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Effect of free distribution of medicines on the process of care for adult patients with type 1 and type 2 diabetes and hypertension: Post-hoc analysis of randomized control trial findings

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ABSTRACT

Objectives

The Carefully Selected and Easily Accessible at No charge Medicines (CLEAN Meds) trial randomized controlled trial showed that patients receiving free access to medicines had improved diabetes and hypertension outcomes compared to patients who had usual access to medicines. In this study, we aimed to test the impact of providing free access to medicine to people with diabetes and hypertension on process of care indicators.

Design

In this post hoc analysis of randomized controlled trial findings we identified process of care indicators for the management of diabetes and hypertension using relevant guidelines. The follow process of care indicators were identified for diabetes management: encounters with healthcare professionals, blood pressure measurements, self-monitoring of blood glucose, annual eye and foot exam, annual administration of the influenza vaccine, and laboratory testing for hemoglobin A1c, LDL-cholesterol, serum creatinine, and urine albumin to creatinine ratio (ACR). We identified the following process of care indicators for hypertension: encounters with healthcare professionals, blood pressure measurements, self-measuring of blood pressure, and serum tests for electrolytes, HbA1c, lipids, and creatinine. Chart extractions were performed for all patients and the indicators for diabetes and hypertension were recorded. We compared the indicators for patients in each arm of the trial.

Results

The study included 268 primary care patients. Free distribution of medicines may improve self-monitoring behaviours (aRR 1.3; 95 % CI 0.7-2.6) and reduce missed primary care appointments for patients with diabetes (aRR 0.8; 95 % CI 0.5-1.3) or hypertension (aRR 0.4; 95 % CI 0.2-0.9). Free distribution may also reduce primary care and consultant appointments and laboratory testing in patients with hypertension.

Conclusions

Improving medicine accessibility for patients with diabetes and hypertension not only improves surrogate health outcomes but also improves the patient experience and may also reduce healthcare costs by encouraging self-monitoring.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study is based on a randomized controlled trial.
- Despite the fact that this was a post-hoc analysis and randomization was not stratified based on these characteristics, we found that the groups were largely balanced.
- Associations identified during post-hoc analyses could be spurious and thus the findings should be viewed as hypothesis-generating.
- The trial this study was based on was conducted with primary care patients in a high-income country who reported cost-related non-adherence and the findings may not apply in other settings.

INTRODUCTION

Managing people with chronic diseases such as diabetes and hypertension with effective medicines and healthcare services can save lives and reduce complications, yet many people do not receive guideline-recommended care.[1–3] One important barrier to optimal care is cost related nonadherence which was reported by 9.6% of people who had received a prescription in the past year. [4] Cost related nonadherence could undermine the provision of healthcare services as people may avoid participating in care if they cannot afford prescribed medicines.[4,5]

Many strategies have been tested to improve the process of care for chronic diseases, with varying success. Resource intensive interventions such as financial incentives to providers and multidisciplinary changes to the primary care team are associated with modest improvements in diabetes and hypertension management.[6,7] Caring for patients with chronic diseases is expensive. [8] The cost and effectiveness of interventions to improve guideline-recommended care are important to consider, since increasing access to effective treatments may reduce costs related to complications, but may increase per-patient costs related to clinicians' monitoring of treatments and more expensive health technologies. [9]

We recently completed the Carefully Selected and Easily Accessible at No charge Medicines (CLEAN Meds) trial, a randomized controlled trial in which patients with self-reported cost-related medication nonadherence were randomly assigned to receive free distribution of medicines from a comprehensive list of essential medicines.[10] The CLEAN Meds trial found that providing Canadian primary care patients with medicines at no charge improved adherence to medication and, for patients with diabetes and hypertension, chronic disease management was improved based on some surrogate outcomes.[10] As previously reported, with free distribution of medicines, hemoglobin A1c levels were 0.4 % lower (95 % CI -0.76 to 0.0) compared with usual access, and systolic blood pressure was 7 mmHg lower (95% CI -11.7 to -2.8) compared with usual access. Given the importance of medication related adherence in patients with chronic diseases, in this post-hoc analysis, we tested the impact on diabetes and

hypertension process of care indicators of providing free access to medicine to people with diabetes and hypertension.

METHODS

Patients

We identified patients in the CLEAN Meds trial with diabetes (with or without hypertension) or only hypertension by identifying all participants prescribed at least one diabetic or anti-hypertensive agent at the start of the trial. Randomization was not stratified based on these conditions. Patients prescribed both a diabetic agent and an anti-hypertensive agent were included only in the diabetes group.

Process of Care Indicators

Using the care goals of diabetes and the Diabetes Canada Guidelines [11] we identified the following process of care indicators for the management of diabetes: encounters with healthcare professionals [in-clinic appointments and telephone appointments with primary care physicians or nurse practitioners], blood pressure measurements, self-monitoring of blood glucose, annual eye exam (with an optometrist or ophthalmologist), foot screening exams (foot care and/or neuropathy screening), annual administration of the influenza vaccine, and laboratory testing for hemoglobin A1c, LDL-cholesterol, serum creatinine, and urine albumin to creatinine ratio (ACR).[11] Glycated hemoglobin (HbA1c) and self-monitoring blood glucose (SMBG) can be used as indicators for the management of glycemic control.

Using the guidelines and the goals of care for hypertension and the Hypertension Canada Guidelines, [12] we identified the following process of care indicators for the management of hypertension: encounters with healthcare professionals, blood pressure measurements, self-measuring of blood pressure (at home or at the pharmacy), and serum tests for electrolytes, HbA1c, lipids, and creatinine.

Since a number of the recommended clinical manoeuvres and other aspects of care (e.g. medicine adjustments) involve patients interacting with healthcare providers, we also assess healthcare encounters that included in person visits and telephone encounters with primary care physicians or nurse practitioners where diabetes or hypertension were documented as being discussed.

Data Collection

Using the PSS Suite software [13], chart extractions were performed for all patients to record the identified process of care indicators for diabetes and hypertension respectively. Two abstracters (OC, HW) were blinded to the patients' intervention status at the time of chart extraction. To ensure reliability of chart extraction, each abstracter completed 5 chart extractions independently and compared findings; there were no disagreements. OC, HW and MA then completed the chart extraction for all participants.

For all patients with diabetes, starting from the patient's start date in the trial to one year later, the following information was recorded from each chart: number of encounters with primary care physicians and nurse practitioners related to diabetes (in-person visits and phone calls were included), number of missed primary care appointments (this is tracked and missed appointments are explicitly stated in the EMR), number of consultant (specialist physician) encounters related to diabetes, number of blood pressure measurements performed at healthcare visits, number of serum hemoglobin A1c (HbA1c) measurements, number of serum LDL-cholesterol (LDL-c) measurements, if serum creatinine (Cr) was measured (binary; done during the year or not), if urine albumin to creatinine ratio (ACR) was measured (binary), if the patient self-monitored their blood glucose levels (binary), if an annual eye screening exam was performed (binary), if an annual foot screening exam was performed (binary), and if the annual influenza vaccine was administered (binary). We also recorded the number of new diabetes medicines each diabetic patient was prescribed and the number of diabetes medicines they stopped taking, during the one year study period. All of this information was found in the charts as expected, however, flu vaccines

may have been given elsewhere, such as at a pharmacy, and may not have been fully captured in chart review.

For all patients with hypertension, starting from the patient's start date in the trial to one year later, the following information was recorded: total number of encounters with primary care physicians and nurse practitioners, number of consultant appointments related to hypertension, number of missed primary care appointments, number of blood pressure measurements performed at healthcare visits; number of serum electrolyte tests [any number of the following tests were included: Na, K, Cl, HCO3- and if a patient had NA, K and CI done on the same day, this was counted as one electrolyte test], number of serum HbA1c measurements, number of serum lipid measurements (any number of the following tests were included: LDL-c, HDL-c, non-HDL-c, triglycerides, cholesterol), number of serum creatinine (Cr) measurements, if the patient self-measures their blood pressure either at home or at a community pharmacy (binary), and the number of new hypertension medicines each patient was prescribed and stopped taking. This information was found in the charts as expected.

Data Analysis

For clinical manoeuvres that are recommended to be performed multiple times during one year (e.g. blood pressure measurements) and for encounters with healthcare professionals we report the rate ratios with 95% confidence intervals that were estimated using a Poisson regression model. We report unadjusted rate ratios and rate ratios adjusted for age, sex and clinic location (urban versus rural). We compared the proportion of patients in each arm receiving clinical manoeuvres that are recommended to be done only once during a one-year period (e.g. annual eye examination for people with diabetes) and report the odds ratio with 95% confidence intervals that was estimated using a logistic regression model. We report unadjusted odds ratios and odds ratios adjusted for age, sex and location (urban versus rural). No p-value threshold was set for these post-hoc and hypothesis generating analyses.

We also compared the net change in medications for hypertension and diabetic patients in the intervention and control arms.

Patient and public involvement

Patients or the public were not involved in the design, conduct, or reporting, or dissemination plans of our research.

RESULTS

Baseline characteristics

Of the 786 patients enrolled in the CLEAN Meds trial, 163 patients were prescribed one or more medicines for diabetes and were included in the diabetes group [including 114 who were also prescribed one or more anti-hypertensive agents], and 105 patients were nondiabetic and prescribed one or more anti-hypertensive agents and included in the hypertension group. We thus included 268 participants in this study. Of the 163 patients with diabetes, 83 patients were in the intervention group receiving free distribution of medicines, while the remaining 80 patients were in the control group receiving standard access to medicines. Of the 105 patients with hypertension, 56 patients were in the intervention group receiving free distribution of medicines, and 49 patients were in the control group receiving standard access to medicines.

Figure 1. Flowchart illustrating study participant inclusion

For this posthoc analysis, the groups are balanced with the exception of hypertension in urban and rural groups. The characteristics of participants in the diabetes and hypertension groups are summarized in Table 1.

Table 1. Baseline participant characteristics.

