

Evaluation of the chronic disease management program for appropriateness of medication adherence and persistence in hypertension and type-2 diabetes patients in Korea

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Abstract

The chronic disease management program (CDMP), a multilevel intervention including copayment reduction and physician incentives, was introduced in 2012 in Korea to improve blood pressure and glycemic control by strengthening the function of clinic as primary care institutions in managing hypertension and diabetes. This study, therefore, aimed to evaluate the effect of CDMP on the appropriateness of medication adherence and persistence in hypertension or type-2 diabetes patients.

A pre-post retrospective study was conducted using claims cohort data from 2010 to 2013. Hypertension or type-2 diabetes patients were selected as the CDMP group, while dyslipidemia patients were the control group. Study groups were further categorized as clinic shifters or non-shifters on the basis of whether hospital use changed to clinic use during the study period. Pre-post changes in adherence and persistence were assessed. Adherence was measured by medication possession ratio (MPR) and categorized as under (<0.8), appropriate (0.8–1.1), and over-adherence (>1.1). Persistence was measured by 12-month cumulative persistence rate.

The pre-post change was significantly improved for appropriate-adherence (hypertension, +6.0%p; diabetes, +6.1%p), 12-month cumulative persistence (hypertension, +6.5%p; diabetes, +10.8%p), and over-adherence (hypertension, –5.3%p; diabetes, –2.8%p) only among the shifters in the CDMP group. Among these, patients visiting the same, single clinic showed a significant increase in appropriate-adherence, whereas those who changed their clinics showed a nonsignificant increase. No significant improvement was verified among the non-shifters in the CDMP group.

CDMP improved medication adherence and persistence by significantly increasing appropriate-adherence and 12-month cumulative persistence rate in hypertension and type-2 diabetes patients. Particularly, CDMP significantly improved over-adherence, which was associated with increasing healthcare costs and hospitalization risk.

Abbreviations: AHDs = antihypertensive drugs, BP = blood pressure, CDMP = chronic disease management program, COC = continuity of care, COCI = continuity of care index, CVD = cardiovascular disease, HbA1c = hemoglobin A1c, KNHIS-NSC = Korea National Health Insurance Service-National Sample Cohort, LLDs = lipid-lowering drugs, MPR = medication possession ratio, OADs = oral antidiabetes drugs, PDC = proportion of days covered, UPI = usual provider continuity index.

Keywords: co-payment reduction, diabetes, hypertension, medication adherence, physician incentive

1. Introduction

Many studies have demonstrated that cardiovascular disease (CVD) deaths, representing 31.4% of all deaths worldwide in 2012,^[1–2] can be prevented by controlling major risk factors

such as high blood pressure (BP), high blood glucose, and obesity.^[3–6] A recent meta-analysis revealed that 10mmHg reduction in systolic BP reduced the risk of major CVD events, coronary heart disease, and stroke by 20%, 17%, and 27%, respectively.^[7]

BP and blood glucose control are significantly associated with medication adherence. According to previous studies, BP control rate was 45% higher in high-adherence patients compared with medium or low-adherence to antihypertensive drugs, and hemoglobin A1c (HbA1c) decreased by 0.16% for each 10% increase in adherence to oral antidiabetic drugs.^[8–9] It has also been demonstrated that high adherence significantly decreased the risk of CVDs, hospitalization, and total medical costs for hypertension and diabetes.^[10–16]

Despite its importance, medication adherence in patients with hypertension and diabetes is suboptimal, ranging from 40% to 80% depending on the study population, and half of the patients discontinued treatments within a year.^[17–22]

In Korea, CVDs are also a major cause of death, with 22.1% attributed to CVDs in 2012, and it is predicted to increase due to a rapidly aging population and lifestyle change.^[23,24] However, only 60% of the patients with hypertension or diabetes are reported to be likely adherent to medications, and less than 40% have their BP or blood glucose under control.^[23,25,26]

Editor: Qinhong Zhang.

J-AK is the first author.

Disclosure of funding: All authors declare that the study was independently conducted without any funding.

All authors declare that they have no conflict of interest.

