



RESEARCH ARTICLE

Assessment of a clinical pharmaceutical service for hypertensive and/or diabetic patients in a primary healthcare center

Paulo Yuri Milen Firmino^{1,2*} , Juliana de Oliveira Carlos², Jonathas de Oliveira Linhares²,
Nirla Rodrigues Romero² , Marta Maria de França Fonteles^{1,2} 

¹Postgraduate Program of Pharmaceutical Sciences, Federal University of Ceará, Fortaleza, CE, Brasil

²Pharmaceutical Care Study Center (CEATENF), Pharmacy Department, Federal University of Ceará, Fortaleza, CE, Brasil

*Corresponding author: yurifirmino@yahoo.com.br

Abstract

Objectives: The present study aimed to assess the short- and long-term outcomes of a clinical service provided by a pharmacist structured in a primary healthcare center (PHC) in Fortaleza, Ceará, Brazil.

Methods: A longitudinal-type study was conducted. Data were collected from pharmacotherapy follow-up (PTF) records from the Pharmaceutical Care Unit of the PHC Dr. Anastácio Magalhães. The PTF was provided to patients diagnosed with hypertension and/or diabetes mellitus. Two groups were formed: records of patients who intended to undergo six months or more of PTF (PTF group) and those who opted not to go through with it after the first session (control). In addition, new blood pressure and glucose measurements were obtained after invitation by phone call at least six months after the completion of the PTF to assess maintenance of the benefits gained. The control patients were invited for this new data collection as well for comparison purposes. Research Ethics Committee approval protocol n°. 329.717.

Results: A total of 224 patients were considered, 109 in the complete PTF group and 115 in the control group, where the following main results were obtained: systolic pressure (mean \pm SD) went from 139.43 \pm 20.6 to 128.31 \pm 16.03 mmHg; diastolic pressure, from 82.45 \pm 11.44 to 77.68 \pm 9.21 mmHg; blood glucose, from 151.78 \pm 75.8 to 121.39 \pm 47.56 mg/dL; and cardiovascular risk, from 21.59 \pm 9.42 to 18.95 \pm 9.06%. In comparison, the control group did not show significant changes on the above parameters. In the post-PTF analysis, the benefits gained tended to be maintained even at least six months after its conclusion.

Conclusions: Thus, the findings of the present study suggest that the provision of the clinical pharmaceutical service assessed at the primary healthcare level offers benefits to patients who attended it for at least six months. Furthermore, the data also suggest that these benefits are maintained in the long term.

Keywords: Pharmaceutical Care. Hypertension. Diabetes Mellitus. Primary Healthcare.

How to cite

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INTRODUCTION

The role of the pharmacist as a healthcare provider for the general public, and specifically for some types of target patients, has been the subject of research around the world. For example, a literature review¹ presented a series of studies involving specific pharmaceutical care for uncontrolled hypertensive patients who reported clinical benefits. In addition, there have been studies that show benefits also in patients with dyslipidemias² and diabetes mellitus³, including those that have demonstrated a reduction in cardiovascular risk in the population served^{4,6}.

Despite the benefits demonstrated over the years by studies involving pharmacotherapy follow-up (PTF), little has yet been evaluated regarding the long-term benefit of a clinical pharmaceutical service. A systematic review⁷ has pointed out this fact, highlighting the need for investigations that explore the persistence of clinical outcomes obtained by educational interventions conducted by pharmacists. A study⁸ evaluated the long-term effects of PTF for diabetics, identifying that some beneficial clinical and humanistic outcomes persisted after 12 months of follow-up while others did not. Thus, there is a need for a review of the pharmaceutical intervention in question and/or the existence of a regular service providing pharmaceutical care, which includes aspects of sustainability.

In this context, the Federal Council of Pharmacy in Brazil has been promoting training in the field of clinical pharmacy, legally establishing the clinical attributions of the pharmacist, approving recognized pharmaceutical concepts and services, and setting up a notable strengthening of the clinical profile of this professional^{9,10}.

However, it should be pointed out that there is no national model of clinical pharmaceutical service with pre-established assessment indicators for patients with chronic diseases in the setting of primary healthcare because of the variable needs and particularities of each region in Brazil. The use of indicators is strategic for monitoring and assessing the quality of health services in general. Thus, they can be considered an important tool for decision-making regarding pharmaceutical services¹¹.

However, there is a need for description and assessment of successful experiences in real practice settings, through process, clinical and humanistic outcomes so these experiences can serve as the basis for future indicators and as examples to be replicated and adapted in different healthcare settings. This process would be extremely important for the first step towards the effective institutionalization of clinical pharmaceutical services in the healthcare network.

In this context, the aim of the present study was, through analyses of short- and long-term clinical outcome parameters, to assess the effectiveness of a clinical pharmaceutical service model, previously established successfully in a primary healthcare center (PHC) in Northeast Brazil.