	Diabetes [n = 163]	**Hypertension [n = 105]**

	Free distribution Number [%] [n = 83]	Usual access Number [%] [n = 80]	Free distribution Number [%] [n = 56]	Usual access Number [%] [n =49]
Women	35 [42.2]	35 [43.8]	22 [39.3]	17 [34.7]
Age [mean, SD]	59 ± 10	58 ± 11.2	60 ± 8.2	61 ± 9.3
Age 65 years or older	25 [30.1]	19 [23.8]	17 [30.4]	16 [32.7]
Ethnicity				
White	42 [50.6]	53 [66.3]	46 [82.1]	34 [69.4]
Black	9 [10.8]	10 [12.5]	2 [3.6]	4 [8.1]
Southeast or East Asian [incl Korean, Japanese, Filipino, Chinese]	6 [7.2]	2 [2.5]	4 [7.1]	2 [4.1]
South Asian	14 [16.9]	9 [11.3]	1 [1.8]	3 [6.1]
Latin American	1 [1.2]	3 [3.8]	0 [0.0]	2 [4.1]
West Asian [including Arab]	2 [2.4]	1 [1.3]	0 [0.0]	0 [0.0]
Mixed or other	9 [10.8]	2 [2.5]	2 [3.6]	4 [8.2]
Declined to provide	0 [0.0]	0 [0.0]	4 [7.1]	0 [0.0]
Main Income source				
Wages and salaries [including self-employed]	44 [53.0]	38 [47.5]	30 [53.6]	28 [57.1]
Pension	22 [26.5]	19 [23.8]	14 [25.0]	9 [18.4]
Social support [e.g. welfare or disability]	11 [13.3]	13 [16.3]	4 [7.1]	8 [16.3]
Unemployment insurance	4 [4.8]	3 [3.8]	4 [7.1]	2 [4.1]
Other	0 [0.0]	1 [1.3]	0 [0.0]	0 [0.0]
Declined to provide	2 [2.4]	6 [7.5]	4 [7.1]	2 [4.1]
Household income*				
$30 000 CAD or less	46 [55.4]	41 [51.3]	23 [41.1]	19 [38.8]
$30 000 to 70 000	24 [28.9]	22 [27.5]	12 [21.4]	12 [24.5]
$70 000 or greater	3 [3.6]	4 [5.0]	4 [7.1]	0 [0.0]
Declined to provide	10 [12.0]	13 [16.3]	17 [30.4]	18 [36.7]
Number of medicines prescribed at baseline [mean, SD]	5 ± 2.8	5 ± 3.1	4 ± 2.0	4 ± 2.6
Urban site	50 [60.2]	48 [60.0]	22 [39.3]	27 [55.1]
Rural site	33 [39.8]	32 [40.0]	34 [60.7]	22 [44.9]

Impact of free distribution of medicines in subgroup of people with diabetes

For patients with diabetes, there was a trend toward slightly more self-monitoring of blood glucose (aRR 1.3; 95 % CI 0.7-2.6; p = 0.45) and small increases in rates of serum creatinine measurement (aOR 1.3; 95 % CI 0.6-2.9; p = 0.48) but not hemoglobin A1c measurements (aRR 1.1; 95 % CI; 0.9-1.3; p = 0.44) for patients receiving free distribution compared to those with usual medicine access (see Table 2). There were no differences in appointments with primary care providers or consultants, but there was a trend toward fewer missed appointments with primary care providers (aRR 0.8; 95 % CI 0.5-1.3; p = 0.39) (see Table 2). There was no difference between the free distribution and usual access groups with respect to net change in medicine prescriptions. Overall, the net change in the number of medicines prescribed to participants receiving free distribution was 14 new starts (a total of 19 new medicines started and 5 medicines stopped; average of 0.17 new medicines per person) and the net change for those with usual access was 14 new starts (a total of 21 new medicines started and 7 medicines stopped; average of 0.18 new medicines per person).

Table 2. Diabetes process of care indicators.

	Free medicine distribution	Usual medicine access	Unadjusted difference	Adjusted difference
Hemoglobin A1c measurements	2 [1-3] [187]	2 [1-3] [160]	1.1 [0.9-1.4] p = 0.27	1.1 [0.9-1.3] p = 0.44
BP measurements	3 [2-5] [278]	3 [2-4] [274]	1.0 [0.8-1.2] p = 0.85	1.0 [0.8-1.2] p = 0.71
LDL-c measurements	1 [0-1] [65]	1 [0-1] [61]	1.0 [0.7-1.5] p = 0.88	1.0 [0.7-1.4] p = 0.96
Urine ACR measured	54 % [45/83]	58 % [46/80]	0.9 [0.5-1.6] p =0.67	0.9 [0.5-1.7] p = 0.70
Serum creatinine measured	82 % [68/83]	76 % [61/80]	1.4 [0.7- 3.0] p =0.37	1.3 [0.6-2.9] p = 0.48
Foot examination performed	63 % [52/83]	61 % [49/80]	1.1 [0.6-2.0] p = 0.85	0.9 [0.5-1.8] p = 0.87
Eye examination performed	42 % [35/83]	43 % [34/80]	1.0 [0.5-1.8] p = 0.97	1.0 [0.5-2.0] p = 0.93

Influenza vaccine administered	29 % [24/83]	28 % [22/80]	1.1 [0.5-2.1] p = 0.84	1.1 [0.5-2.2] p = 0.84
Self-monitoring of blood glucose	54 % [45/83]	48 % [38/80]	1.3 [0.7-2.4] p = 0.39	1.3 [0.7-2.6] p = 0.45
Primary care encounters related to diabetes	3 [1-5] [258]	3 [1-4] [243]	1.0 [0.8-1.3] p = 0.85	1.0 [0.8-1.3] p = 0.90
Consultant encounters related to diabetes	0 [0-1] [49]	0 [0-1] [51]	0.9 [0.5-1.6] p = 0.79	1.0 [0.6-1.8] p = 0.96
Missed primary care appointments	0 [0-1] [43]	0 [0-1] [49]	0.9 [0.5- 1.4] p = 0.54	0.8 [0.5-1.3] p = 0.39
Total number of encounters and manoeuvres [assign 0 or 1 for binary indicators; exclude missed appointments]	11 [9-17] [1039]	12 [9-16] [1106]	1.0 [0.9-1.2] p = 0.74	1.0 [0.9 to 1.2] p = 0.85

Count indicators are reported as the median number of measurements or encounters with the IQR and the sum of all measurements or encounters. Binary indicators are reported as a proportion. Differences are adjusted for age, sex, and site and reported as rate ratio or odds ratio with the 95% confidence interval and p value.

Impact of free distribution of medicines in subgroup of people with hypertension

Among hypertension patients, free distribution was associated with less serum creatinine [aRR 0.6; 95 % CI 0.4 -1.0; p =0.04] and electrolyte measuring (aRR 0.6; 95 % CI 0.4-1.0; p = 0.04) and fewer missed appointments (aRR 0.4; 95 % CI 0.2-0.9; p = 0.03) (see Table 3). There were trends towards fewer encounters with primary care providers (aRR 0.9; 0.7-1.1; p = 0.25) and consultants (aRR 0.6; 95 % CI 0.1-4.6; p = 0.61) but similar self-monitoring of blood pressure (aOR 1.1; 95 % CI 0.4-3.2; p = 0.86) (see Table 3). There was no difference in blood pressuring measuring in clinic. There were slightly more new medicine starts in participants receiving free distribution. Overall, the net change in the number of medicines prescribed to intervention participants was 15 new starts (a total of 20 new medicines started

and 5 medicines stopped; average: 0.27 new medicines per person) and the net change for control participants was 0 (a total of 9 new medicines started and 9 medicines stopped).

Table 3. Hypertension process of care indicators.

	Free medicine distribution	Usual medicine access	Unadjusted difference	Adjusted difference
BP measurements	3 [2-4] [173]	3 [2-4] [160]	1.0 [0.7- 1.2] p = 0.67	1.00 [0.8-1.3] p = 0.92
Hemoglobin A1c measurements	0 [0-1] [37]	1 [0-1] [42]	0.8 [0.5- 1.2] p = 0.27	0.8 [0.5-1.3] p = 0.41
Lipid measurements	0 [0-1] [36]	1 [0-1] [37]	0.9 [0.5- 1.4] p =0.49	0.9 [0.6-1.5] p = 0.70
Serum creatinine measurements	1 [0-1.3] [78]	1 [0-3] [110]	0.6 [0.4- 1.0] p = 0.05	0.6 [0.4 -1.0] p =0.04
Serum electrolyte measurements	1 [0-1] [66]	1 [0-3] [103]	0.6 [0.3-0.9] p = 0.02	0.6 [0.4-1.0] p = 0.04
Primary care encounters	5 [3-7] [287]	5 [3-9] [302]	0.8 [0.7-1.1] p = 0.11	0.9 [0.7-1.1] p = 0.25
Consultant encounters related to hypertension	0 [0-0] [5]	0 [0-1] [5]	0.9 [0.1-6.1] p = 0.89	0.6 [0.1-4.6] p = 0.61
Missed primary care appointments	0 [0-0] [14]	0 [0-1] [44]	0.3 [0.1- 0.6] p = 0.00	0.4 [0.2-0.9] p = 0.03
Self-monitoring of blood pressure	21 % [12/56]	18 % [9/49]	1.2 [0.5-3.2] p = 0.70	1.1 [0.4-3.2] p = 0.86
Total number of encounters and manoeuvres [assign 0 or 1 for binary indicators; exclude missed appointments]	12 [8-15] [694]	15 [8-20] [768]	0.8 [0.6-1.0] p = 0.04	0.8 [0.7-1.0] p = 0.10

Count indicators are reported as the median number of measurements or encounters with the IQR and the sum of all measurements or encounters. Binary indicators are reported as a proportion. Differences are adjusted for age, sex, and site and reported as odds ratio or rate ratio with the 95% confidence interval and p value.

DISCUSSION

In this post-hoc analysis of randomized controlled trial findings, free distribution of medicines to people with diabetes or hypertension was not associated with more visits to primary care providers or consultants and, in fact, patients with hypertension had less laboratory monitoring and slightly fewer visits. Free distribution may slightly increase self-monitoring and reduce missed appointments.

The modest reductions in laboratory testing of serum creatinine and electrolytes for patients with hypertension may reflect appropriate clinical judgement against repeat testing. The Canadian guidelines recommend that the frequency of laboratory testing should be guided by clinical judgement and no specific intervals are mentioned in the guidelines. Clinicians may have been less likely to order laboratory testing in patients receiving free distribution because they had slightly better control of their blood pressure, possibly due to the greater number of medicines prescribed. These tests may also have been ordered less frequently because patients had fewer visits, potentially because they were self-monitoring. Systematic reviews have reported improved glycemic control in diabetic patients performing self-monitoring of blood glucose, and reduced blood pressure in patients with hypertension self-measuring their blood pressure.[14,15] Thus, the observed trend towards more self-monitoring, if real, could reflect improved patient motivation, better disease control, or different guidance from clinicians. A 2018 randomized controlled trial found that using self-monitored blood pressure readings to titrate anti-hypertensive treatments led to a significant reduction in blood pressure compared to the use of clinic readings to guide care.[16] In this trial, patients with hypertension had substantially better blood pressure control. The improvements in disease control and usefulness of self-measured blood pressure readings may have resulted in clinicians asking patients to monitor their blood pressure at home rather than attend clinic; this would explain both the increase in self-monitoring and the reduction in clinic visits. A 1985 controlled trial of the effects of medical insurance on health spending and health status reported lower

blood pressure with free care, though the cause of the difference was additional contact with physicians under free care. [17]

The reduction in missed appointments observed here may be explained by an improved clinician-patient relationship and better perceived disease control. The reduction in missed appointments did not relate to needing to attend appointments in order to get their free medications, as the study pharmacist had access to their electronic medical record, could communicate with primary care providers, and medications were mailed to participants. A 2004 study of patient perceptions found that emotional barriers [including the fear of bad news] and perceived disrespect by the healthcare system caused patients to miss primary care appointments.[18] Additionally, a 2014 cross-sectional survey reported that patients with hypertension with no medication coverage and high medication costs were more likely to miss appointments.[19] Patients may not take their medicines due to cost and may miss appointments due to feelings of embarrassment or guilt over this; this may be obviated by free distribution of medicines.