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Medicine (2017) 96:14(e6577)

Received: 6 November 2016 / Received in final form: 28 February 2017 /

Accepted: 19 March 2017

<http://dx.doi.org/10.1097/MD.00000000000006577>

Medication adherence is known to be related to continuity of care (COC), which might render healthcare providers more accountable for managing their patients continuously.^[27,28] The Korean health care delivery system, however, is not well established to ensure continuity of care at the primary care level. Moreover, patients tend to prefer using the outpatient service in hospitals rather than clinics, although the treatment costs and copayment rates are higher in hospitals compared with clinics.^[29] According to the Korea health insurance statistics yearbook, the outpatient cost per visit day was 2.7 times higher in hospitals than in clinics in 2012, and the outpatient expenditure of the hospitals increased by 92.0% in 2012 compared with that in 2006; the outpatient expenditure of the clinics increased by 41.6% in the same period.^[29] Consequently, the financial burden of outpatient care has increased and the function of a clinic as a primary care institution has been undermined over the years.

Therefore, the Korean government attempted to complement this fragmented system by incorporating a component of the managed care system of the chronic disease management program (CDMP) in 2012.

The CDMP aimed to improve BP and glycemic control for hypertension and type-2 diabetes patients by strengthening the function of clinics as primary healthcare. To participate in the CDMP, patients are required to designate a preferred clinic to receive treatments for hypertension or type-2 diabetes and register with the CDMP. Patients are allowed to change their preferred clinics. The CDMP has encouraged patients to use clinic outpatient services by providing a multilevel intervention consisting of copayment reduction and physician incentives. For patients who receive continuous treatments in clinics for hypertension or type-2 diabetes, the copayment rate for the consultation fee is reduced to 20% from 30%. Financial incentive is also provided to clinics participating in the CDMP.

This study, therefore, aimed to evaluate the effect of the CDMP on medication adherence and persistence in hypertension and type-2 diabetes patients. Even though the majority of

studies evaluating the interventions' effect focused on whether the developed interventions improved poor-adherence,^[20,30,31] it has been demonstrated that not only undersupply but also oversupply, both of which were considered inappropriate adherence, was associated with undesirable healthcare outcome.^[32-39] Stroupe et al^[32-34] found that medication oversupply was associated with higher probability of hospitalization for hypertension patients, and several studies showed that medical costs were significantly higher for oversupply patients.^[33-38]

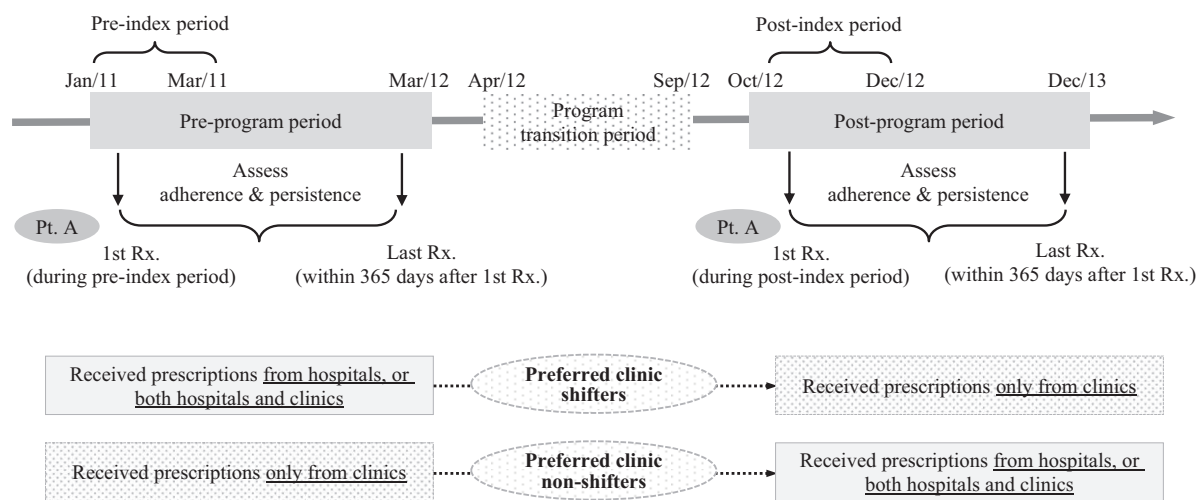
However, there are not many studies that have evaluated the impact of the intervention on appropriate-adherence as well as over-adherence. Therefore, here, pre-post changes were compared not only with the overall medication possession rate, but also to the appropriateness level of medication adherence, and to persistence between program participants as clinic shifters and program non-participants as clinic non-shifters.

2. Methods

2.1. Study design and population

This was a pre-post and retrospective study, consisting of a 12-month pre-period before implementing CDMP and a 12-month postperiod following a 6-month transition period after CDMP implementation, from January 1, 2011 through December 31, 2013. The first 3 months in both periods were defined as the index period and the first prescription of each patient identified in the index period was considered as the index prescription in the preperiod and postperiod. Patients were followed for 365 days after the date of index prescription in both periods, and pre-post changes in adherence and persistence were examined (Fig. 1).

