newly diagnosed between 1999 and 2013 in the LHDB, 919 patients with diabetes participating in the DSCP with

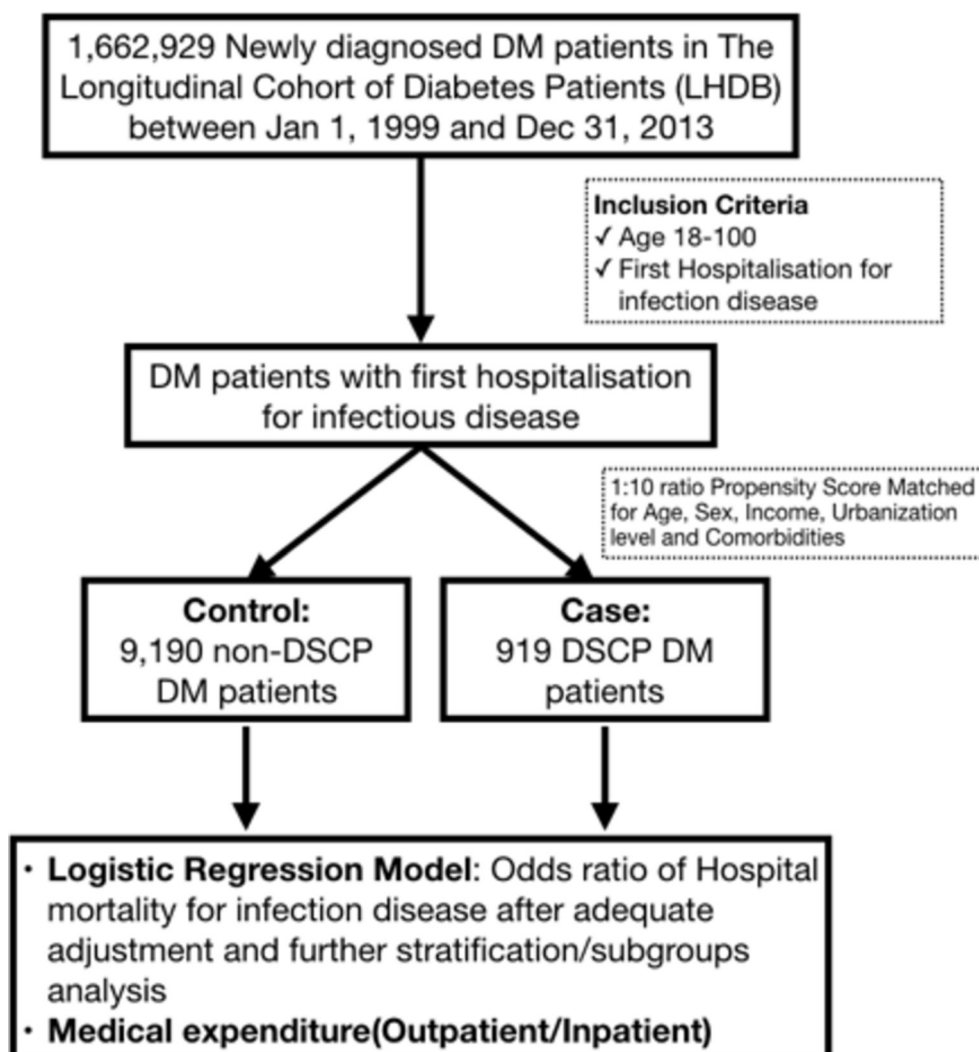


Figure 1 Participant selection process. DM, diabetes mellitus; DSCP, Diabetes Shared Care Program.

the first hospitalisation for infection were retrieved (figure 1). Meanwhile, we conducted a 1:10 ratio propensity score match for patients who were not enrolled in the programme according to their age, sex, income, urbanisation level and comorbidities.^{14 15} A total of 9190 propensity score-matched patients with diabetes who did not participate in the DSCP were assigned to the comparison group.

Patient and public involvement

Because the LHDB contains deidentified secondary data for research, our study was exempt from requiring informed consent from the participants. Thereby, no patient or public was involved in this study.

