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Five-year cost-effectiveness of patient empowerment programme (PEP) for type 2 diabetes mellitus in primary care

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ABSTRACT

This study evaluated the short-term cost-effectiveness of the Patient Empowerment Programme (PEP) for diabetes mellitus in Hong Kong. Propensity score matching was used to select a matched group of PEP and non-PEP subjects. A societal perspective was adopted to estimate the cost of PEP. The outcome measures were the cumulative incidence of all-cause mortality and diabetic complication over a five-year follow-up and the number needed to treat (NNT) to avoid one event. The incremental cost-effectiveness ratio (ICER) of cost per event avoided was calculated using the PEP cost per subject multiplied by the NNT. The PEP cost per subject from the societal perspective was US$247. There was a significantly lower cumulative incidence of all-cause mortality (2.9% vs 4.6%, $p<0.001$), any diabetic complication (9.5% vs 10.8%, $p=0.001$) and CVD events (6.8% vs 7.6%, $p=0.018$), in the PEP group. The costs per death from any cause, DM complication or case of CVD avoided were US$14,465, US$19,617 and US$30,796, respectively. The extra amount allocated to running PEP was small and it appears cost-effective in the short-term as an addition to RAMP.

INTRODUCTION

Self-management education programmes were shown to be effective in systematic reviews, but whether such programmes are also cost-effective is important to health care decision makers to allocate limited resources efficiently. Our recent systematic review identified 12 cost-effective studies published between January 2003 and September 2015 but none was carried out on an Asian population who might have different response to education interventions for culture and practical reasons.[1]

A Patient Empowerment Programme (PEP) for Diabetes Mellitus (DM) was launched by the Hong Kong (HK) Hospital Authority (HA) in 2010, aiming to enhance subjects' disease-specific knowledge and self-management skills, promote self-efficacy and modify lifestyles. Detailed descriptions of the programme are available elsewhere.[2-8] Apart from the PEP, the HA introduced a multi-disciplinary Risk Assessment and Management Programme (RAMP) in 2009 to provide regular check-ups and complication screening to all DM subjects in public general outpatient clinics (GOPCs) that provide primary care services.[9] Over 90% of the PEP subjects currently participate in RAMP serving as routine clinical practice. We therefore interested to evaluate the cost-effectiveness of PEP as additional to RAMP using empirical cost and effectiveness data from a cohort with up to five years of follow up.

MATERIALS AND METHODS

Evaluating the five-year effectiveness of PEP

We selected subjects with DM who had joined RAMP on or before 31 March 2012 and have attended at least one PEP session within 180 days of their first RAMP assessment as the PEP group, while those who had not joined PEP by 30 Nov 2015 were defined as the non-PEP

group. We excluded subjects who had any pre-defined diabetic complications including cardiovascular disease (CVD), diabetic retinopathy (DR), nephropathy or neuropathy; and those who had specialist medical clinic attendances within 6 months on or before their baseline visit; and those did not have complete data at baseline. Propensity score matching was used to match the two groups on socio-demographic factors, clinical baseline measures, clinical characteristics, and health service utilization at baseline.

The outcome used was the first occurrence of any CVD complication, DR (including sight threatening diabetic retinopathy), end stage renal disease (ESRD), neuropathy or mortality from any cause during the five-year follow up period.

Costing of PEP

A societal perspective was adopted to estimate the cost of the programme which included NGO resource costs, HA administrative costs as well as costs to the community and to subjects attending PEP. We converted them to a per subject cost and the final PEP cost per subject was the sum of the above four categories. All costs are originally calculated in HK$ and converted into US$ for reporting (1US$=7.8HK$).

A structured questionnaire was distributed to the NGOs in all seven geographical clusters in HK to collect data on expenditures in setting up in the first year of operation, and in running PEP each year. HA administrative costs were obtained from the HA Finance Division to estimate the costs spent on PEP at head office and cluster office.