Because the Korea National Health Insurance Service-National Sample Cohort (KNHIS-NSC) data, a representative cohort database of the Korean population, did not have an identifier for CDMP participants, it was impossible to determine these participants directly from the data. However, those who



Pt. A=patient A, Rx=prescription.

Figure 1. Study design.

participated in the CDMP must have received prescriptions only from clinics. Accordingly, patients who received prescriptions only from clinics in the postperiod could be considered participating patients. However, for patients who received prescriptions only from clinics in both the preperiod and postperiod, it was difficult to determine if they continued their clinic visit to participate in the CDMP or if they maintained their behavior as usual. Therefore, patients who shifted to clinic visit in the postperiod were defined as participating patients and were called clinic-shifters. In contrast, patients who shifted to hospital or both hospital and clinic visit in the postperiod were defined as non-participating patients and were called clinic non-shifters. To investigate any potential selection bias due to defined participants using pre-post changes in medical institutions, patients with dyslipidemia, which was not covered by the CDMP, were selected as the control group. This control group was also further categorized into clinic shifters or non-shifters using pre-post changes in medical institutions. The differences in pre-post changes in adherence and persistence between the shifters and non-shifters within the CDMP group were compared with those in the control group.

Patients with hypertension, type-2 diabetes, or dyslipidemia were identified using medications prescribed to patients, and the Anatomical Therapeutic Chemical Code was used to classify these medications. Antihypertensive drugs (AHDs) included β -blockers (C07), calcium-channel blockers (C08), and angiotensin-converting enzyme inhibitors and angiotensin receptor blockers (C09). Oral antidiabetes drugs (OADs) included sulfonylurea (A10H), biguanides (A10J), glitazones (A10K), α -glucosidase inhibitors (A10L), glinides (A10M), DPP-IV inhibitors (A10N), GLP-1 agonists (A10S), and others (A10X). Lipid-regulating and antiatheroma preparations (C10) were classified as lipid-lowering drugs (LLDs).

For enrollment in the study, patients were required to have received prescriptions with AHDs, OADs, or LLDs during the index period and to have met the criteria for clinic shifters or non-shifters. Of this population, patients were excluded if they were aged <20 years as of the date of index prescription in the pre-period; died or were hospitalized during the study period; received insulin during the study period (because insulin is mainly dispensed within medical institutions in Korea, we were unable to estimate adherence or persistence precisely using pharmacy claims); or received prescriptions with AHDs, OADs, or LLDs from a public healthcare center not covered by the CDMP. Additionally, to recruit only those patients who required continuous treatments, patients were excluded if they received only 1 prescription with AHDs, OADs, or LLDs within 6 months after index prescription in the pre-period, or the total prescription days within this period was less than 14 days (Fig. 2).^[2,3] For the control group, patients were additionally excluded if they were enrolled in the CDMP group, or received AHDs or OADs from clinics during the study period. Those who had received AHDs, OADs, or LLDs during the previous 12 months from the date of index prescription in the pre-period were considered as patients having a history of treatments with AHDs, OADs, or LLDs.

2.2. Data source

This study used KNHIS-NSC data provided by the Korean National Health Insurance Service (NHIS), which is a single-insurer covering the entire Korean population and providing national health insurance and medical aid programs. KNHIS-NSC data were randomly sampled from the 2002 database,