Outcome evaluation

This study aimed to evaluate whether the DSCP influenced the outcomes of infection-related hospitalisation in patients with diabetes. The index hospitalisation was defined as the first admission due to infectious disease after the patients participated in the DSCP. The primary outcome was the hospital mortality rate during the index hospitalisation. The secondary outcomes were the length of hospital stay, medical cost and complications between the DSCP and non-DSCP participants. We also analysed the difference in mortality ORs according to the infection sites between the DSCP and non-DSCP groups.

Diabetes Shared Care Program

The DSCP was initiated by Taiwan's Bureau of National Health Insurance (BNHI) in 2001 to enhance the quality and efficiency of type 2 diabetes care.¹³ This programme financially encourages the healthcare provider to provide patients with diabetes with multiple laboratory tests annually (eg, HbA1c, total cholesterol, low-density lipoprotein (LDL)) and other related health examinations (eg, for eyes or feet).¹³ Physicians specialising in metabolic disorders or who had taken part in a training programme for type 2 diabetes shared care were eligible to enrol individual patients.¹³ All patients enrolled were required to receive education and comprehensive care for type 2 diabetes by the BNHI.¹³ Therefore, DSCP participants received integrated care from physicians, diabetes educators and dietitians, whereas the non-DSCP participants received care from only physicians. However, the time between the enrolment date and index hospitalisation date was recorded.

Statistics

Descriptive analysis was used to compare the basic characteristics of the DSCP and non-DSCP groups. Demographic information, including age, sex, income, urbanisation level, comorbidities and medical resource utilisation, was collected retrospectively for a period of 1 year. A 1:10 ratio of propensity score-matched comparison was conducted based on the patient's age, sex, insurance premium, urbanisation level and comorbidities.^{14 15} The OR was calculated using the logistical regression model after

adjusting for potential confounders to determine the effect of the DSCP on mortality in patients with diabetes hospitalised for infection. Further stratification analyses were conducted to examine which group of patients with type 2 diabetes benefited the most from the DSCP during hospitalisation for infectious diseases. Statistical analyses were performed using the SAS V.9.4 statistical package (SAS Institute). A p value of 0.05 was considered significant.

RESULTS

The demographic characteristics and comorbidities of patients with type 2 diabetes who did and did not participate in the DSCP are shown in table 1. The mean ages of the DSCP and non-DSCP participants were 61.77±13.91 and 61.61±14.88 years old, respectively (p=0.74). There were no significant differences in the age, sex, income, urbanisation level or baseline comorbidities between each group. However, the DSCP participants were more likely to receive aspirin, statins, biguanide, sulfonylurea, thiazolidinedione and insulin.

The hospital outcomes during index hospitalisation for infection between the DSCP and non-DSCP participants are shown in table 2. In terms of the mortality rate during hospitalisation, the DSCP group showed a significantly lower rate (2.18% vs 4.82%, p=0.0003). Stratification analysis of the different infectious diseases showed that the DSCP participants exhibited a lower frequency of respiratory (26.22% vs 30.24%, p=0.0112) and gastrointestinal infections (8.49% vs 13.04%, p<0.0001). In addition, primary bacteraemia (12.4% vs 16.72%, p=0.0007) and sepsis (10.12% vs 14.67%, p=0.0002) were less frequent in the DSCP group. However, a higher frequency of genitourinary infections (32.64% vs 28.96%, p=0.019) and musculoskeletal system infections (21.87% vs 16.72%, p<0.0001) were reported in the DSCP group. Regarding the rate of mechanical ventilation requirement and intensive care unit admission, no significant differences were observed between the groups. The length of hospital stay was also not significantly different between the two groups.

The logistical regression model was conducted to measure the OR of hospital mortality associated with the DSCP in different infection classifications (table 3). For primary bacteraemia, the mortality rate was improved significantly in the DSCP group (adjusted OR=0.49, 95% CI 0.20 to 0.66, p=0.0399). Although no significant difference was noted, the mortality rates of respiratory infection (adjusted OR=0.5, 95% CI 0.25 to 1.00, p=0.051) and sepsis (adjusted OR=0.55, 95% CI 0.27 to 1.10, p=0.0916) were lower in the DSCP group.