Our study found that there was only a small non-significant increase in hemoglobin A1c monitoring and serum creatinine monitoring in patients with diabetes. Our findings suggest that financial barriers to medication access may not deter patients with diabetes from engaging in necessary health visits and screening related to the management of their condition. In contrast, a study of American patients with diabetes found that lower cost-related nonadherence was associated with improved compliance to annual diabetes recommendations.[5] Financial incentives to clinicians, audit and feedback interventions, and reminders to clinicians can achieve modest reductions in hemoglobin A1c, and our study found a small increase in the frequency of HbA1c monitoring with free medicine distribution.[6]

The results of this study post-hoc analysis of trial findings suggest that improving access to chronic disease medicines will not substantially increase costs associated with outpatient visits. To the contrary, in this study free distribution appeared to increase self-monitoring, reduce visits for hypertension and reduce the total number of healthcare encounters and manoeuvres performed in a year, without changing

the likelihood of visits for diabetes. Increasing access to medicines may encourage self-monitoring practices, reduce in-person visits, and decrease laboratory investigations performed. Free distribution of medicines may not only improve blood pressure control but could also reduce the per-person costs associated with the management of hypertension.

Strengths of this study include the fact that the results are based on a randomized controlled trial. Participants differed with respect to income level, ethnicity and location (urban versus rural). Despite the fact that this was a post-hoc analysis and randomization was not stratified based on these characteristics, we found that the groups were largely balanced; except for urban status. There are also some limitations in this analysis. Associations identified during post-hoc analyses could be spurious and thus the findings should be viewed as hypothesis-generating.[20] The trial was not designed to have sufficient power to detect differences in some of the outcomes examined in this study so the failure to identify associations should be interpreted with caution. Since the trial was unblinded, patients and clinicians could have been motivated by allocation to free access to improve the process of care. The trial was conducted with primary care patients in a high-income country who reported cost-related non-adherence and the findings may not apply in other settings. The study was based on a review of primary care charts that do not reflect every actual encounter (e.g. visits to other providers).

CONCLUSION

This post-hoc analysis of randomized controlled trial results found that free distribution of medicines may improve self-monitoring behaviours and reduce missed primary care appointments for patients with diabetes or hypertension. Free distribution may also reduce primary care and consultant appointments and laboratory testing in patients with hypertension. Additionally, free distribution of medicines improves disease control and improves patients' self-reported care. [21] Overall, these findings suggest that improving medicine accessibility for patients with diabetes and hypertension not only improves surrogate health outcomes but also improves the patient experience and may also reduce healthcare costs by

encouraging self-monitoring practices. The hypotheses generated by this post-hoc analysis of randomized controlled trial findings could be tested in future studies.

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AUTHOR CONTRIBUTIONS

OC contributed to the data curation, formal analysis, investigation, methodology, visualization, writing the original draft and reviewing and editing. HW contributed to the data curation, formal analysis, investigation, writing the original draft and reviewing and editing. MA contributed to the data curation, formal analysis, and reviewing and editing. BM contributed to the methodology, validation, investigation, resources and reviewing and editing. BS contributed to the methodology, validation, investigation, resources and reviewing and editing. NP contributed to the conceptualization, methodology, validation, formal analysis, investigation, resources, writing the original draft, reviewing and editing.

DATA AVAILABILITY

Deidentified participant data is available upon reasonable request from the corresponding author.

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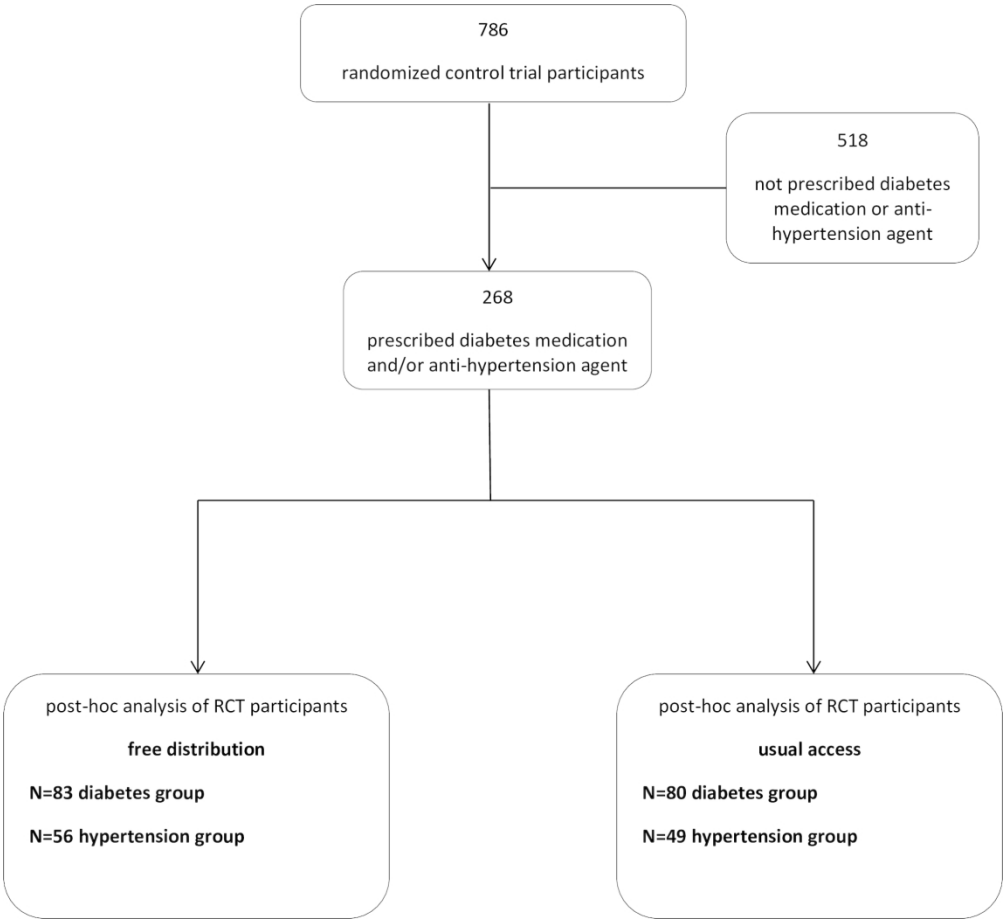

Figure 1. Flowchart illustrating study participant inclusion

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Effect of free distribution of medicines on the process of care for adult patients with type 1 and type 2 diabetes and hypertension: Post-hoc analysis of randomized control trial findings

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Effect of free distribution of medicines on the process of care for adult patients with type 1 and type 2 diabetes and hypertension: Post-hoc analysis of randomized control trial findings

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ABSTRACT

Objectives

The Carefully Selected and Easily Accessible at No charge Medicines (CLEAN Meds) trial randomized controlled trial showed that patients receiving free access to medicines had improved diabetes and hypertension outcomes compared to patients who had usual access to medicines. In this study, we aimed to test the impact of providing free access to medicine to people with diabetes and hypertension on process of care indicators.

Design

In this post hoc analysis of randomized controlled trial findings we identified process of care indicators for the management of diabetes and hypertension using relevant guidelines. The follow process of care indicators were identified for diabetes management: encounters with healthcare professionals, blood pressure measurements, self-monitoring of blood glucose, annual eye and foot exam, annual administration of the influenza vaccine, and laboratory testing for hemoglobin A1c, LDL-cholesterol, serum creatinine, and urine albumin to creatinine ratio (ACR). We identified the following process of care indicators for hypertension: encounters with healthcare professionals, blood pressure measurements, self-measuring of blood pressure, and serum tests for electrolytes, HbA1c, lipids, and creatinine. Chart extractions were performed for all patients and the indicators for diabetes and hypertension were recorded. We compared the indicators for patients in each arm of the trial.

Results

The study included 268 primary care patients. Free distribution of medicines may improve self-monitoring behaviours (aRR 1.3; 95 % CI 0.7-2.6) and reduce missed primary care appointments for patients with diabetes (aRR 0.8; 95 % CI 0.5-1.3) or hypertension (aRR 0.4; 95 % CI 0.2-0.9). Free distribution may also reduce primary care and consultant appointments and laboratory testing in patients with hypertension.

Conclusions

Improving medicine accessibility for patients with diabetes and hypertension not only improves surrogate health outcomes but also improves the patient experience and may also reduce healthcare costs by encouraging self-monitoring.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study is based on a randomized controlled trial.
- Despite the fact that this was a post-hoc analysis and randomization was not stratified based on these characteristics, we found that the groups were largely balanced.
- Associations identified during post-hoc analyses could be spurious and thus the findings should be viewed as hypothesis-generating.
- The trial this study was based on was conducted with primary care patients in a high-income country who reported cost-related non-adherence and the findings may not apply in other settings.

INTRODUCTION

Managing people with chronic diseases such as diabetes and hypertension with effective medicines and healthcare services can save lives and reduce complications, yet many people do not receive guideline-recommended care.[1–3] One important barrier to optimal care is cost related nonadherence which was reported by 9.6% of people who had received a prescription in the past year. [4] Cost related nonadherence could undermine the provision of healthcare services as people may avoid participating in care if they cannot afford prescribed medicines.[4,5]

Many strategies have been tested to improve the process of care for chronic diseases, with varying success. Resource intensive interventions such as financial incentives to providers and multidisciplinary changes to the primary care team are associated with modest improvements in diabetes and hypertension management.[6,7] Caring for patients with chronic diseases is expensive. [8] The cost and effectiveness of interventions to improve guideline-recommended care are important to consider, since increasing access to effective treatments may reduce costs related to complications, but may increase per-patient costs related to clinicians' monitoring of treatments and more expensive health technologies. [9]

We recently completed the Carefully Selected and Easily Accessible at No charge Medicines (CLEAN Meds) trial, a randomized controlled trial in which patients with self-reported cost-related medication nonadherence were randomly assigned to receive free distribution of medicines from a comprehensive list of essential medicines.[10] The CLEAN Meds trial found that providing Canadian primary care patients with medicines at no charge improved adherence to medication and, for patients with diabetes and hypertension, chronic disease management was improved based on some surrogate outcomes.[10] As previously reported, with free distribution of medicines, hemoglobin A1c levels were 0.4 % lower (95 % CI -0.76 to 0.0) compared with usual access, and systolic blood pressure was 7 mmHg lower (95% CI -11.7 to -2.8) compared with usual access. We undertook this post-hoc analysis both to help understand

why the intervention was beneficial in some circumstances and why the intervention did not have a large benefit in general or any benefit for some participants. Given the importance of medication related adherence in patients with chronic diseases, in this post-hoc analysis, we tested the impact on diabetes and hypertension process of care indicators of providing free access to medicine to people with diabetes and hypertension.