The set-up cost for NGOs and HA was divided by the number of subjects who attended at least one PEP session in that cluster, while the ongoing cost was divided by the number of subjects in that cluster in the corresponding financial year and then was averaged across the years. Finally, these per cluster costs were averaged across all clusters.

The NGOs reported on the time of volunteers spent on PEP. These were annualized and valued at the hourly wages of the specific staff, if noted, or the median hourly wage for the Hong Kong population.[10] The use of NGO's own, or other unpaid, venues for PEP were valued based on the rental cost of paid venues reported in that year. These costs were summed and divided by the corresponding number of subjects, and averaged across clusters and years.

A self-administered questionnaire was distributed to 475 subjects in all clusters to collect the travel cost and time used by subjects and accompanying person(s) attending the PEP. Time spent attending PEP sessions was measured as an average of 2.5 hours for disease-specific sessions and 2 hours for generic sessions and each participant attended on average four sessions with two disease-specific and two generic sessions for each subject and 6% of subjects had a companion. Travel and attendance time was valued using the median hourly wage for subjects and their companions.[10] Co-payments were paid by some subjects but ignored as a transfer payment under the societal perspective.

Statistical analysis

The characteristics of the matched PEP and non-PEP groups were compared by independent t-test or chi-squared tests. Five-year cumulative incidence of the outcomes was calculated for each type of event and compared between the groups by chi-squared tests. All statistical analyses were performed in STATA 13 while the cost and cost-effectiveness analysis were done in excel.

Cost-effectiveness Analysis

Only the extra costs of PEP in additional to routine health care were considered since both groups attended RAMP. We did not discount the cost since the programme cost was onetime

cost only i.e. all present cost. The number needed to treat (NNT) to avoid one event over five-year was estimated for outcomes which was significantly different between groups. The incremental cost-effectiveness ratio (ICER) was calculated using the PEP cost per subject multiplied by the NNT giving us cost per complication or death avoided during the study period. One-way sensitivity analysis was conducted to test the uncertainties surrounding the PEP cost per subject using the minimum to maximum values of costs reported by the NGOs. Effectiveness was tested with the 95% confidence interval (CI) for events of PEP groups constructed based on Poisson distribution.

RESULTS

Characteristics of the matched PEP and non-PEP groups

After excluding ineligible subjects, there were 11,600 subjects in the PEP group remained for matching which yielded 11,581 matched pairs (Appendix 1). There were no significant differences between the matched groups (Appendix 2).

Five-year effectiveness of PEP

The mean follow-up for PEP and non-PEP groups was 53 and 55 months, respectively. There was a significantly lower cumulative incidence of all-cause mortality (2.9% vs 4.6%, $p<0.001$), any diabetic complication (9.5% vs 10.8%, $p=0.001$) and CVD events (6.8% vs 7.6%, $p=0.018$), in the PEP group than in the non-PEP group (Appendix 3). There was no significant difference in the cumulative incidences of DR, ESRD or neuropathy.

PEP cost per subject

The total societal PEP cost per subject was US$247 with a range across NGOs of US$191 to US$297 (Table 1). Among these 57% were the provider costs; 38% were the subjects' and families' costs; and, 5% were community costs.

Cost-effectiveness of PEP

The incremental cost of PEP versus non-PEP group was the programme cost above and NNT to avoid a death from any cause is 58, resulting in an ICER of US$14,465 per death (Table 2). The cost to avoid one CVD death was US$68,192. To avoid any DM complication, the NNT is 79 and this gives an ICER of US$19,617. The ICER to avoid a CVD event is US$30,796, to avoid a stroke is US$42,747 and to avoid a heart failure event is US$58,450. Varying the cost of the programme did not have a large impact on the ICERs, but varying the effectiveness may increase the ICER up to two times of the base case.