The medical care expenditures in the DSCP and non-DSCP groups are shown in figure 2. The medical expenditures of the outpatient department during a 1-year period were significantly higher in the DSCP group (NT\$73 956±39 259 vs NT\$56 050±30 645). No significant difference in the total medical expenditures

Table 1 Demographic characteristics and comorbidities in patients with diabetes who did and did not participate in the Diabetes Shared Care Program (DSCP)

	After PS matching*				P values
	Diabetes Shared Care Program				
	No (n=9190, 90.91%)		Yes (n=919, 9.09%)		
	n	%	n	%	
Sex					0.8242
Female	3995	43.47	396	43.09	
Male	5195	56.53	523	56.91	
Age (years)					0.1122
18–29	176	1.92	10	1.09	
30–39	559	6.08	49	5.33	
40–49	1364	14.84	136	14.8	
50–59	2124	23.11	217	23.61	
60–69	1964	21.37	209	22.74	
70–79	1930	21	212	23.07	
≥80	1073	11.68	86	9.36	
Mean (±SD)†	61.61 (14.88)		61.77 (13.91)		0.7369†
Insurance premium (NT\$)					0.9102
<20 000	4138	45.03	413	44.94	
20 000–40 000	3982	43.33	398	43.31	
40 000–60 000	882	9.6	86	9.36	
≥60 000	188	2.05	22	2.39	
Urbanisation level					0.9817
1 (highest)	1353	14.72	138	15.02	
2	2770	30.14	270	29.38	
3	2248	24.46	230	25.03	
4	2010	21.87	198	21.55	
5 (lowest)	809	8.8	83	9.03	
Baseline comorbidity					
HTN	6500	70.73	652	70.95	0.89
Hyperlipidaemia	4558	49.60	465	50.60	0.5628
COPD	2841	30.91	285	31.01	0.9512
PAOD	931	10.13	102	11.10	0.3554
IHD	3254	35.41	332	36.13	0.6644
CLD	2181	23.73	224	24.37	0.663
CKD	3403	37.03	351	38.19	0.4861
Stroke	2465	26.82	249	27.09	0.8592
Cancer	1136	12.36	118	12.84	0.6746
CCI score					0.1011
0	190	2.07	18	1.96	
1	1129	12.29	91	9.90	
≥2	7871	85.65	810	88.14	
Drug					
NSAID	3818	41.55	390	42.44	0.6008
Aspirin	910	9.90	116	12.62	0.0092
Statin	1728	18.80	212	23.07	0.0017

Continued

Table 1 Continued

	After PS matching*				
	Diabetes Shared Care Program				
	No (n=9190, 90.91%)		Yes (n=919, 9.09%)		P values
n	%	n	%		
Clopidogrel	340	3.70	43	4.68	0.1382
Biguanides	3081	33.53	438	47.66	<0.0001
DPP-4 inhibitors	248	2.70	34	3.70	0.0789
Sulfonylureas	3556	38.69	533	58.00	<0.0001
Thiazolidinedione	548	5.96	105	11.43	<0.0001
Other OAD	955	10.39	173	18.82	<0.0001
Insulin	983	10.7	228	24.81	<0.0001

X² test.

*Propensity score matching included the following variables: age, sex, insurance premium, urbanisation and baseline comorbidities.

†Two-sample t-test.

‡Fisher's exact test.

§Antidiabetic agents include biguanides, DPP-4 inhibitors, other OAD, sulfonylureas, thiazolidinedione and insulin.

CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; HTN, hypertension; IHD, ischaemic heart disease; NSAID, non-steroidal anti-inflammatory drug; OAD, oral antidiabetic drug; PAOD, peripheral arterial occlusion disease; PS, propensity score.

before the index hospitalisation between the two groups was noted (NT\$182 988±233 434 vs NT\$176 253±314 730) (p=0.4212). However, the total medical expenditures during the index hospitalisation were significantly higher in the non-DSCP group (NT\$72 454±30 429 vs NT\$86 385±29 350) (p=0.0066).