METHODS

Patients

We identified patients in the CLEAN Meds trial with diabetes (with or without hypertension) or only hypertension by identifying all participants prescribed at least one diabetic or anti-hypertensive agent at the start of the trial. Randomization was not stratified based on these conditions. Because anti-hypertensives such as ACE inhibitors and angiotensin receptor blockers are a standard part of diabetes management (even when blood pressure is "normal"), we included patients who were prescribed both a diabetic agent and an anti-hypertensive agent only in the diabetes group.

Process of Care Indicators

Using the care goals of diabetes and the Diabetes Canada Guidelines [11] we identified the following process of care indicators for the management of diabetes: encounters with healthcare professionals [in-clinic appointments and telephone appointments with primary care physicians or nurse practitioners], blood pressure measurements, self-monitoring of blood glucose, annual eye exam (with an optometrist or ophthalmologist), foot screening exams (foot care and/or neuropathy screening), annual administration of the influenza vaccine, and laboratory testing for hemoglobin A1c, LDL-cholesterol, serum creatinine, and urine albumin to creatinine ratio (ACR).[11] Glycated hemoglobin (HbA1c) and self-monitoring blood glucose (SMBG) can be used as indicators for the management of glycemic control.

Using the guidelines and the goals of care for hypertension and the Hypertension Canada Guidelines, [12] we identified the following process of care indicators for the management of hypertension: encounters with healthcare professionals, blood pressure measurements, self-measuring of blood pressure (at home or at the pharmacy), and serum tests for electrolytes, HbA1c, lipids, and creatinine.

Since a number of the recommended clinical manoeuvres and other aspects of care (e.g. medicine adjustments) involve patients interacting with healthcare providers, we also assess healthcare encounters that included in person visits and telephone encounters with primary care physicians or nurse practitioners where diabetes or hypertension were documented as being discussed.

Data Collection

Patients' primary care electronic medical records (EMRs) were accessed using the PS Suite software (an EMR provider that is used by the sites from which trial participants were recruited) [13]and information for the identified process of care indicators for diabetes and hypertension were identified and abstracted. Two abstracters (OC, HW) were blinded to the patients' intervention status at the time of chart abstraction. To ensure reliability of chart abstraction, each abstracter completed 5 chart abstractions independently and compared findings; there were no disagreements. OC, HW and MA then completed the chart abstractions for all participants.

For all patients with diabetes, starting from the patient's start date in the trial to one year later, the following information was recorded from each chart: number of encounters with primary care physicians and nurse practitioners related to diabetes (in-person visits and phone calls were included), number of missed primary care appointments (this is tracked and missed appointments are explicitly stated in the EMR), number of consultant (specialist physician) encounters related to diabetes, number of blood pressure measurements performed at healthcare visits, number of serum hemoglobin A1c (HbA1c)

measurements, number of serum LDL-cholesterol (LDL-c) measurements, if serum creatinine (Cr) was measured (binary; done during the year or not), if urine albumin to creatinine ratio (ACR) was measured (binary), if the patient self-monitored their blood glucose levels (binary), if an annual eye screening exam was performed (binary), if an annual foot screening exam was performed (binary), and if the annual influenza vaccine was administered (binary). We also recorded the number of new diabetes medicines each diabetic patient was prescribed and the number of diabetes medicines they stopped taking, during the one year study period. All of this information was found in the charts as expected, however, flu vaccines may have been given elsewhere, such as at a pharmacy, and may not have been fully captured in chart review.

For all patients with hypertension, starting from the patient's start date in the trial to one year later, the following information was recorded: total number of encounters with primary care physicians and nurse practitioners, number of consultant appointments related to hypertension, number of missed primary care appointments, number of blood pressure measurements performed at healthcare visits; number of serum electrolyte tests [any number of the following tests were included: Na, K, Cl, HCO3- and if a patient had NA, K and CI done on the same day, this was counted as one electrolyte test], number of serum HbA1c measurements, number of serum lipid measurements (any number of the following tests were included: LDL-c, HDL-c, non-HDL-c, triglycerides, cholesterol), number of serum creatinine (Cr) measurements, if the patient self-measures their blood pressure either at home or at a community pharmacy (binary), and the number of new hypertension medicines each patient was prescribed and stopped taking. This information was found in the charts as expected.

Data Analysis

For clinical manoeuvres that are recommended to be performed multiple times during one year (e.g. blood pressure measurements) and for encounters with healthcare professionals we report the rate ratios with

95% confidence intervals that were estimated using a Poisson regression model. We report unadjusted rate ratios and rate ratios adjusted for age, sex and clinic location (urban versus rural). We compared the proportion of patients in each arm receiving clinical manoeuvres that are recommended to be done only once during a one-year period (e.g. annual eye examination for people with diabetes) and report the odds ratio with 95% confidence intervals that was estimated using a logistic regression model. We report unadjusted odds ratios and odds ratios adjusted for age, sex and location (urban versus rural). No p-value threshold was set for these post-hoc and hypothesis generating analyses.

We also compared the net change in medications for hypertension and diabetic patients in the intervention and control arms. As part of the intervention, some patients had to switch medicines within a class. We thus used net changes as a measure that would treat both groups similarly and captured whether or not management had "intensified" by adding more agents.

Patient and public involvement

Patients or the public were not involved in the design, conduct, or reporting, or dissemination plans of our research.

RESULTS

Baseline characteristics

Of the 786 patients enrolled in the CLEAN Meds trial, 163 patients were prescribed one or more medicines for diabetes and were included in the diabetes group [including 114 who were also prescribed one or more anti-hypertensive agents], and 105 patients were nondiabetic and prescribed one or more anti-hypertensive agents and included in the hypertension group. We thus included 268 participants in this study. Of the 163 patients with diabetes, 83 patients were in the intervention group receiving free distribution of medicines, while the remaining 80 patients were in the control group receiving standard access to medicines. Of the 105 patients with hypertension, 56 patients were in the intervention group

receiving free distribution of medicines, and 49 patients were in the control group receiving standard access to medicines. Study participant inclusion is illustrated in Figure 1.

Figure 1. Flowchart illustrating study participant inclusion

For this posthoc analysis, the groups are balanced with the exception of hypertension in urban and rural groups. The characteristics of participants in the diabetes and hypertension groups are summarized in Table 1.

Table 1. Baseline participant characteristics.

	Diabetes [n = 163]		**Hypertension [n = 105]**	
	Free distribution Number [%] [n = 83]	**Usual access Number [%] [n = 80]**	**Free distribution Number [%] [n = 56]**	**Usual access Number [%] [n =49]**
Women	35 [42.2]	35 [43.8]	22 [39.3]	17 [34.7]
Age [mean, SD]	59 ± 10	58 ± 11.2	60 ± 8.2	61 ± 9.3
Age 65 years or older	25 [30.1]	19 [23.8]	17 [30.4]	16 [32.7]
Ethnicity				
White	42 [50.6]	53 [66.3]	46 [82.1]	34 [69.4]
Black	9 [10.8]	10 [12.5]	2 [3.6]	4 [8.1]
Southeast or East Asian [incl Korean, Japanese, Filipino, Chinese]	6 [7.2]	2 [2.5]	4 [7.1]	2 [4.1]
South Asian	14 [16.9]	9 [11.3]	1 [1.8]	3 [6.1]
Latin American	1 [1.2]	3 [3.8]	0 [0.0]	2 [4.1]
West Asian [including Arab]	2 [2.4]	1 [1.3]	0 [0.0]	0 [0.0]
Mixed or other	9 [10.8]	2 [2.5]	2 [3.6]	4 [8.2]
Declined to provide	0 [0.0]	0 [0.0]	4 [7.1]	0 [0.0]
Main Income source				
Wages and salaries [including self-employed]	44 [53.0]	38 [47.5]	30 [53.6]	28 [57.1]
Pension	22 [26.5]	19 [23.8]	14 [25.0]	9 [18.4]
Social support [e.g. welfare or disability]	11 [13.3]	13 [16.3]	4 [7.1]	8 [16.3]
Unemployment insurance	4 [4.8]	3 [3.8]	4 [7.1]	2 [4.1]
Other	0 [0.0]	1 [1.3]	0 [0.0]	0 [0.0]
Declined to provide	2 [2.4]	6 [7.5]	4 [7.1]	2 [4.1]

Household income*				
$30 000 CAD or less	46 [55.4]	41 [51.3]	23 [41.1]	19 [38.8]
$30 000 to 70 000	24 [28.9]	22 [27.5]	12 [21.4]	12 [24.5]
$70 000 or greater	3 [3.6]	4 [5.0]	4 [7.1]	0 [0.0]
Declined to provide	10 [12.0]	13 [16.3]	17 [30.4]	18 [36.7]
Number of medicines prescribed at baseline [mean, SD]	5 ± 2.8	5 ± 3.1	4 ± 2.0	4 ± 2.6
Urban site	50 [60.2]	48 [60.0]	22 [39.3]	27 [55.1]
Rural site	33 [39.8]	32 [40.0]	34 [60.7]	22 [44.9]

Impact of free distribution of medicines in subgroup of people with diabetes

For patients with diabetes, there weresmall increases in rates of serum creatinine measurement (aOR 1.3; 95 % CI 0.6-2.9; p = 0.48) but not hemoglobin A1c measurements (aRR 1.1; 95 % CI; 0.9-1.3; p = 0.44) for patients receiving free distribution compared to those with usual medicine access. There no substantial difference in self-monitoring of blood glucose (aRR 1.3; 95% CI 0.7 – 2.6; p=0.45) (see Table 2). There were no differences in appointments with primary care providers or consultants, but there was a trend toward fewer missed appointments with primary care providers (aRR 0.8; 95 % CI 0.5-1.3; p = 0.39) (see Table 2). There was no difference between the free distribution and usual access groups with respect to net change in medicine prescriptions. Overall, the net change in the number of medicines prescribed to participants receiving free distribution was 14 new starts (a total of 19 new medicines started and 5 medicines stopped; average of 0.17 new medicines per person) and the net change for those with usual access was 14 new starts (a total of 21 new medicines started and 7 medicines stopped; average of 0.18 new medicines per person).

Table 2. Diabetes process of care indicators.