DISCUSSION

The estimated cost of PEP per subject was around US$128-US$256, depending on whether the subject costs were included or not. Of the NGO-ongoing cost, staff cost and other operating expense costs caused greatest variability while equipment and venue rentals did not cause a lot of variation. The variation in staff cost could be explained by different grades of staffs used, different number or working hours of staff used.

The additional cost to avoid a death from any cause by PEP was US$14,465 (HK$112,827). A local estimate of the statistical value of life saved in HK was at least HK$10 million.[11] By this measure, the cost to avoid one death was far below the value and so PEP could be

considered cost-effective. Diabetic complications are usually associated with extra health service costs. For example, one study in HK estimated the health service cost for subject with CVD was 2.88 to 7.04 times higher in event year and 1.33 to 2.43 times higher in subsequent year than subject without CVD.[12] It would be expected that the PEP cost could be compensated for the reduction in health service utilization due to prevention of complications. In the current calculation of cost-effectiveness, we did not include the health service costs in the costing part to avoid double counting of the benefits in dollar values since it has already counted in the effectiveness part, i.e. reduction in complications.

The advantage of this study was that the five-year follow-up period would allow us to observe the difference in development of diabetic complications between groups rather than only surrogate outcomes i.e. HbA1c, blood pressure which commonly used in other short-term CEA studies. The comprehensive estimate of the programme cost in this study was also important for the quality of the cost-effectiveness findings. The limitation was that this study was not a RCT, therefore we need to be cautious of claiming the association of PEP on the reduced incidence as a causal association. As RCT is not always practical in a service setting, we generated two similar groups based on the characteristics for which we have data. The baseline characteristics of our matched groups were all comparable in demographic, clinical risk factors and health service utilization. Nonetheless we must admit to the possibility that the two groups may differ in some aspects which are not reflected in the variables we have. Our further analyses on changes in DM knowledge score and clinical measurements of the PEP group stratified by the number of PEP sessions showed an expected trend with larger improvement in knowledge and clinical risk factors from those who attended more sessions (Appendix 4). This supports the view that the association between PEP and the improved outcomes could be causal.

There have been a few studies on the cost-effectiveness of self-management education programmes but none were directly comparable to the PEP programme. Similar to our group based structured diabetes education programme in primary care setting, a programme named DESMOND in UK was found to be cost-effective from provider perspective with an ICER of £5,387 per QALY gained using a life-time model.[13] Another programme also with diabetes group education structure in South Africa was shown to be cost-effective from societal perspective with an ICER of US$1,862 per QALY gained using a life-time model.[14] Neither of these studies calculated the cost per complication or death prevented but both studies supported the cost-effectiveness of self-management education programmes which is consistent with our conclusion.

In conclusion, the extra amount allocated to running PEP was not very great and it appears to be cost-effective over five years. This was a lifestyle education programme taken in addition to the routine care offered in the RAMP programme and, as others have shown, might be even more cost-effective when taking a life time horizon.

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Author contributions: J.X.L. researched data and wrote the manuscript. S.M.M wrote the manuscript. C.S. and J. C. researched data and contributed to the methods and results of the

manuscript. C.K.H.W., W.C.W.W. and C.L.K. L. reviewed and edited the manuscript. W.C.W.W. is the guarantor of this work.

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Tables

Appendices

Table 1. Summary of average PEP costs per subject

Costs	Cost per subject (US$)	Range (min to max)
HA administration costs (excluding payments to NGOs)	**53**	NA
Head office level (including Head office Team, IT Development & Maintenance, Other Operating costs)	22	
Cluster level (including Cluster Support Office)	31	
NGOs resources costs	**88**	**43-139**
Set-up cost (staff, equipment and others)	5	1-12
On-going cost	83	42-129
Staff	69	39-87
Venue rental	4	0-12
Equipment	1	0-2
Other operating expenses	9	1-49
Costs to the society	**13**	**2-46**
Cost of volunteers	8	0-33
NGO's own or unpaid venues	5	0-12
Costs to subjects attending PEP	**94**	**85-106**
Time cost for subjects in attending PEP sections	65	64-66
Time cost for accompany person in attending PEP secessions	4	1-7
Travelling cost and time for subjects (2-way)	23	18-31
Travelling cost and time for accompany person (2-way)	1	0.3-4
Societal perspective: average PEP costs/subject	**247**	**191-297**