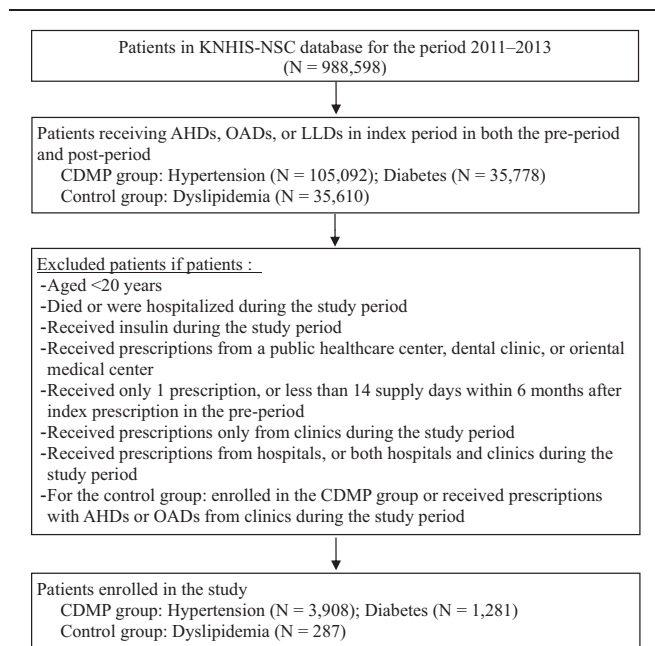


Figure 2. Flowchart for selection of the study population. AHD=antihypertensive drug, CDMP=chronic disease management program, KNHIS-NSC=Korea National Health Insurance Service-National Sample Cohort, LLD=lipid-lowering drug, OAD=oral antidiabetic drug.

stratified for sex, age, income level quantile, and health insurance type. KNHIS-NSC data covered the period between January 1, 2002 and December 31, 2013 and contained medical treatment claims, pharmacy claims, and eligibility data for a population of approximately 1 million beneficiaries, which represented 2.2% of all national health beneficiaries in 2002.

Medical treatment claims contained details of outpatient services and hospitalization such as visit date, hospitalization period, diagnosis code, prescribed drug, treatment provider, and treatment cost. Pharmacy claims contained details such as dispensed drug, dispense date, days of supply, dispensing cost, and prescribing provider. Eligibility data contained demographic information such as age, sex, year of death, cause of death, income level quantile, type of disability, and date of registration for disability. All the claims data were linked by de-identified patient codes and provider codes to protect personal information.

This study was approved by the Review Committee of Research Support of the National Health Insurance Service (NHIS-2015-2-068) and the Institutional Review Board of SungKyungKwan University (SKKU-2015-07-001-002).

2.3. Measures

The effectiveness of the CDMP was evaluated by using adherence and persistence measures. Adherence was measured by medication possession ratio (MPR) using a fixed 1-year period, which was calculated as total days of supply of the study medications prescribed in 365-day period starting with the date of index prescription divided by 365 days. The MPR was considered as standard measure for evaluation of adherence using claim data and best predictor of future hospitalization.^[40,41]

For evaluation of appropriate-adherence, patients with MPR 0.8 to 1.1 were categorized as appropriate-adherent. The MPR of 0.8 was chosen as the lower threshold for appropriate-adherence because several studies have suggested that patients receiving at

least 80% of their medications were more likely to achieve therapeutic responses and were associated with lower risk of hospitalization.^[13,16,33,42] Unlike the lower threshold, setting the upper threshold was controversial because there are fewer studies evaluating the association between the upper threshold and healthcare outcomes. However, several studies have shown that an MPR >1.1 was associated with increasing healthcare costs and hospitalization risk.^[32,34,37] Therefore, the MPR of 1.1 was chosen as the upper threshold for this study. For additional analysis, the MPR was categorized as under-adherence with MPR <0.8, appropriate-adherence with MPR 0.8–1.1, and over-adherence with MPR >1.1.

Persistence was measured by the proportion of patients persistent in a 365-day period starting with the date of index prescription. Patients were considered persistent if they renewed their previous prescription within a defined grace period from the ending of the previous prescription. The grace period was defined as a time period equal to one-half the days of supply of the previous prescription.^[43,44] For example, a patient with a 30-day prescription was considered persistent if the patient received the following prescription within 15 days from the ending of the previous prescription.

Further analysis was conducted on the clinic shifters in the CDMP group to determine whether continuity of outpatient care affected adherence and persistence. The clinic shifters were categorized into same, single clinic-users, and multiple clinic-users (≥ 2), depending on whether patients changed their clinics in the postperiod because the CDMP allowed patients to change their clinic.

2.4. Statistical analysis

Descriptive analysis was conducted to describe baseline characteristics of the study populations. Baseline characteristics between the shifters and non-shifters in the CDMP and control group were compared using a *t* test for continuous variables and chi-square

test for categorical variables. The cumulative persistence rate was estimated using the Kaplan–Meier survival analysis.

Pre-post changes in MPR were assessed using a paired *t* test within the group, and pre-post changes in appropriate-adherence and cumulative persistence rates were assessed using the McNemar test. All analyses were conducted using SAS software, version 9.3 (SAS, Cary, NC). All reported *P* values were 2-sided, and statistical significance was set at $P < 0.05$.

3. Results

3.1. Baseline characteristics

Among 988,598 patients in the KNHIS-NSC data, 5476 patients were eligible for the study. The baseline characteristics for each group are shown in Table 1.