Table 2 Hospital outcomes during index hospitalisation for infectious disease between patients with diabetes who did and did not participate in the DSCP

	After PS matching*				
	Diabetes Shared Care Program (DSCP)				
	No (n=9190, 90.91%)		Yes (n=919, 9.09%)		P values
n	%	n	%		
Infection classification					
Central nervous	48	0.52	7	0.76	0.3469
Respiratory	2779	30.24	241	26.22	0.0112
Cardiovascular	43	0.47	1	0.11	0.1812†
Gastrointestinal	1198	13.04	78	8.49	<0.0001
Genitourinary	2661	28.96	300	32.64	0.0191
Musculoskeletal	1537	16.72	201	21.87	<0.0001
Primary bacteraemia	1537	16.72	114	12.4	0.0007
Device-related infection	138	1.5	15	1.63	0.7572
Other/undetermined	1039	11.31	130	14.15	0.0103
Sepsis	1348	14.67	93	10.12	0.0002
Procedures (during hospitalisation)					
Mechanical ventilation	922	10.03	84	9.14	0.3889
Intensive care unit	1441	15.68	126	13.71	0.1157
Mortality	443	4.82	20	2.18	0.0003
Length of hospital stay, days (means, SD)	11.76 (29.24)		11.36 (11.78)		0.4203‡

X² test.

*Propensity score matching included the following variables: age, sex, insurance premium, urbanisation and baseline comorbidities.

†Fisher's exact test.

‡Two-sample t-test.

PS, propensity score.

Table 3 Logistical regression model measuring the ORs and 95% CIs of mortality associated with the Diabetes Shared Care Program stratified by infection classification

Variable	Mortality		Crude		Adjusted*	
	No n (%)	Yes n (%)	OR (95% CI)	P values	OR (95% CI)	P values
Infection classification						
Central nervous	6 (12.50)	2 (28.57)	2.8 (0.44 to 17.80)	0.2752	–	–
Respiratory	190 (6.84)	9 (3.73)	0.53 (0.27 to 1.05)	0.0669	0.5 (0.25 to 1.00)	0.051
Cardiovascular	0	0	–	–	–	–
Gastrointestinal	34 (2.84)	2 (2.56)	0.9 (0.21 to 3.82)	0.8875	1.06 (0.24 to 4.74)	0.9433
Genitourinary	50 (1.88)	0	–	–	–	–
Musculoskeletal	10 (0.65)	1 (0.50)	0.76 (0.10 to 6.00)	0.7977	0.67 (0.08 to 6.01)	0.7212
Primary bacteraemia	273 (17.76)	10 (8.77)	0.45 (0.23 to 0.86)	0.0166	0.49 (0.25 to 0.97)	0.0399
Device related	5 (3.62)	0	–	–	–	–
Other/undetermined	17 (1.64)	1 (0.77)	0.47 (0.06 to 3.53)	0.46	0.42 (0.05 to 3.42)	0.4165
Sepsis	267 (19.81)	10 (10.75)	0.49 (0.25 to 0.95)	0.0356	0.55 (0.27 to 1.10)	0.0916

*Adjusted for age, sex, insurance premium, urbanisation level and comorbidities in a logistical regression model.

The forest plot in figure 3 shows the stratification of ORs of the DSCP efficacy. In our stratification analysis, men participating in the DSCP had a lower OR for mortality rate (adjusted OR=0.36) compared with women. Therefore, men may have benefited more from this programme. The efficacy of DSCP in infectious diseases was much more obvious in male patients (adjusted OR=0.36, 95% CI 0.20 to 0.66, $p=0.0009$), patients aged 70–79 years (adjusted OR=0.25, 95% CI 0.09 to 0.70, $p=0.008$) and patients with

the low and lowest incomes (adjusted OR=0.32, 95% CI 0.12 to 0.87, $p=0.0256$ and adjusted OR=0.41, 95% CI 0.23 to 0.73, $p=0.0022$, respectively).

DISCUSSION

Our study demonstrated that the patients with type 2 diabetes enrolled in the DSCP were associated with better outcomes from infection-related hospitalisation. Among