Note: NA = not applicable; HA = Hospital Authority; NGO = Non-Governmental Organization

Table 2. Short-term cost-effectiveness of PEP versus non-PEP from a societal perspective

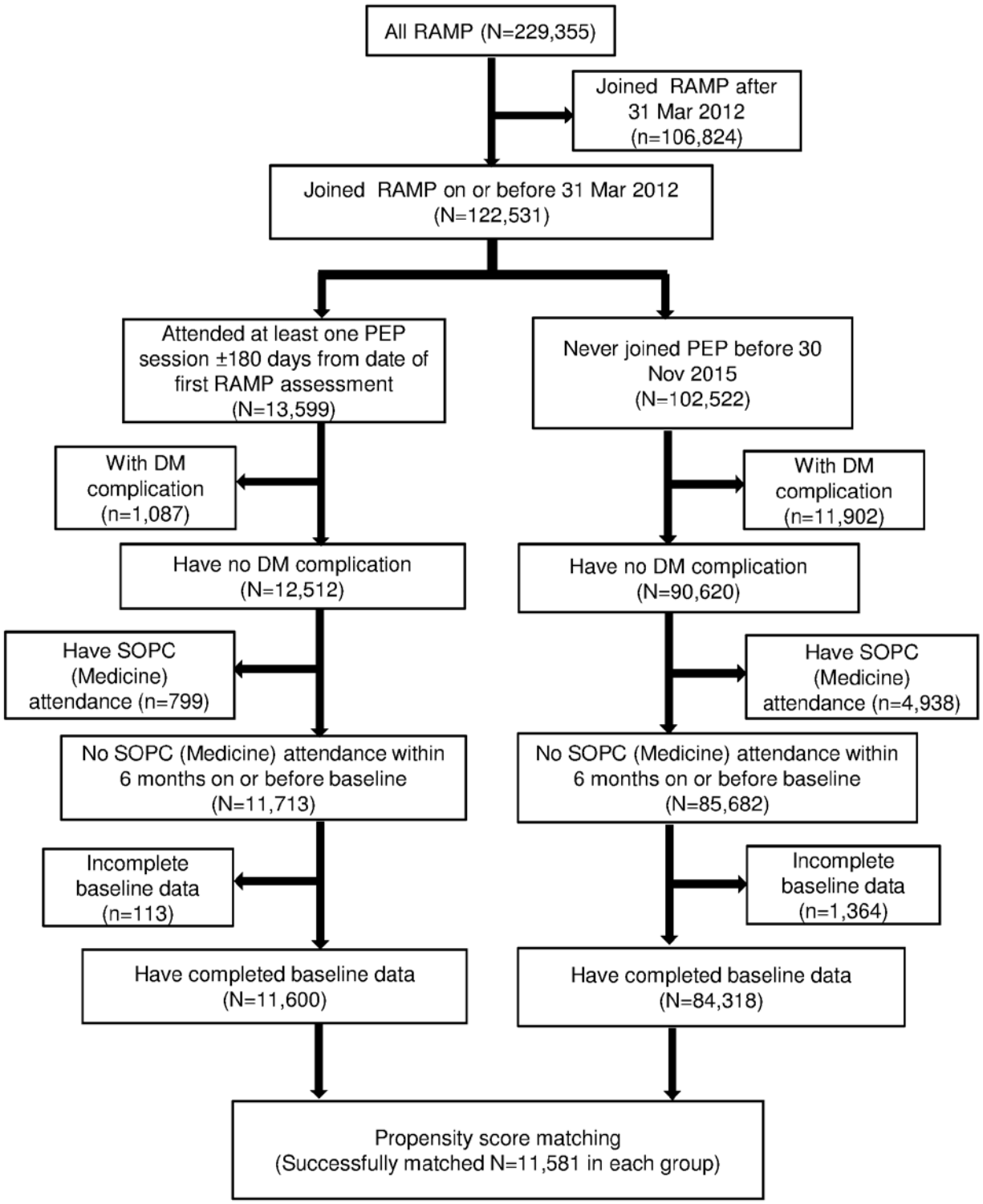
Endpoint	No. of observed events, n (%)		NNT	ICER (Cost/event avoided) (US$)		
	Non PEP (N=11581)	PEP (N=11581)		Base-case	Sensitivity on cost*	Sensitivity on effect**
All deaths	536 (4.6%)	338 (2.9%)	58	14,465	11,143-17,389	12,238-17,683
CVD deaths	72 (0.6%)	30 (0.3%)	276	68,192	52,532-81,979	54,310-91,607
Any complication (CVD, DR, ESRD, Neuropathy)	1245 (10.8%)	1099 (9.5%)	79	19,617	15,112-23,583	13,575-35,349
CVD events	875 (7.6%)	782 (6.8%)	125	30,796	23,724-37,023	19,377-74,995
Stroke events	395 (3.4%)	328 (2.8%)	173	42,747	32,930-51,390	27,943-90,915
Heart failure events	209 (1.8%)	160 (1.4%)	236	58,450	45,027-70,268	38,813-118,312