The control group had no significant differences in baseline characteristics between the clinic shifters and non-shifters. However, the CDMP group showed significant differences in sex and previous use of the study medications in the hypertension group, and income level in the diabetes group.

3.2. Medication possession ratio (MPR)

As shown in Table 2, pre-post changes in the mean overall-MPR were significantly increased in the non-shifters in both the CDMP and control group ($P < 0.001$), whereas the hypertension shifters in the CDMP group showed a significant decrease ($P < 0.001$) and the diabetes shifters showed no significant change ($P = 0.560$). The shifters in the control group showed a nonsignificant increase of 0.0004 ($P = 0.858$) in the mean-overall MPR.

3.3. Appropriate medication adherence

Pre-post changes in the appropriate-adherence rate showed different trends between the CDMP and control group. For the CDMP group, the shifters showed a significant increase in the

Table 1
Comparison of baseline characteristics of the study populations.

Variable, n (%)	CDMP group						Control group		
	Hypertension			Diabetes			Dyslipidemia		
	Clinic shifters	Clinic non-shifters	<i>P</i>	Clinic shifters	Clinic non-shifters	<i>P</i>	Clinic shifters	Clinic non-shifters	<i>P</i>
Total	2506	1402		890	391		174	113	
Gender			<0.001			0.395			0.790
Male	1248 (49.8%)	601 (42.9%)		483 (54.3%)	202 (51.7%)		49 (28.2%)	34 (30.1%)	
Female	1258 (50.2%)	801 (57.1%)		407 (45.7%)	189 (48.3%)		125 (71.8%)	79 (69.9%)	
Age group			0.222			0.088			0.782
<50 yr	462 (18.4%)	231 (15.5%)		162 (18.2%)	63 (16.1%)		21 (12.1%)	15 (13.3%)	
50–59 yr	770 (30.7%)	443 (31.6%)		279 (31.4%)	125 (32.0%)		83 (47.7%)	48 (42.5%)	
60–69 yr	719 (28.7%)	387 (27.6%)		275 (30.9%)	104 (26.6%)		47 (27.0%)	36 (31.9%)	
≥70 yr	555 (22.2%)	341 (24.3%)		174 (19.6%)	99 (25.3%)		23 (13.2%)	14 (12.4%)	
Previous use of study drugs			<0.001			0.688			0.648
No	249 (9.9%)	90 (6.4%)		88 (9.9%)	42 (10.7%)		36 (20.7%)	20 (17.7%)	
Yes	2257 (90.1%)	1312 (93.6%)		802 (90.1%)	349 (89.3%)		138 (79.3%)	93 (82.3%)	
Income level			0.889			<0.001			0.935
Medical aid	111 (4.4%)	67 (4.8%)		32 (3.6%)	27 (6.9%)		8 (4.6%)	4 (3.5%)	
≤50%	898 (35.8%)	483 (34.5%)		345 (38.8%)	128 (32.7%)		54 (31.0%)	38 (33.6%)	
51–80%	689 (27.5%)	395 (28.2%)		264 (29.7%)	94 (24.0%)		48 (27.6%)	34 (30.1%)	
81–90%	355 (14.2%)	207 (14.8%)		95 (10.7%)	68 (17.4%)		24 (13.8%)	15 (13.3%)	
≥91%	453 (18.1%)	250 (17.8%)		154 (17.3%)	74 (18.9%)		40 (23.0%)	22 (19.5%)	

P value was calculated using a *t* test for continuous variables and a chi-squared test for categorical variables.

CDMP = chronic disease management program, yr = year.

Table 2
Comparison of adherence and persistence rate in the pre-period and post-period.