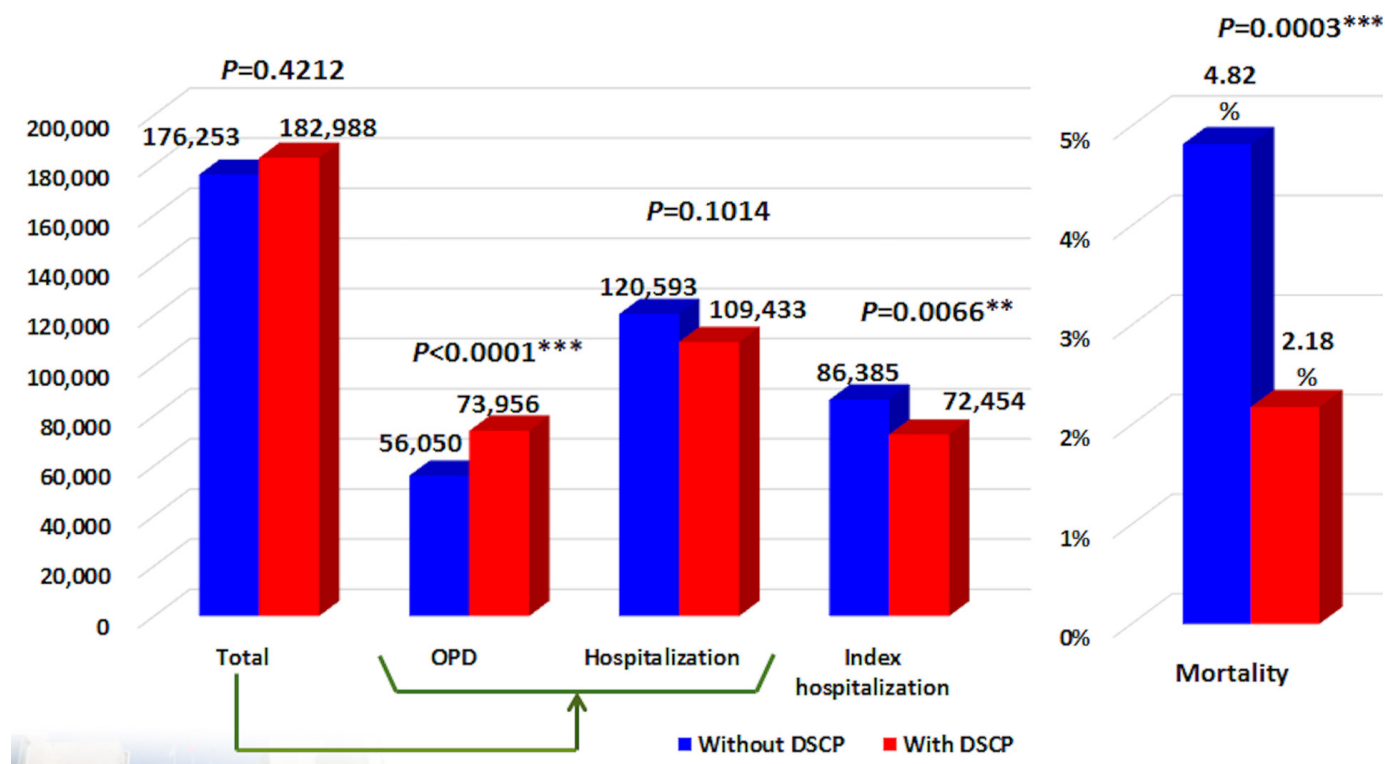


Figure 2 Cost and mortality rate in patients with diabetes with and without DSCP participation. DSCP, Diabetes Shared Care Program; OPD, outpatient department.