CVD=Cardiovascular Disease; IHD= Ischaemic Heart Disease; DR=Diabetic Retinopathy; STDR=Sight Threatening Diabetic Retinopathy; ESRD= End Stage Renal Disease; NNT=number needed to treat; ICER=incremental cost-effectiveness ratio

* PEP cost per subject was tested using the minimum to maximum values of costs reported by the NGOs.

** 95% CI for events of PEP groups were constructed based on Poisson distribution. The minimum and maximum NNT were calculated using the 95% CI and to generate the range of ICERs

Appendix 1. Flowchart of subjects' selection



Note: RAMP= Risk Assessment and Management Programme; PEP =Patient Empowerment Programme; DM = Diabetes Mellitus; SOPC = Specialist Outpatient Clinic

Appendix 2. Demographic and Clinical Characteristics

		Matched		Before matching
	p-value*	PEP	Non-PEP	Non-PEP
Socio-demographic characteristics				
N		11581	11581	84318
Sex, n (%)				
Female	0.474	6614 (57.1)	6560 (56.6)	45256 (53.7)
Male		4967 (42.9)	5021 (43.4)	39062 (46.3)
Age, mean (SD)	0.196	63.1 (9.8)	63.3 (10.7)	64.3 (11.6)
Current smoker, n (%)	0.921	894 (7.7)	886 (7.7)	9851 (11.7)
Under CSSA, n (%)	0.285	1370 (11.8)	1423 (12.3)	12926 (15.3)
Education				
No formal education		1453 (12.6)	1444 (12.5)	16778 (19.9)
Primary	0.660	4575 (39.5)	4642 (40.1)	32122 (38.1)
Secondary		4797 (41.4)	4715 (40.7)	30627 (36.3)
Tertiary		756 (6.5)	780 (6.7)	4791 (5.7)
HA clusters				
A		1464 (12.6)	1523 (13.2)	11909 (14.1)
B		963 (8.3)	995 (8.6)	4391 (5.2)
C		2026 (17.5)	2053 (17.7)	8821 (10.5)
D	0.503	1237 (10.7)	1284 (11.1)	10732 (12.7)
E		1466 (12.7)	1421 (12.3)	22377 (26.5)
F		3886 (33.6)	3795 (32.8)	16685 (19.8)
G		539 (4.7)	510 (4.4)	9403 (11.2)
Clinical characteristics				
Self-reported duration of DM, mean (SD)	0.536	6.6 (6.3)	6.6 (5.8)	7.8 (6.5)
History of hypertension, n(%)	0.873	8274 (71.4)	8263 (71.4)	61953 (73.5)
Use of anti-hypertensive drugs, n(%)	0.808	8691 (75.1)	8675 (74.9)	64307 (76.3)
Use of lipid lowing drugs, n(%)	0.261	3789 (32.7)	3709 (32.0)	22111 (26.2)
On oral anti-diabetic drug, n (%)	0.075	9651 (83.3)	9549 (82.5)	73436 (87.1)