Measures	CDMP group				Control group	
	Hypertension		Diabetes		Dyslipidemia	
	Clinic shifters	Clinic non-shifters	Clinic shifters	Clinic non-shifters	Clinic shifters	Clinic non-shifters
Total (n)	2506	1402	890	391	174	113
MPR (mean ± SD)						
Pre-period	0.93 (0.19)	0.89 (0.17)	0.90 (0.17)	0.88 (0.19)	0.73 (0.25)	0.58 (0.30)
Postperiod	0.91 (0.16)	0.96 (0.22)	0.91 (0.16)	0.93 (0.18)	0.73 (0.27)	0.74 (0.31)
Absolute change in mean	-0.02	0.07	0.003	0.05	0.004	0.15
P value*	<0.001	<0.001	0.560	<0.001	0.858	<0.001
Appropriate-adherence (%; MPR 0.8–1.1)						
Pre-period	79.1%	80.2%	77.2%	78.3%	49.4%	29.2%
Postperiod	85.1%	75.2%	83.3%	82.6%	53.5%	49.6%
Absolute change in %	6.0%p	-5.1%p	6.1%p	4.3%p	4.0%p	20.4%p
P value†	<0.001	<0.001	<0.001	0.062	0.354	<0.001
Over-adherence (%; MPR >1.1)						
Pre-period	6.3%	1.0%	3.6%	1.3%	0.6%	0.0%
Postperiod	1.0%	9.9%	0.8%	4.6%	0.0%	3.5%
Absolute change in %	-5.3%p	8.9%p	-2.8%p	3.3%p	-0.6%p	3.5%p
P value*	<0.001	<0.001	<0.001	0.007	0.319	0.045
Under-adherence (%; MPR <0.8)						
Pre-period	14.6%	18.8%	19.2%	20.5%	50.0%	70.8%
Postperiod	14.0%	14.9%	16.0%	12.8%	46.6%	46.9%
Absolute change in %	-0.7%p	-3.9%p	-3.3%p	-7.7%p	-3.5%p	-23.9%p
P value*	0.40	<0.001	0.021	<0.001	0.424	<0.001
12-month cumulative persistence rate (%; 12 mo)‡						
Pre-period	58.9%	59.1%	54.3%	56.8%	28.7%	20.4%
Postperiod	65.4%	58.0%	65.1%	62.2%	33.3%	35.4%
Absolute change in %	6.5%p	-1.1%p	10.8%p	5.4%p	4.6%p	15.1%p
P value†	<0.001	0.493	<0.001	0.081	0.319	0.006
Average days' supply (mean ± SD)						
Pre-period	49.2 (26.1)	37.8 (15.1)	47.9 (26.1)	33.5 (12.6)	54.4 (30.9)	37.5 (17.1)
Postperiod	42.1 (18.1)	44.8 (22.9)	39.4 (16.9)	41.6 (20.4)	43.7 (19.4)	51.7 (27.6)
Absolute change in mean	-7.2	7.0	-8.5	8.1	-10.7	14.2
P value*	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

CDMP = chronic disease management program, MPR = medication possession ratio.

* P value was calculated using a paired *t* test.

† P value was calculated using the McNemar test.

‡ Cumulative persistence rate was calculated using the Kaplan–Meier survival analysis.

appropriate-adherence rate, increasing 6.0%p in the hypertension ($P < 0.001$) and 6.1%p in the diabetes groups ($P < 0.001$), whereas the non-shifters showed a significant decrease of 5.1%p in the former ($P < 0.001$) but no significant change in the latter groups ($P = 0.062$). In contrast, the non-shifters in the control group showed a significant increase of 20.4%p ($P < 0.001$), whereas the shifters showed a nonsignificant increase of 4.0%p ($P = 0.354$; Table 2).

Among the shifters in the CDMP group, patients visiting the same, single clinic showed a significant increase of 6.3%p in the hypertension ($P < 0.001$) and 6.4%p in the diabetes group ($P < 0.001$), whereas those who changed their clinics in the postperiod showed a nonsignificant increase (Table 3).

3.4. Inappropriate medication adherence

Under-adherence reduced in all groups, and the magnitude of the change was larger in the non-shifters compared with the shifters. Similar to the mean MPR, the non-shifters in the control group showed the largest significant change ($P < 0.001$). However, over-adherence decreased significantly only among the shifters in the CDMP group ($P < 0.001$), decreasing 5.3%p in the hypertension and 2.8%p in the diabetes groups. The non-shifters in the CDMP group showed a significant increase of 8.9%p in the

hypertension ($P < 0.001$) and 3.3%p in the diabetes groups ($P = 0.007$). However, the shifters in the control group showed a nonsignificant increase ($P = 0.319$), whereas the non-shifters showed a significant increase of 3.5%p ($P = 0.045$; Table 2).

3.5. Cumulative persistence rate

In the CDMP group, only the shifters showed a significant increase in the 12-month cumulative persistence rate ($P < 0.001$), increasing 6.5%p in the hypertension and 10.8%p in the diabetes groups. In contrast, in the control group, only the non-shifters showed a significant increase ($P = 0.004$; Table 2).

Similar to the appropriate-adherence, the shifters who did not change their preferred clinic in the postperiod showed a significant increase of 8.3%p in the hypertension ($P < 0.001$) and 10.8%p in the diabetes group ($P < 0.001$), whereas those who changed their preferred clinics showed a significant increase of 10.9%p only in the diabetes group ($P = 0.047$; Table 3).