	Free medicine distribution	Usual medicine access	Unadjusted difference	Adjusted difference
Hemoglobin A1c measurements	2 [2] [187]	2 [2] [160]	1.1 [0.9-1.4] p = 0.27	1.1 [0.9-1.3] p = 0.44

BP measurements	3 [7] [278]	3 [7] [274]	1.0 [0.8-1.2] p = 0.85	1.0 [0.8-1.2] p = 0.71
LDL-c measurements	1[1] [65]	1 [1] [61]	1.0 [0.7-1.5] p = 0.88	1.0 [0.7-1.4] p = 0.96
Urine ACR measured	54 % [45/83]	58 % [46/80]	0.9 [0.5-1.6] p =0.67	0.9 [0.5-1.7] p = 0.70
Serum creatinine measured	82 % [68/83]	76 % [61/80]	1.4 [0.7- 3.0] p =0.37	1.3 [0.6-2.9] p = 0.48
Foot examination performed	63 % [52/83]	61 % [49/80]	1.1 [0.6-2.0] p = 0.85	0.9 [0.5-1.8] p = 0.87
Eye examination performed	42 % [35/83]	43 % [34/80]	1.0 [0.5-1.8] p = 0.97	1.0 [0.5-2.0] p = 0.93
Influenza vaccine administered	29 % [24/83]	28 % [22/80]	1.1 [0.5-2.1] p = 0.84	1.1 [0.5-2.2] p = 0.84
Self-monitoring of blood glucose	54 % [45/83]	48 % [38/80]	1.3 [0.7-2.4] p = 0.39	1.3 [0.7-2.6] p = 0.45
Primary care encounters related to diabetes	3 [6] [258]	3 [5] [243]	1.0 [0.8-1.3] p = 0.85	1.0 [0.8-1.3] p = 0.90
Consultant encounters related to diabetes	1 [1] [49]	1 [1] [51]	0.9 [0.5-1.6] p = 0.79	1.0 [0.6-1.8] p = 0.96
Missed primary care appointments	1 [1] [43]	1 [1] [49]	0.9 [0.5- 1.4] p = 0.54	0.8 [0.5-1.3] p = 0.39
Total number of encounters and manoeuvres [assign 0 or 1 for binary indicators; exclude missed appointments]	13 [42] [1106]	13 [38] [1039]	1.0 [0.9-1.2] p = 0.74	1.0 [0.9 to 1.2] p = 0.85

Count indicators are reported as the mean number of measurements or encounters with the variance and the sum of all measurements or encounters. Binary indicators are reported as a proportion. Differences are adjusted for age, sex, and site and reported as rate ratio or odds ratio with the 95% confidence interval and p value.

Impact of free distribution of medicines in subgroup of people with hypertension

Among hypertension patients, free distribution was associated with less serum creatinine [aRR 0.6; 95 % CI 0.4 -1.0; p =0.04] and electrolyte measuring (aRR 0.6; 95 % CI 0.4-1.0; p = 0.04) and fewer missed appointments (aRR 0.4; 95 % CI 0.2-0.9; p = 0.03) (see Table 3). There were trends towards fewer encounters with primary care providers (aRR 0.9; 0.7-1.1; p = 0.25) and consultants (aRR 0.6; 95 % CI 0.1-4.6; p = 0.61) but similar self-monitoring of blood pressure (aOR 1.1; 95 % CI 0.4-3.2; p = 0.86) (see Table 3). There was no difference in blood pressuring measuring in clinic. There were slightly more new medicine starts in participants receiving free distribution. Overall, the net change in the number of medicines prescribed to intervention participants was 15 new starts (a total of 20 new medicines started and 5 medicines stopped; average: 0.27 new medicines per person) and the net change for control participants was 0 (a total of 9 new medicines started and 9 medicines stopped).

Table 3. Hypertension process of care indicators.

	Free medicine distribution	Usual medicine access	Unadjusted difference	Adjusted difference
BP measurements	3 [4] [173]	3 [5] [160]	1.0 [0.7- 1.2] p = 0.67	1.00 [0.8-1.3] p = 0.92
Hemoglobin A1c measurements	1 [1] [37]	1 [1] [42]	0.8 [0.5- 1.2] p = 0.27	0.8 [0.5-1.3] p = 0.41
Lipid measurements	1 [1] [36]	1 [1] [37]	0.9 [0.5- 1.4] p =0.49	0.9 [0.6-1.5] p = 0.70
Serum creatinine measurements	1 [4] [78]	2 [13] [110]	0.6 [0.4- 1.0] p = 0.05	0.6 [0.4 -1.0] p =0.04
Serum electrolyte measurements	1 [3] [66]	2 [11] [103]	0.6 [0.3-0.9] p = 0.02	0.6 [0.4-1.0] p = 0.04
Primary care encounters	5 [9] [287]	6 [14] [302]	0.8 [0.7-1.1] p = 0.11	0.9 [0.7-1.1] p = 0.25
Consultant encounters related to hypertension	0 [0] [5]	0 [0] [5]	0.9 [0.1-6.1] p = 0.89	0.6 [0.1-4.6] p = 0.61
Missed primary care appointments	0 [0] [14]	0 [4] [44]	0.3 [0.1- 0.6] p = 0.00	0.4 [0.2-0.9] p = 0.03

Self-monitoring of blood pressure	21 % [12/56]	18 % [9/49]	1.2 [0.5-3.2] p = 0.70	1.1 [0.4-3.2] p = 0.86
Total number of encounters and manoeuvres [assign 0 or 1 for binary indicators; exclude missed appointments]	12 [43] [694]	16 [97] [768]	0.8 [0.6-1.0] p = 0.04	0.8 [0.7-1.0] p = 0.10

Count indicators are reported as the mean number of measurements or encounters with the variance and the sum of all measurements or encounters. Binary indicators are reported as a proportion. Differences are adjusted for age, sex, and site and reported as odds ratio or rate ratio with the 95% confidence interval and p value.

DISCUSSION

In this post-hoc analysis of randomized controlled trial findings, free distribution of medicines to people with diabetes or hypertension was not associated with more visits to primary care providers or consultants and, in fact, patients with hypertension had less laboratory monitoring and slightly fewer visits. Free distribution may slightly increase self-monitoring and reduce missed appointments.

The modest reductions in laboratory testing of serum creatinine and electrolytes for patients with hypertension may reflect appropriate clinical judgement against repeat testing. The Canadian guidelines recommend that the frequency of laboratory testing should be guided by clinical judgement and no specific intervals are mentioned in the guidelines. Clinicians may have been less likely to order laboratory testing in patients receiving free distribution because they had slightly better control of their blood pressure, possibly due to the greater number of medicines prescribed. These tests may also have been ordered less frequently because patients had fewer visits, potentially because they were self-monitoring. Systematic reviews have reported improved glycemic control in diabetic patients performing self-monitoring of blood glucose, and reduced blood pressure in patients with hypertension self-measuring their blood pressure.[14,15] Thus, the observed trend towards more self-monitoring, if real, could reflect improved patient motivation, better disease control, or different guidance from clinicians. A 2018

randomized controlled trial found that using self-monitored blood pressure readings to titrate anti-hypertensive treatments led to a significant reduction in blood pressure compared to the use of clinic readings to guide care.[16] In this trial, patients with hypertension had a lower systolic blood pressure after one year . The improvements in disease control and usefulness of self-measured blood pressure readings may have resulted in clinicians asking patients to monitor their blood pressure at home rather than attend clinic; this would explain both the increase in self-monitoring and the reduction in clinic visits. A 1985 controlled trial of the effects of medical insurance on health spending and health status reported lower blood pressure with free care, though the cause of the difference was additional contact with physicians under free care. [17]

The reduction in missed appointments observed here may be explained by an improved clinician-patient relationship and better perceived disease control. The reduction in missed appointments did not relate to needing to attend appointments in order to get their free medications, as the study pharmacist had access to their electronic medical record, could communicate with primary care providers, and medications were mailed to participants. A 2004 study of patient perceptions found that emotional barriers [including the fear of bad news] and perceived disrespect by the healthcare system caused patients to miss primary care appointments.[18] Additionally, a 2014 cross-sectional survey reported that patients with hypertension with no medication coverage and high medication costs were more likely to miss appointments.[19] Patients may not take their medicines due to cost and may miss appointments due to feelings of embarrassment or guilt over this; this may be obviated by free distribution of medicines.

Our study found that there was only a small non-significant increase in hemoglobin A1c monitoring and serum creatinine monitoring in patients with diabetes. Our findings suggest that financial barriers to medication access may not deter patients with diabetes from engaging in necessary health visits and screening related to the management of their condition. In contrast, a study of American patients with diabetes found that lower cost-related nonadherence was associated with improved compliance to annual

diabetes recommendations.[5] Financial incentives to clinicians, audit and feedback interventions, and reminders to clinicians can achieve modest reductions in hemoglobin A1c, and our study found a small increase in the frequency of HbA1c monitoring with free medicine distribution.[6]

The results of this study post-hoc analysis of trial findings suggest that improving access to chronic disease medicines will not substantially increase costs associated with outpatient visits. To the contrary, in this study free distribution appeared to increase self-monitoring, reduce visits for hypertension and reduce the total number of healthcare encounters and manoeuvres performed in a year, without changing the likelihood of visits for diabetes. Increasing access to medicines may encourage self-monitoring practices, reduce in-person visits, and decrease laboratory investigations performed. Free distribution of medicines may not only improve blood pressure control but could also reduce the per-person costs associated with the management of hypertension.

Strengths of this study include the fact that the results are based on a randomized controlled trial. Participants differed with respect to income level, ethnicity and location (urban versus rural). Despite the fact that this was a post-hoc analysis and randomization was not stratified based on these characteristics, we found that the groups were largely balanced; except for urban status. There are also some limitations in this analysis. Associations identified during post-hoc analyses could be spurious and thus the findings should be viewed as hypothesis-generating.[20] The study population is a subset of the CLEAN Meds trial, and only included those with diabetes or hypertension based on whether they were prescribed at least one diabetic or anti-hypertensive agent at the start of the trial; this reduced sample size is a limitation. The trial was not designed to have sufficient power to detect differences in some of the outcomes examined in this study so the failure to identify associations should be interpreted with caution. Since the trial was unblinded, patients and clinicians could have been motivated by allocation to free access to improve the process of care. The trial was conducted with primary care patients in a high-income country who reported cost-related non-adherence and the findings may not apply in other settings.

The study was based on a review of primary care charts that do not reflect every actual encounter (e.g. visits to other providers).

CONCLUSION

This post-hoc analysis of randomized controlled trial results found that free distribution of medicines may improve self-monitoring behaviours and reduce missed primary care appointments for patients with diabetes or hypertension. Free distribution may also reduce primary care and consultant appointments and laboratory testing in patients with hypertension. Additionally, free distribution of medicines improves disease control and improves patients' self-reported care. [21] Overall, these findings suggest that improving medicine accessibility for patients with diabetes and hypertension not only improves surrogate health outcomes but also improves the patient experience and may also reduce healthcare costs by encouraging self-monitoring practices. The hypotheses generated by this post-hoc analysis of randomized controlled trial findings could be tested in future studies.

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COMPETING INTERESTS STATEMENT

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AUTHOR CONTRIBUTIONS

OC contributed to the data curation, formal analysis, investigation, methodology, visualization, writing the original draft and reviewing and editing. HW contributed to the data curation, formal analysis, investigation, writing the original draft and reviewing and editing. MA contributed to the data curation, formal analysis, and reviewing and editing. BM contributed to the methodology, validation, investigation, resources and reviewing and editing. BS contributed to the methodology, validation, investigation, resources and reviewing and editing. NP contributed to the conceptualization, methodology, validation, formal analysis, investigation, resources, writing the original draft, reviewing and editing.

DATA AVAILABILITY

Deidentified participant data is available upon reasonable request from the corresponding author.