On insulin, n (%)	0.311	118 (1.0)	134 (1.2)	1294 (1.5)
Chronic kidney disease, n (%)	0.513	1099 (9.5)	1070 (9.2)	11566 (13.7)
Charlson's index	0.793	3.7 (1.1)	3.7 (1.2)	3.5 (1.3)
BMI, kg/m^2	0.202	25.6 (4.0)	25.5 (3.9)	25.5 (3.9)
HbA1c, %	0.398	7.4 (1.3)	7.4 (1.4)	7.2 (1.3)
Systolic blood pressure, mmHg	0.806	134.3 (17.8)	134.2 (16.9)	135.7 (17.5)
Diastolic blood pressure, mmHg	0.532	75.8 (10.7)	75.7 (10.4)	74.9 (10.3)
Total cholesterol to HDL ratio, mmol/L	0.911	4.0 (1.2)	4.0 (1.2)	4.1 (1.2)
LDL-cholesterol, mmol/L	0.988	2.9 (0.8)	2.9 (0.8)	2.9 (0.8)
Triglyceride, mmol/L	0.842	1.6 (0.9)	1.6 (1.1)	1.5 (1.0)

Health service utilization in the past 12 months				
A&E attendance, mean (SD)	0.744	0.31 (0.9)	0.32 (0.8)	0.34 (1.0)
In-patient admission, mean (SD)	0.115	0.09 (0.4)	0.10 (0.4)	0.11 (0.4)
GOPC attendance, mean (SD)	0.765	5.16 (2.4)	5.17 (2.6)	5.14 (2.3)
SOPC attendance, mean (SD)	0.944	1.31 (2.4)	1.31 (2.6)	1.25 (2.5)

CSSA=comprehensive social security assistance; PEP=patient empowerment programme; BMI = Body Mass Index ; HbA1c = Hemoglobin A1c; LDL-C = Low Density Lipoprotein - Cholesterol; HDL-C High Density Lipoprotein - Cholesterol; A&E= Accident and Emergency; GOPC = General Outpatient Clinic; SOPC = Specialist Outpatient Clinic;
*by t-test or Chi2 test

Appendix 3. Five-year cumulative incidence of complications

	Cumulative number and incidence of complication events				
	Non-PEP (N=11581)		PEP (N=11581)		p-value
	n	%	n	%	
All deaths	**536**	4.6%	**338**	2.9%	<0.001
CVD deaths	**72**	0.6%	**30**	0.3%	<0.001
Cancer deaths	**194**	1.7%	**137**	1.2%	0.002
Respiratory deaths	**112**	1.0%	**46**	0.4%	<0.001
Any complication (CVD, DR, ESRD, Neuropathy)	**1245**	10.8%	**1099**	9.5%	0.001
CVD events	**875**	7.6%	**782**	6.8%	0.018
IHD events	**395**	3.4%	**380**	3.3%	0.584
Stroke events	**395**	3.4%	**328**	2.8%	0.011
Heart failure events	**209**	1.8%	**160**	1.4%	0.010
DR events	**321**	2.8%	**279**	2.4%	0.082
STDR events	**49**	0.4%	**47**	0.4%	0.838
ESRD events	**128**	1.1%	**121**	1.0%	0.656
Neuropathy events	**33**	0.3%	**23**	0.2%	0.181