4. Discussion

This study found that the CDMP, a multilevel intervention providing financial benefits to both patients, who receive continuous treatments in preferred clinics for hypertension and

Table 3**Adherence and persistence rate per number of preferred clinics visited in the post-period.**

Measures	Preferred clinic shifters in CDMP group			
	Hypertension		Diabetes	
	Using same, single clinic	Using ≥ 2 clinics	Using same, single clinic	Using ≥ 2 clinics
Total (n, %)	2064 (82.4%)	442 (17.6%)	761 (85.5%)	129 (14.5%)
Appropriate-adherence (%; MPR 0.8–1.1)				
Pre-period	79.6%	76.7%	77.4%	76.0%
Post-program period	85.9%	81.0%	83.8%	79.8%
Absolute change in %	6.3%p	4.3%p	6.4%p	3.9%p
P value*	<0.001	0.056	<0.001	0.336
12-month cumulative persistence rate (%; 12 mo) [†]				
Pre-period	59.4%	57.0%	55.3%	48.1%
Postperiod	67.6%	55.2%	66.1%	58.9%
Absolute change in %	8.3%p	–1.8%p	10.8%p	10.9%p
P value*	<0.001	0.547	<0.001	0.047

CDMP = chronic disease management program, MPR = medication possession ratio.

* P value was calculated using the McNemar test.

[†] 12-month cumulative persistence rate was calculated using the Kaplan–Meier survival analysis.

type-2 diabetes, and physicians in preferred clinics, which meet requirements of post-quality assessment, was associated with improved appropriateness of medication adherence and persistence in hypertension and type-2 diabetes patients. Furthermore, the program significantly reduced over-adherence, which was associated with increasing healthcare costs and hospitalization risk.^[32–36]

These findings suggest that the CDMP encouraged patients to change healthcare utilization from hospitals to clinics, which resulted in continuous treatments in preferred clinics, and healthcare providers to have more accountability for managing their patients continuously. Consequently, it might improve the COC, which could lead to improved medication adherence and persistence. The association between COC and adherence was demonstrated by previous studies.^[27,28,45] According to the study by Warren et al^[28], a usual provider continuity index (UPI) of $\geq 75\%$ was associated with an increased likelihood of adherence. Chen et al^[27] reported that patients with higher continuity of care index (COCI) scores were more likely to adhere to medications than those with lower COCI scores. Moreover, the study found that the COC was significantly associated with healthcare outcomes. The probability of hospitalization for patients with high COCI scores was significantly lower than that for those with low COCI scores.^[27] Furthermore, Cheng and Chen^[45] reported that the COC, either at the physician or institution level, was negatively associated with duplicated medications. In our study, compared with the patients who changed their preferred clinic, those who did not showed higher rates of appropriate adherence and persistence, suggesting that the magnitudes of improvements in adherence and persistence are related to the COC at the clinic level. These results might indicate that using the same preferred clinic contributes to improve COC, which leads to better adherence and persistence.

Our findings of improvements in adherence were similar to those reported in previous studies assessing the effect of copayment reduction policy.^[20–22,30,31,46,47] A systematic review showed that reduced out-of-pocket expenses improved medication adherence across clinical conditions among interventions developed to improve adherence at policy level.^[21] A study assessing the effect of a concession card that provided discounts on out-of-pocket costs for prescribed medications showed that reduced copayment significantly improved the continuation and

adherence to statins. The study suggested that higher out-of-pocket costs affected the frequency and continuation of dispensing statin prescriptions.^[48] Additionally, several studies showed that integrated multiple-level interventions were more effective in improving adherence than single interventions.^[21,22,46]

This study also found that the CDMP significantly improved over-adherence. The prevalence and negative impacts of oversupply on healthcare outcomes and healthcare costs have been reported by previous studies.^[32–36] According to the study assessing the association between medication supplies and healthcare costs in older adults, over-adherence (MPR >1.2) was commonly observed for treatment with oral hypoglycemics, antihypertensives, and statins in 53%, up to 52%, and up to 35.5% of the patients, respectively.^[32] Moreover, oversupply was associated with 16% and 11% higher probability of hospitalization for patients with complicated and uncomplicated hypertension, respectively.^[32–34] Furthermore, several studies showed that medical costs were significantly higher in oversupply patients.^[33–36]