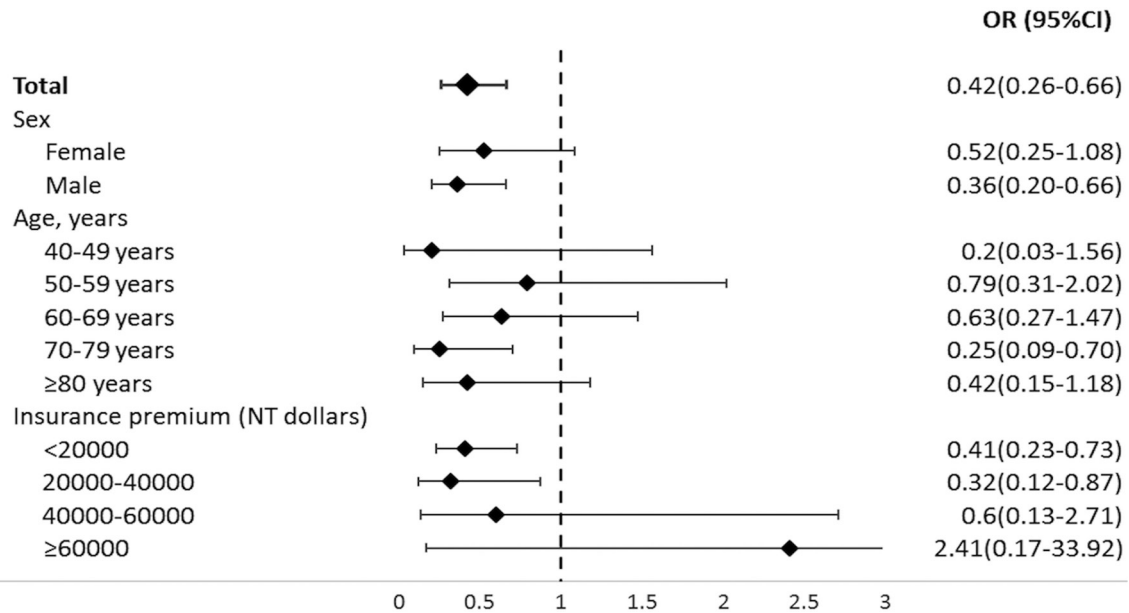


Figure 3 Stratification analysis of Diabetes Shared Care Program (DSCP) efficacy in infectious conditions with hospitalisation.

patients enrolled in the DSCP, the in-hospital mortality rate was significantly lower than that of patients not enrolled in the DSCP (2.18% vs 4.82%, $p=0.0003$). The total medical expenditures during the index hospitalisation were significantly lower in the DSCP group (NT\$72 454±30 429 vs NT\$86 385±29 350, $p=0.0066$). Even without statistical significance, the DSCP group had lower requirements of mechanical ventilation support and intensive care unit admission. The medical expenditure of index hospitalisation was also significantly lower in the DSCP group (NT\$72 454±30 429 vs NT\$86 385±29 350, which are equal to US\$2468.70 vs US\$2944.02). A previous study also reported that the DSCP increased the total expenses in type 2 diabetic care to approximately US\$100 (equal to NT\$3000) per person per year, which indeed lowers the costs of hospitalisation.¹³ In stratification analysis of DSCP efficacy in infectious conditions with hospitalisation, male patients, patients aged between 70 and 79 years and patients with insurance premiums below NT\$40 000 (equal to US\$1333.33) benefited more from the DSCP.

Pay for performance with the DSCP was established in 2001 in Taiwan and has proven to be cost-effective, especially in patients with type 2 diabetes with hypertension and hyperlipidaemia.^{1 5 8} The programme was first launched in August 1996 in I-Lan County, which is located in northeastern Taiwan.¹ The DSCP was then implemented nationwide in Taiwan. The number of patients participating in this programme has increased gradually since 2001.^{1 12} This programme aims to provide comprehensive type 2 diabetic care by integrating physical and psychosocial support. The DSCP sets an 'ABC' goal for diabetic management (A: HbA1c <7.0%, B: blood pressure <130/80 mm Hg, C: LDL cholesterol <100 mg/dL/total cholesterol <160 mg/dL).¹ This programme also encourages healthcare providers with financial incentives to perform regular follow-up visits and exams for

better monitoring and controlling diabetes.¹³ In terms of medication, the classes of antidiabetic, antihypertensive and antilipidemic medications were prescribed individually according to the patient's care plan, comorbidity and other patient factors.⁹ In addition to medical treatments, patients who participate in the DSCP are educated about self-care, nutrition supplements and other health issues related to diabetes by certificated diabetes specialists, nurses and dietitians.⁹ Chen *et al*¹⁶ illustrated that the duration of enrolment in this programme was positively correlated with the care quality and compliance.¹⁶ Patients with type 2 diabetes with 1 year of participation in the DSCP also benefited more than those participating fewer than 3 months.^{8 16}

Hao *et al*⁹ found that patients enrolled in the DSCP had significantly improved systolic and diastolic blood pressure. Lipid profiles, including high-density lipoprotein and LDL, showed significant improvements after participation in the DSCP for 3 years.⁹ Kornelius *et al*¹² also reported that patients engaged in the DSCP had a 14% reduction in cardiovascular events, a 16% reduction in stroke risk and a 22% reduction in all-cause mortality. These authors also found that patients with lower incomes and those of older age were at higher risk of cardiovascular complications.¹²