CVD=Cardiovascular Disease; IHD= Ischaemic Heart Disease; DR=Diabetic Retinopathy; STDR=Sight Threatening Diabetic Retinopathy; ESRD= End Stage Renal Disease

Appendix 4. Pre and Post-programme knowledge score and change in clinical measurement over five years by number of sessions

		No. of PEP session attended							
	Overall	1 PEP session	2 PEP sessions	3 PEP sessions	4 PEP sessions	5 PEP sessions	6 PEP sessions	7 PEP sessions	≥8 PEP sessions
Knowledge score									
N	6325	199	1032	174	547	362	1160	2606	245
Pre	3.98	3.69	3.80	4.22	4.36	3.91	4.22	3.81	4.78
Post	7.38	6.41	6.48	6.47	6.95	7.14	7.65	7.84	7.82
Post - Pre	3.40*	2.72*	2.68*	2.25*	2.58*	3.23*	3.44*	4.02*	3.04*
Clinical risk factors									
N	11581	1708	3328	552	908	588	1349	2718	430
HbA1c (%)									
Pre	7.38	7.41	7.42	7.27	7.42	7.40	7.28	7.40	7.22
Post**	6.98	7.05	7.01	6.93	6.94	6.95	6.84	7.01	6.90
Post - Pre	-0.40*	-0.36*	-0.41*	-0.34*	-0.48*	-0.45*	-0.44*	-0.39*	-0.32*
SBP (mmHg)									
Pre	134.26	133.86	133.78	134.62	135.49	133.93	135.55	133.86	135.52
Post**	129.42	130.03	129.81	128.68	128.32	128.68	128.92	129.79	127.48
Post - Pre	-4.85*	-3.84*	-3.97*	-5.93*	-7.17*	-5.25*	-6.63*	-4.07*	-8.03*
DBP (mmHg)									
Pre	75.83	75.68	75.70	76.08	75.89	76.60	76.33	75.13	78.93
Post**	71.86	71.82	71.97	71.91	72.13	71.79	71.90	71.44	73.22
Post - Pre	-3.97*	-3.86*	-3.73*	-4.17*	-3.76*	-4.81*	-4.43*	-3.68*	-5.71*
LDL-C (mmol/l)									
Pre	2.88	2.92	2.86	2.89	2.93	2.90	2.92	2.86	2.80
Post**	2.23	2.26	2.24	2.23	2.23	2.18	2.21	2.24	2.17
Post - Pre	-0.65*	-0.65*	-0.62*	-0.66*	-0.71*	-0.72*	-0.71*	-0.62*	-0.62*
BMI (kg/m^2)									
Pre	25.58	25.60	25.60	25.69	25.32	25.37	25.54	25.56	26.29
Post**	25.35	25.42	25.42	25.40	25.05	25.19	25.32	25.23	26.07
Post - Pre	-0.23*	-0.18*	-0.19*	-0.29*	-0.26*	-0.18*	-0.22*	-0.32*	-0.21

*p-value <0.05 by t-test
**Clinical measurement at 60-month or last available record after intervention
HbA1c = Hemoglobin A1c; SBP= Systolic Blood Pressure ; DBP= Diastolic Blood Pressure; LDL-C = Low Density Lipoprotein - Cholesterol; BMI = Body Mass Index;

Appendix 5. CHEERS checklist—Items to include when reporting economic evaluations of health interventions

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Page 2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Page 3
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 3-4
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Page 3-4
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 4
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Page 5-6
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 4
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 6
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 4
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Page 4
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	not applicable
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	not applicable
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 4-5
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	not applicable

Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 4
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	not applicable
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	not applicable
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 5-6
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Page 6-7
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Page 6-7
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Page 7
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	not applicable
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	not applicable
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Page 7-9
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 9-10
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 10