In terms of inappropriate adherence, we found that under-adherence decreased across all studied groups, especially the clinic non-shifters showed a larger decrease compared with the shifters in both groups. Similarly, the mean MPR significantly increased in the non-shifters in both groups, whereas the shifters showed a significant decrease in the hypertension group but nonsignificant changes in the diabetes and control groups. These results seem to favor the non-shifters and are difficult to explain. However, these conflicting results could potentially be due to the increased average days' supply among the non-shifters. The average days' supply increased among the non-shifters in both the CDMP and control groups, whereas it decreased among the shifters in both groups (Table 2). The association of days' supply and medication adherence has been reported by previous studies.^[49,50] A study investigating the prevalence and predictors of oversupply in diabetes patients found that receiving at least 1 90-day prescription fill was associated with lower odds of undersupply and higher odds of oversupply compared with patients with none.^[49] Further, a study evaluating the effect of policy change in days' supply found that a reduced days' supply decreased medication adherence for chronic diseases as measured by the proportion of days covered (PDC).^[50] According to the

study, the decrease in allowed days' supply from 100 days to 34 days substantially decreased medication adherence for AHDs, OADs, and statins.^[50] Therefore, it was assumed that the increased average days' supply might reduce undersupply and increase oversupply in the non-shifters, and consequently it might increase the mean level of medication adherence (MPR). This finding also indicated that the mean MPR level might not be appropriate for evaluating the effect of a developed intervention on medication adherence if the intervention affected the days' supply because of the association between days' supply and medication adherence.^[49,50] Therefore, the appropriateness of medication adherence using the categorized adherence (under-, appropriate-, and over-adherence) may be considered an effective index to assess the effectiveness of an intervention that can change the days' supply.

Several limitations should be considered when interpreting our results. First, the participants were defined using changes in medical institutes during the study period because the data used for this study did not have an indicator to identify patients participating in the CDMP. Consequently, this could have affected the results. Therefore, a control group, consisting of patients with dyslipidemia, which was not covered by the CDMP, was included in the study to investigate the impact of changes in medical institutes on adherence and persistence. The observed nonsignificant improvement in adherence and persistence in the clinic shifters of the control group suggests that the significant improvements in the shifters of the CDMP group were the effect of the CDMP rather than a consequence of changes in medical institutes.

Second, the eligible patients for the study were those who received the study medications in the index periods in both the preperiod and postperiod. Therefore, there might be a possibility that patients more likely to adhere to the medications were enrolled in the study. According to Park et al,^[23] the 3-year mean MPR is higher than the 1-year and 2-year mean MPR in hypertension and diabetes patients. Moreover, we excluded patients who were hospitalized during the study period because the pharmacy claims database did not include prescription records for hospitalized patients. This could explain the higher MPR across all groups in our study as compared with that in previous studies.^[17,19,23]

Third, appropriate-adherence was defined as MPR of 0.8 to 1.1. Therefore, the results obtained would likely be different if a different threshold was used.

Fourth, because of the limitation of the pharmacy claim data, it was not possible to determine whether patients actually took the medications as prescribed and also switching medications for clinical reasons could not be distinguished from preventable duplication of medications. Furthermore, the reasons for discontinuation of medications were not reported. Therefore, it was not possible to distinguish discontinuation due to therapeutic needs such as adverse events or insufficient therapeutic results from discontinuation due to poor adherence.

Finally, in our study, the analyses were focused on evaluating the overall impact of the CDMP on medication adherence and persistence to determine whether CDMP implementation led to improved adherence and persistence in patients with hypertension or type-2 diabetes. Even though CDMP's positive impact on adherence and persistence was demonstrated by our study, it was not clear how the CDMP intervention contributed to improved adherence and persistence, including the impact of its individual components. Future studies should be thus needed to determine why and how the CDMP intervention affects medication

adherence and persistence and the component of the multilevel intervention that has more impact on improving adherence and persistence. Thus, these limitations of our study could limit the generalizability of our results.

5. Conclusion

In conclusion, this study demonstrates that the CDMP, a multilevel intervention consisting of co-payment reduction and physician incentive, can play an important role in improving adherence and persistence, particularly in achieving appropriate-adherence level in hypertension and type-2 diabetes patients. Further, it also indicates that improving continuity of care, with interventions such as preferred clinics, contributes to improved adherence and persistence. Given these findings, our study suggests that incorporating components used in the managed care system can improve healthcare outcomes in countries with a fragmented healthcare system such as is present in Korea. Additionally, measuring appropriateness of medication adherence may be an effective index to assess the impact of an intervention on medication adherence.

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