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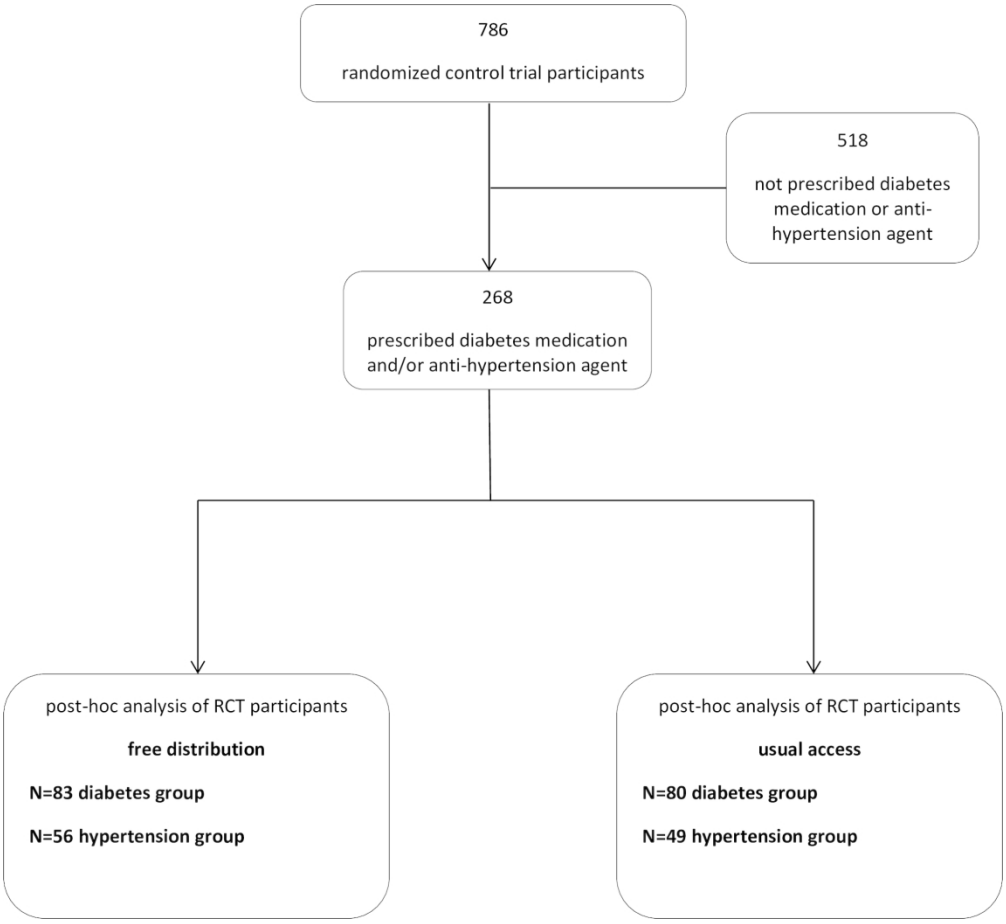

Figure 1. Flowchart illustrating study participant inclusion

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Effect of free distribution of medicines on the process of care for adult patients with type 1 and type 2 diabetes and hypertension: Post-hoc analysis of randomized control trial findings

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Effect of free distribution of medicines on the process of care for adult patients with type 1 and type 2 diabetes and hypertension: Post-hoc analysis of randomized control trial findings

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ABSTRACT

Objectives

The Carefully Selected and Easily Accessible at No charge Medicines (CLEAN Meds) trial randomized controlled trial showed that patients receiving free access to medicines had improved diabetes and hypertension outcomes compared to patients who had usual access to medicines. In this study, we aimed to test the impact of providing free access to medicine to people with diabetes and hypertension on process of care indicators.

Design

In this post hoc analysis of randomized controlled trial findings we identified process of care indicators for the management of diabetes and hypertension using relevant guidelines. The following process of care indicators were identified for diabetes management: encounters with healthcare professionals, blood pressure measurements, self-monitoring of blood glucose, annual eye and foot exam, annual administration of the influenza vaccine, and laboratory testing for hemoglobin A1c, LDL-cholesterol, serum creatinine, and urine albumin to creatinine ratio (ACR). We identified the following process of care indicators for hypertension: encounters with healthcare professionals, blood pressure measurements, self-measuring of blood pressure, and serum tests for electrolytes, HbA1c, lipids, and creatinine. Chart extractions were performed for all patients and the indicators for diabetes and hypertension were recorded. We compared the indicators for patients in each arm of the trial.

Results

The study included 268 primary care patients. Free distribution of medicines may improve self-monitoring behaviours (aRR 1.30; 95 % CI 0.66-2.57) and reduce missed primary care appointments for patients with diabetes (aRR 0.80; 95 % CI 0.48-1.33) or hypertension (aRR 0.41; 95 % CI 0.18-0.90). Free distribution may also reduce primary care and consultant appointments and laboratory testing in patients with hypertension.

Conclusions

Improving medicine accessibility for patients with diabetes and hypertension not only improves surrogate health outcomes but also improves the patient experience and may also reduce healthcare costs by encouraging self-monitoring.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study is based on a randomized controlled trial.
- Despite the fact that this was a post-hoc analysis and randomization was not stratified based on these characteristics, we found that the groups were largely balanced.
- Associations identified during post-hoc analyses could be spurious and thus the findings should be viewed as hypothesis-generating.
- The trial this study was based on was conducted with primary care patients in a high-income country who reported cost-related non-adherence and the findings may not apply in other settings.

INTRODUCTION

Managing people with chronic diseases such as diabetes and hypertension with effective medicines and healthcare services can save lives and reduce complications, yet many people do not receive guideline-recommended care.[1–3] One important barrier to optimal care is cost related nonadherence which was reported by 9.6% of people who had received a prescription in the past year. [4] Cost related nonadherence could undermine the provision of healthcare services as people may avoid participating in care if they cannot afford prescribed medicines.[4,5]

Many strategies have been tested to improve the process of care for chronic diseases, with varying success. Resource intensive interventions such as financial incentives to providers and multidisciplinary changes to the primary care team are associated with modest improvements in diabetes and hypertension management.[6,7] Caring for patients with chronic diseases is expensive. [8] The cost and effectiveness of interventions to improve guideline-recommended care are important to consider, since increasing access to effective treatments may reduce costs related to complications, but may increase per-patient costs related to clinicians' monitoring of treatments and more expensive health technologies. [9]

We recently completed the Carefully Selected and Easily Accessible at No charge Medicines (CLEAN Meds) trial, a randomized controlled trial in which patients with self-reported cost-related medication nonadherence were randomly assigned to receive free distribution of medicines from a comprehensive list of essential medicines.[10] The CLEAN Meds trial found that providing Canadian primary care patients with medicines at no charge improved adherence to medication and, for patients with diabetes and hypertension, chronic disease management was improved based on some surrogate outcomes.[10] As previously reported, with free distribution of medicines, hemoglobin A1c levels were 0.4 % lower (95 % CI -0.76 to 0.0) compared with usual access, and systolic blood pressure was 7 mmHg lower (95% CI -11.7 to -2.8) compared with usual access.

We undertook this post-hoc analysis both to help understand why the intervention was beneficial in some circumstances and why the intervention did not have a large benefit in general or any benefit for some participants. Improving access to medicines could improve the process of care as patients who are nonadherent may lack motivation for participating in care. Participation in diabetes education is associated with both better quality of diabetes care and greater adherence to diabetes medicines, indicating that medicine adherence and quality of care may improve together. [11] On the other hand, improved adherence and better disease control could also lead to less participation in care. Patient-centred medical homes is associated with improved quality of diabetes care but not with better medicine adherence, suggesting that the process of care and medicine adherence can be uncoupled. [12] Given the importance of medication related adherence in patients with chronic diseases, in this post-hoc analysis, we tested the impact on diabetes and hypertension process of care indicators of providing free access to medicine to people with diabetes and hypertension.

METHODS

Patients

We identified patients in the CLEAN Meds trial with diabetes (with or without hypertension) or only hypertension by identifying all participants prescribed at least one diabetic or anti-hypertensive agent at the start of the trial. Randomization was not stratified based on these conditions. Because anti-hypertensives such as ACE inhibitors and angiotensin receptor blockers are a standard part of diabetes management (even when blood pressure is "normal"), we included patients who were prescribed both a diabetic agent and an anti-hypertensive agent only in the diabetes group.

Process of Care Indicators

Using the care goals of diabetes and the Diabetes Canada Guidelines [13]) we identified the following process of care indicators for the management of diabetes: encounters with healthcare professionals [in-clinic appointments and telephone appointments with primary care physicians or nurse practitioners], blood pressure measurements, self-monitoring of blood glucose, annual eye exam (with an optometrist or ophthalmologist), foot screening exams (foot care and/or neuropathy screening), annual administration of the influenza vaccine, and laboratory testing for hemoglobin A1c, LDL-cholesterol, serum creatinine, and urine albumin to creatinine ratio (ACR).[13] Glycated hemoglobin (HbA1c) and self-monitoring blood glucose (SMBG) can be used as indicators for the management of glycemic control.

Using the guidelines and the goals of care for hypertension and the Hypertension Canada Guidelines, [14] we identified the following process of care indicators for the management of hypertension: encounters with healthcare professionals, blood pressure measurements, self-measuring of blood pressure (at home or at the pharmacy), and serum tests for electrolytes, HbA1c, lipids, and creatinine.

Since a number of the recommended clinical manoeuvres and other aspects of care (e.g. medicine adjustments) involve patients interacting with healthcare providers, we also assess healthcare encounters that included in person visits and telephone encounters with primary care physicians or nurse practitioners where diabetes or hypertension were documented as being discussed.

Data Collection

Patients' primary care electronic medical records (EMRs) were accessed using the PS Suite software (Telus Health) and information for the identified process of care indicators for diabetes and hypertension were identified and abstracted. Two abstracters (OC, HW) were blinded to the patients' intervention status at the time of chart abstraction. To ensure reliability of chart abstraction, each abstracter completed 5 chart abstractions independently and compared findings; there were no disagreements. OC, HW and MA then completed the chart abstractions for all participants.

For all patients with diabetes, starting from the patient's start date in the trial to one year later, the following information was recorded from each chart: number of encounters with primary care physicians and nurse practitioners related to diabetes (in-person visits and phone calls were included), number of missed primary care appointments (this is tracked and missed appointments are explicitly stated in the EMR), number of consultant (specialist physician) encounters related to diabetes, number of blood pressure measurements performed at healthcare visits, number of serum hemoglobin A1c (HbA1c) measurements, number of serum LDL-cholesterol (LDL-c) measurements, if serum creatinine (Cr) was measured (binary; done during the year or not), if urine albumin to creatinine ratio (ACR) was measured (binary), if the patient self-monitored their blood glucose levels (binary), if an annual eye screening exam was performed (binary), if an annual foot screening exam was performed (binary), and if the annual influenza vaccine was administered (binary). We also recorded the number of new diabetes medicines each diabetic patient was prescribed and the number of diabetes medicines they stopped taking, during the one year study period. All of this information was found in the charts as expected, however, flu vaccines may have been given elsewhere, such as at a pharmacy, and may not have been fully captured in chart review.