In addition, the immune system is compromised in patients with diabetes, and these patients are more likely to develop infectious diseases. Previous studies have reported that diabetes may lead to deleterious effects on both the cellular and humoral immune system, causing patients with diabetes to be more susceptible to infection.^{17 18} In terms of pathophysiology, decreased perception, tissue hypoxaemia, reduced tissue perfusion and impaired leucocyte function develop in patients with diabetes.¹⁹ These changes also include decreased leucocyte function, altered microvascular responses

and changes in the complement cascade and cytokine network.^{17 18} Furthermore, leucocyte responsiveness in patients with diabetes has been proven to be inversely related to the hyperglycaemic status.^{18 20} These changes make patients with diabetes more vulnerable to infections, such as foot ulcers and urinary tract infections.^{21 22} Moreover, patients with diabetes are prone to infections caused by resistant pathogens.²² Mor *et al* reported that patients with diabetes had a higher rate of hospital-treated infections, with especially increased rates of emphysematous cholecystitis, abscess, tuberculosis and septicæmia.¹¹ However, such adverse effects could be reversed after adequate glycaemic control.^{18 23–27}

In our study, DSCP participants had significantly higher prevalence of genitourinary infection and musculoskeletal infection. This phenomenon could be explained by the prevalence of these infectious diseases in patients with type 2 diabetes and the regular follow-up of the DSCP participants. Previous studies showed that patients with diabetes have higher prevalence of genitourinary tract infection and diabetic foot infection.^{21 28 29} As the DSCP provides participants with routine laboratory analysis and self-care education, these common infections could be detected earlier and be treated more aggressively. Moreover, given routinely visits and follow-up, the frequencies of infection-related hospitalisation due to respiratory disease, primary bacteraemia and sepsis were significantly decreased in DSCP participants. This might be associated with the regular monitoring and early intervention in the care programme (DSCP). In the logistical regression model, each mortality rate stratified by infection classification was reduced in the DSCP group. In addition, the overall mortality rate was significantly reduced.

Taiwan's NHI programme is a universal health insurance system covering nearly 99% of its residents.¹³ This programme has been adopted by the Taiwanese government since March 1995.³⁰ The revenue for the NHI programme comes from several sources (employees, employers and government, both nationally and locally).³⁰ The insured are classified into six main categories and 15 subcategories based on their job and income. The percentage of the premium paid by the insured for each category varies from 0% for low-income citizens to 100% for the self-employed.³⁰ The DSCP is a programme of care in Taiwan's NHI programme. Our study demonstrated the forest plot (figure 3) for the stratification of ORs of the efficacy of DSCP, finding that DSCP participants with premiums lower than NT\$40 000 benefited more from the DSCP. For the nearly 99% of citizens covered by Taiwan National Insurance, those with lower incomes may have more accessibility to medical aids. While participating in the DSCP, these individuals could benefit more from receiving diabetes-related education and monitoring during every visit.

This study has some limitations. This study was not a randomised controlled trial, and randomly assigning the patients with diabetes into the DSCP and non-DSCP groups was difficult. In addition, since the physicians were

free to recruit their participants, selection bias may also be present. One previous study reported that physicians might exclude sicker patients from this programme.³¹

CONCLUSION

In this study, we found that participation in the DSCP was associated with a lower risk of hospital mortality in infectious conditions. Older patients, male patients and patients with lower socioeconomic statuses showed higher cost-effectiveness in this programme. This finding may promote healthcare providers distributing this health resource more efficiently.

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Contributors Conception and design: CHC and MSH. Data analysis and interpretation: SYH, DHTY, CKH, CMC, JHC and VCRH. Manuscript writing: CHC, MSH and SHM. Final approval and critical revision: CKH and MSH.

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Competing interests None declared.

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Data sharing statement According to the requirement of the International Committee of Medical Journal Editors, we are willing to share the study protocol and statistical analysis process. However, the deidentified data of the patients included in our study were not released to the researchers because of special restriction of the Taiwan National Health Insurance Research Database. After the study is published, the above-mentioned information should be easily available by direct contact with the corresponding author.

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