For all patients with hypertension, starting from the patient's start date in the trial to one year later, the following information was recorded: total number of encounters with primary care physicians and nurse practitioners, number of consultant appointments related to hypertension, number of missed primary care appointments, number of blood pressure measurements performed at healthcare visits; number of serum electrolyte tests [any number of the following tests were included: Na, K, Cl, HCO3- and if a patient had NA, K and CI done on the same day, this was counted as one electrolyte test], number of serum HbA1c measurements, number of serum lipid measurements (any number of the following tests were included: LDL-c, HDL-c, non-HDL-c, triglycerides, cholesterol), number of serum creatinine (Cr) measurements,

if the patient self-measures their blood pressure either at home or at a community pharmacy (binary), and the number of new hypertension medicines each patient was prescribed and stopped taking. This information was found in the charts as expected.

Data Analysis

For clinical manoeuvres that are recommended to be performed multiple times during one year (e.g. blood pressure measurements) and for encounters with healthcare professionals we report the rate ratios with 95% confidence intervals that were estimated using a negative binomial regression model. We report unadjusted rate ratios and rate ratios adjusted for age, sex and clinic location (urban versus rural). We compared the proportion of patients in each arm receiving clinical manoeuvres that are recommended to be done only once during a one-year period (e.g. annual eye examination for people with diabetes) and report the odds ratio with 95% confidence intervals that was estimated using a logistic regression model. We report unadjusted odds ratios and odds ratios adjusted for age, sex and location (urban versus rural). No p-value threshold was set for these post-hoc and hypothesis generating analyses.

We also compared the net change in medications for hypertension and diabetic patients in the intervention and control arms. As part of the intervention, some patients had to switch medicines within a class. We thus used net changes as a measure that would treat both groups similarly and captured whether or not management had "intensified" by adding more agents.

Patient and public involvement

Patients or the public were not involved in the design, conduct, or reporting, or dissemination plans of our research.

RESULTS

Baseline characteristics

Of the 786 patients enrolled in the CLEAN Meds trial, 163 patients were prescribed one or more medicines for diabetes and were included in the diabetes group [including 114 who were also prescribed one or more anti-hypertensive agents], and 105 patients were nondiabetic and prescribed one or more anti-hypertensive agents and included in the hypertension group. We thus included 268 participants in this study. Of the 163 patients with diabetes, 83 patients were in the intervention group receiving free distribution of medicines, while the remaining 80 patients were in the control group receiving standard access to medicines. Of the 105 patients with hypertension, 56 patients were in the intervention group receiving free distribution of medicines, and 49 patients were in the control group receiving standard access to medicines. Study participant inclusion is illustrated in Figure 1.

Figure 1. Flowchart illustrating study participant inclusion

For this posthoc analysis, the groups are balanced with the exception of hypertension in urban and rural groups. The characteristics of participants in the diabetes and hypertension groups are summarized in Table 1.

Table 1. Baseline participant characteristics.

	Diabetes [n = 163]		**Hypertension [n = 105]**	
	Free distribution Number [%] [n = 83]	**Usual access Number [%] [n = 80]**	**Free distribution Number [%] [n = 56]**	**Usual access Number [%] [n =49]**
Women	35 [42.2]	35 [43.8]	22 [39.3]	17 [34.7]
Age [mean, SD]	59 ± 10	58 ± 11.2	60 ± 8.2	61 ± 9.3
Age 65 years or older	25 [30.1]	19 [23.8]	17 [30.4]	16 [32.7]
Ethnicity				
White	42 [50.6]	53 [66.3]	46 [82.1]	34 [69.4]
Black	9 [10.8]	10 [12.5]	2 [3.6]	4 [8.1]
Southeast or East Asian [incl Korean, Japanese, Filipino, Chinese]	6 [7.2]	2 [2.5]	4 [7.1]	2 [4.1]
South Asian	14 [16.9]	9 [11.3]	1 [1.8]	3 [6.1]
Latin American	1 [1.2]	3 [3.8]	0 [0.0]	2 [4.1]

West Asian [including Arab]	2 [2.4]	1 [1.3]	0 [0.0]	0 [0.0]
Mixed or other	9 [10.8]	2 [2.5]	2 [3.6]	4 [8.2]
Declined to provide	0 [0.0]	0 [0.0]	4 [7.1]	0 [0.0]
Main Income source				
Wages and salaries [including self-employed]	44 [53.0]	38 [47.5]	30 [53.6]	28 [57.1]
Pension	22 [26.5]	19 [23.8]	14 [25.0]	9 [18.4]
Social support [e.g. welfare or disability]	11 [13.3]	13 [16.3]	4 [7.1]	8 [16.3]
Unemployment insurance	4 [4.8]	3 [3.8]	4 [7.1]	2 [4.1]
Other	0 [0.0]	1 [1.3]	0 [0.0]	0 [0.0]
Declined to provide	2 [2.4]	6 [7.5]	4 [7.1]	2 [4.1]
Household income*				
$30 000 CAD or less	46 [55.4]	41 [51.3]	23 [41.1]	19 [38.8]
$30 000 to 70 000	24 [28.9]	22 [27.5]	12 [21.4]	12 [24.5]
$70 000 or greater	3 [3.6]	4 [5.0]	4 [7.1]	0 [0.0]
Declined to provide	10 [12.0]	13 [16.3]	17 [30.4]	18 [36.7]
Number of medicines prescribed at baseline [mean, SD]	5 ± 2.8	5 ± 3.1	4 ± 2.0	4 ± 2.6
Urban site	50 [60.2]	48 [60.0]	22 [39.3]	27 [55.1]
Rural site	33 [39.8]	32 [40.0]	34 [60.7]	22 [44.9]

Impact of free distribution of medicines in subgroup of people with diabetes

For patients with diabetes, there were small increases in rates of serum creatinine measurement (aOR 1.33; 95 % CI 0.61-2.91; p = 0.48) but not hemoglobin A1c measurements (aRR 1.09; 95 % CI; 0.88-1.34; p = 0.44) for patients receiving free distribution compared to those with usual medicine access. There was a small increase self-monitoring of blood glucose (aRR 1.30; 95% CI 0.66 – 2.57; p=0.45) (see Table 2). There were no differences in appointments with primary care providers or consultants, but there was a trend toward fewer missed appointments with primary care providers (aRR 0.80; 95 % CI 0.48-1.33; p = 0.39) (see Table 2). There was no difference between the free distribution and usual access groups with respect to net change in medicine prescriptions. Overall, the net change in the number of medicines prescribed to participants receiving free distribution was 14 new starts (a total of 19 new medicines started and 5 medicines stopped; average of 0.17 new medicines per person) and the net change

for those with usual access was 14 new starts (a total of 21 new medicines started and 7 medicines stopped; average of 0.18 new medicines per person).

Table 2. Diabetes process of care indicators.

	Free medicine distribution	Usual medicine access	Unadjusted difference	Adjusted difference
Hemoglobin A1c measurements	2 [2] [187]	2 [2] [160]	1.13 [0.91-1.39] p = 0.27	1.09 [0.88-1.34] p = 0.44
BP measurements	3 [7] [278]	3 [7] [274]	0.98 [0.78-1.23] p = 0.85	0.96 [0.77-1.19] p = 0.71
LDL-c measurements	1[1] [65]	1 [1] [61]	1.03 [0.72-1.46] p = 0.88	0.99 [0.70-1.41] p = 0.96
Urine ACR measured	54 % [45/83]	58 % [46/80]	0.88 [0.47-1.63] p =0.67	0.88 [0.47-1.67] p = 0.70
Serum creatinine measured	82 % [68/83]	76 % [61/80]	1.41 [0.66- 3.02] p =0.37	1.33 [0.61-2.91] p = 0.48
Foot examination performed	63% [52/83]	61% [49/80]	1.06 [0.56-2.00] p = 0.85	0.94 [0.49-1.84] p = 0.87
Eye examination performed	42 % [35/83]	43 % [34/80]	0.99 [0.53-1.84] p = 0.97	1.03 [0.53-2.01] p = 0.93
Influenza vaccine administered	29 % [24/83]	28 % [22/80]	1.07 [0.54-2.12] p = 0.84	1.08 [0.52-2.22] p = 0.84
Self-monitoring of blood glucose	54 % [45/83]	48 % [38/80]	1.31 [0.71-2.42] p = 0.39	1.30 [0.66-2.57] p = 0.45
Primary care encounters related to diabetes	3 [6] [258]	3 [5] [243]	1.02 [0.81-1.30] p = 0.85	1.02 [0.81-1.28] p = 0.90
Consultant encounters related to diabetes	1 [1] [49]	1 [1] [51]	0.93 [0.53-1.62] p = 0.79	1.01 [0.59-1.75] p = 0.96
Missed primary care appointments	1 [1] [43]	1 [1] [49]	0.85 [0.50- 1.44] p = 0.54	0.80 [0.48-1.33] p = 0.39
Total number of encounters and manoeuvres [assign 0 or 1 for	13 [42] [1106]	13 [38] [1039]	1.03 [0.88-1.19] p = 0.74	1.01 [0.88 to 1.17] p = 0.85

binary indicators; exclude missed appointments]				

Count indicators are reported as the mean number of measurements or encounters with the variance and the sum of all measurements or encounters. Binary indicators are reported as a proportion. Differences are adjusted for age, sex, and site and reported as rate ratio or odds ratio with the 95% confidence interval and p value.

Impact of free distribution of medicines in subgroup of people with hypertension

Among hypertension patients, free distribution was associated with a lower rate of serum creatinine [aRR 0.61; 95 % CI 0.38 -0.97; p =0.04] and electrolyte measuring (aRR 0.59; 95 % CI 0.36-0.98; p = 0.04), and fewer missed appointments (aRR 0.41; 95 % CI 0.18-0.90; p = 0.03) (see Table 3). There were trends towards fewer encounters with primary care providers (aRR 0.90; 0.71-1.10; p = 0.25) and consultants (aRR 0.59; 95 % CI 0.07-4.62; p = 0.61) but similar self-monitoring of blood pressure (aOR 1.10; 95 % CI 0.38-3.17; p = 0.86) (see Table 3). There was no difference in blood pressuring measuring in clinic. There were slightly more new medicine starts in participants receiving free distribution. Overall, the net change in the number of medicines prescribed to intervention participants was 15 new starts (a total of 20 new medicines started and 5 medicines stopped; average: 0.27 new medicines per person) and the net change for control participants was 0 (a total of 9 new medicines started and 9 medicines stopped).

Table 3. Hypertension process of care indicators.

	Free medicine distribution	Usual medicine access	Unadjusted difference	Adjusted difference
BP measurements	3 [4] [173]	3 [5] [160]	0.95 [0.74-1.22] p = 0.67	0.99 [0.77-1.27] p = 0.92
Hemoglobin A1c measurements	1 [1] [37]	1 [1] [42]	0.77 [0.49- 1.22] p = 0.27	0.83 [0.53-1.30] p = 0.41
Lipid measurements	1 [1] [36]	1 [1] [37]	0.85 [0.54- 1.35] p =0.49	0.91 [0.57-1.46] p = 0.70

Serum creatinine measurements	1 [4] [78]	2 [13] [110]	0.62 [0.39- 1.00] p = 0.05	0.61 [0.38 -0.97] p =0.04
Serum electrolyte measurements	1 [3] [66]	2 [11] [103]	0.56 [0.34-0.93] p = 0.02	0.59 [0.36-0.98] p = 0.04
Primary care encounters	5 [9] [287]	6 [14] [302]	0.83 [0.66-1.05] p = 0.11	0.9 [0.71-1.10] p = 0.25
Consultant encounters related to hypertension	0 [0] [5]	0 [0] [5]	0.88 [0.13-6.10] p = 0.89	0.59 [0.07-4.62] p = 0.61
Missed primary care appointments	0 [0] [14]	0 [4] [44]	0.28 [0.12- 0.64] p = 0.00	0.41 [0.18-0.90] p = 0.03
Self-monitoring of blood pressure	21 % [12/56]	18 % [9/49]	1.21 [0.46-3.18] p = 0.70	1.10 [0.38-3.17] p = 0.86
Total number of encounters and manoeuvres [assign 0 or 1 for binary indicators; exclude missed appointments]	12 [43] [694]	16 [97] [768]	0.79 [0.63-1.00] p = 0.04	0.83 [0.67-1.04] p = 0.10

Count indicators are reported as the mean number of measurements or encounters with the variance and the sum of all measurements or encounters. Binary indicators are reported as a proportion. Differences are adjusted for age, sex, and site and reported as odds ratio or rate ratio with the 95% confidence interval and p value.

DISCUSSION

In this post-hoc analysis of randomized controlled trial findings, free distribution of medicines to people with diabetes or hypertension was not associated with more visits to primary care providers or consultants and, in fact, patients with hypertension had less laboratory monitoring and slightly fewer visits. Free distribution may slightly increase self-monitoring and reduce missed appointments.

The modest reductions in laboratory testing of serum creatinine and electrolytes for patients with hypertension may reflect appropriate clinical judgement against repeat testing. The Canadian guidelines

recommend that the frequency of laboratory testing should be guided by clinical judgement and no specific intervals are mentioned in the guidelines. Clinicians may have been less likely to order laboratory testing in patients receiving free distribution because they had slightly better control of their blood pressure, possibly due to the greater number of medicines prescribed. These tests may also have been ordered less frequently because patients had fewer visits, potentially because they were self-monitoring. Systematic reviews have reported improved glycemic control in diabetic patients performing self-monitoring of blood glucose, and reduced blood pressure in patients with hypertension self-measuring their blood pressure.[15,16] Thus, the observed trend towards more self-monitoring, if real, could reflect improved patient motivation, better disease control, or different guidance from clinicians. A 2018 randomized controlled trial found that using self-monitored blood pressure readings to titrate anti-hypertensive treatments led to a significant reduction in blood pressure compared to the use of clinic readings to guide care.[17] In this trial, patients with hypertension had a lower systolic blood pressure after one year . The improvements in disease control and usefulness of self-measured blood pressure readings may have resulted in clinicians asking patients to monitor their blood pressure at home rather than attend clinic; this would explain both the increase in self-monitoring and the reduction in clinic visits. A 1985 controlled trial of the effects of medical insurance on health spending and health status reported lower blood pressure with free care, though the cause of the difference was additional contact with physicians under free care. [18]

The reduction in missed appointments observed here may be explained by an improved clinician-patient relationship and better perceived disease control. The reduction in missed appointments did not relate to needing to attend appointments in order to get their free medications, as the study pharmacist had access to their electronic medical record, could communicate with primary care providers, and medications were mailed to participants. A 2004 study of patient perceptions found that emotional barriers [including the fear of bad news] and perceived disrespect by the healthcare system caused patients to miss primary care appointments.[19] Additionally, a 2014 cross-sectional survey reported that patients with hypertension

with no medication coverage and high medication costs were more likely to miss appointments.[20] Patients may not take their medicines due to cost and may miss appointments due to feelings of embarrassment or guilt over this; this may be obviated by free distribution of medicines.

Our study found that there was only a small non-significant increase in hemoglobin A1c monitoring and serum creatinine monitoring in patients with diabetes. Our findings suggest that financial barriers to medication access may not deter patients with diabetes from engaging in necessary health visits and screening related to the management of their condition. In contrast, a study of American patients with diabetes found that lower cost-related nonadherence was associated with improved compliance to annual diabetes recommendations.[5] Financial incentives to clinicians, audit and feedback interventions, and reminders to clinicians can achieve modest reductions in hemoglobin A1c, and our study found a small increase in the frequency of HbA1c monitoring with free medicine distribution.[6]

The results of this study post-hoc analysis of trial findings suggest that improving access to chronic disease medicines will not substantially increase costs associated with outpatient visits. To the contrary, in this study free distribution appeared to increase self-monitoring, reduce visits for hypertension and reduce the total number of healthcare encounters and manoeuvres performed in a year, without changing the likelihood of visits for diabetes. Increasing access to medicines may encourage self-monitoring practices, reduce in-person visits, and decrease laboratory investigations performed. Free distribution of medicines may not only improve blood pressure control but could also reduce the per-person costs associated with the management of hypertension.

Strengths of this study include the fact that the results are based on a randomized controlled trial. Participants differed with respect to income level, ethnicity and location (urban versus rural). Despite the fact that this was a post-hoc analysis and randomization was not stratified based on these characteristics, we found that the groups were largely balanced; except for urban status. There are also some limitations in this analysis. Associations identified during post-hoc analyses could be spurious and thus the findings

should be viewed as hypothesis-generating.[21] The study population is a subset of the CLEAN Meds trial, and only included those with diabetes or hypertension based on whether they were prescribed at least one diabetic or anti-hypertensive agent at the start of the trial; this reduced sample size is a limitation. The trial was not designed to have sufficient power to detect differences in some of the outcomes examined in this study so the failure to identify associations should be interpreted with caution. We separated participants with diabetes from those with hypertension while we could have analysed some shared outcomes (e.g. blood pressure measurement) using a single group with a larger sample size. Since the trial was unblinded, patients and clinicians could have been motivated by allocation to free access to improve the process of care. The trial was conducted with primary care patients in a high-income country who reported cost-related non-adherence and the findings may not apply in other settings. The study was based on a review of primary care charts that do not reflect every actual encounter (e.g. visits to other providers).

CONCLUSION

This post-hoc analysis of randomized controlled trial results found that free distribution of medicines may improve self-monitoring behaviours and reduce missed primary care appointments for patients with diabetes or hypertension. Free distribution may also reduce primary care and consultant appointments and laboratory testing in patients with hypertension. Additionally, free distribution of medicines improves disease control and improves patients' self-reported care. [22] Overall, these findings suggest that improving medicine accessibility for patients with diabetes and hypertension not only improves surrogate health outcomes but also improves the patient experience and may also reduce healthcare costs by encouraging self-monitoring practices. The hypotheses generated by this post-hoc analysis of randomized controlled trial findings could be tested in future studies.

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COMPETING INTERESTS STATEMENT

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AUTHOR CONTRIBUTIONS

OC contributed to the data curation, formal analysis, investigation, methodology, visualization, writing the original draft and reviewing and editing. HW contributed to the data curation, formal analysis, investigation, writing the original draft and reviewing and editing. MA contributed to the data curation, formal analysis, and reviewing and editing. BM contributed to the methodology, validation, investigation, resources and reviewing and editing. BS contributed to the methodology, validation, investigation, resources and reviewing and editing. RW contributed to methodology, formal analysis, investigation, and reviewing and editing. NP contributed to the conceptualization, methodology, validation, formal analysis, investigation, resources, writing the original draft, reviewing and editing.

DATA AVAILABILITY

Deidentified participant data is available upon reasonable request from the corresponding author.

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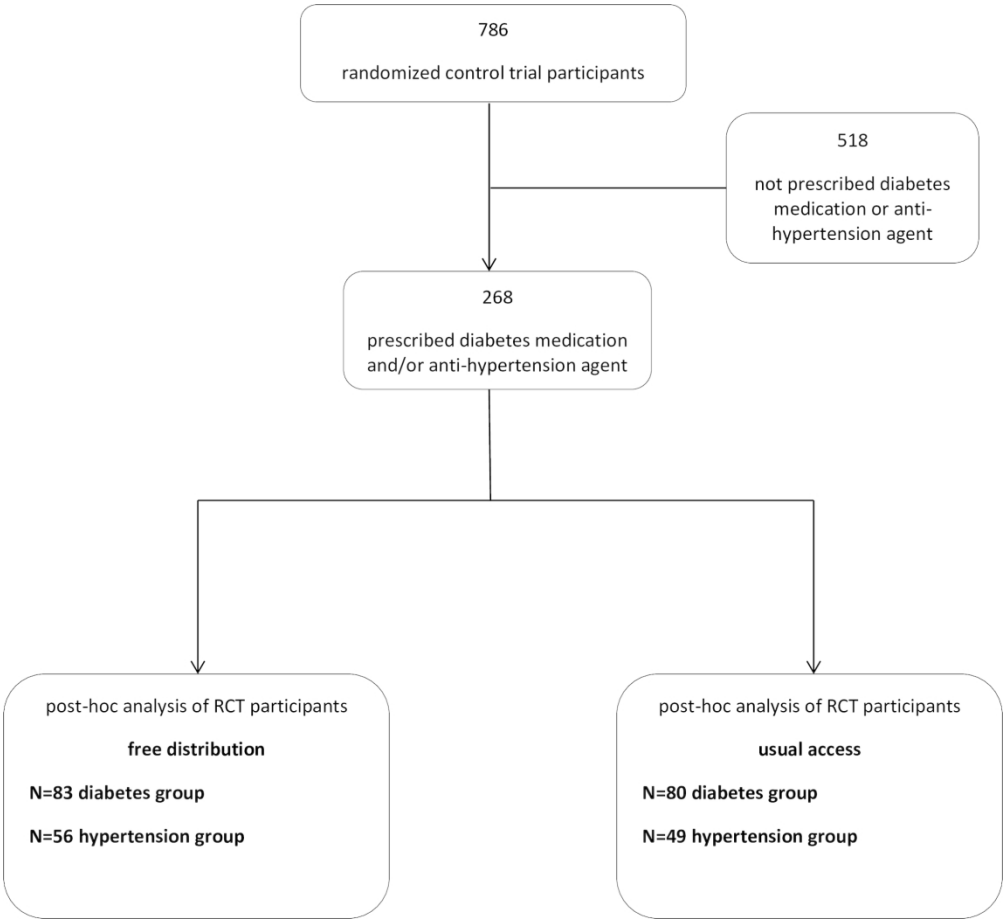

Figure 1. Flowchart illustrating study participant inclusion

190x173mm (300 x 300 DPI)