MATERIAL AND METHODS

General description of study

We conducted a longitudinal type study focused on the assessment of a service, particularly a clinical pharmaceutical service for hypertensive and/or diabetic patients, established in the pharmaceutical care unit (PCU) located in the PHC Dr. Anastácio Magalhães of Unified Health System Regional III, in Fortaleza, Ceará, Brazil. The study period was from July 2013 to May 2016 and clinical outcome data were used for this assessment.

Study location

The PCU assessed is a unit that provides pharmaceutical services in the public health system which was developed, as a partnership between the PHC direction board and the Federal University of Ceará, at the end of 2008 by the Center for Pharmaceutical Care Studies (CEATENF) and aimed to include, in addition to the healthcare professionals already involved, the pharmacist in the care process of the patient/user seen at the PHC. The PCU operates each weekday morning and afternoon in a specific room under a team of pharmacists and pharmacy students previously trained by CEATENF.

The primary target patients considered for the services offered by the PCU were adults previously diagnosed with systemic arterial hypertension and/or diabetes mellitus, where in the first visit or subsequent visits, the following was found: a) through the *physician* at the PHC, the existence of uncontrolled levels of blood pressure and/or glucose, under treatment or not, and/or existence of cardiovascular risk factors; b) through the *nurse* responsible for the registry of hypertensive and diabetic patients in the institution, the existence of a patient/user with control difficulty and with problems adhering to treatment; c) through the *pharmacist* in charge of the PHC dispensing pharmacy, at the time of dispensation, the need for education on the proposed pharmacotherapy and/or use of two or more medications for hypertension and/or diabetes; and d) through the *PCU team*, the presence of problems with adherence, difficulty in understanding the prescribed pharmacotherapy or achieving therapeutic goals.

The identified target patients were asked to participate in the service and were taken to the office designated for the PTF service.

Description of the Pharmaceutical Service Provided by the PCU

The pharmaceutical service provided by the PCU in question was PTF. The group of patients under PTF, in addition to the healthcare usually provided at the PHC, was targeted for health education, detection, resolution, and prevention of drug therapy problems, the incentive to adherence to the prescribed treatment, and lifestyle modification according to their health problem. PTF was based on a nine-month individualized care plan for each patient included in the service, with flexible interview intervals of approximately two months. In the study, the minimum six-month time to set up a complete PTF was stipulated on the basis of previous experience reported by the PCU team regarding the average time necessary to achieve most of the therapeutic goals with each patient.

Although the primary target patients of the PCU were those diagnosed with hypertension and/or diabetes, the PTF provided considered all health problems presented and medications used by the patients, as understood by the theoretical framework referred to by the national Federal Pharmacy Council¹⁰.

During the provision of the service by the PCU, not all patients seen followed a care plan of at least six months duration (complete PTF) because of various reasons. Those reasons were related to personal preferences of those patients, such as: lack of interest in the PTF, distance from the PHC, and lack of time to meet the PTF appointments. For purposes of comparison, this group of patients was considered the "control" in the study. Patients in the "control group" received pharmaceutical advice only during the first meeting with the PCU team, where information was collected. These patients maintained contact with the PCU team nevertheless, and subsequently, more data were collected through a new invitation by the PCU team or by choice of the patient themselves for a new meeting to assess the therapeutic goals achieved even without the PTF.

Data collection

Data collection was performed by the retrospective researcher during the study period and included records archived in the PCU regarding the PTF of all patients seen from the beginning of the activities of the PCU until the end of May 2016.

The PTF assessment was done through the data collected from the records of the patient visits, which included, besides general socio-demographic data, laboratory tests and blood pressure measurements carried out by the PCU team, identification of drug therapy problems, and calculation of cardiovascular risk according to the Framingham global risk score recommended by the Brazilian Society of Cardiology^{12,13}.

Retrospective data collection was based on the review and analysis of the monitoring and outcome records used by the PCU during PTF. During the process, therefore, relevant data were extracted for the analysis and determination of clinical outcomes.

The researchers, therefore, collected data from records of the beginning of the PTF and the end of it from each patient as registered by the PCU team. The data from the control group

were collected from the records of the first meeting and the last one. Furthermore, the researchers carried out an extra data collection meeting with all patients at least six months after the end of the PTF period or at the last meeting with each one. Thus, the results analyzed included those at the beginning and the end of the care process and post-PTF.

The phase of collection of the post-PTF clinical outcomes was performed through new single interviews with each patient that was assisted in any form by the PCU team (complete or incomplete PTF) or pre-scheduled telephone contact with them. This interview was carried out at least six months after the end of the PTF or at the last meeting with the PCU team. At the time of the interview, new clinical parameters (i.e., blood pressure and glycemia) were collected. The laboratory tests were obtained by the last set of tests performed on the patients, and they were requested to be done at the time of the appointment to set up the interview. Tests that were performed up to two months before the day of the post-PTF interview were accepted.

The purpose of the post-PTF interview was to assess the maintenance of the benefits gained through the complete PTF and to compare it to those patients who did not go through the PTF. This purpose was explained to the patient during the telephone appointment.

For the data collection process, the following variables were considered of interest for this study:

- o Cardiovascular risk rate (%)
- o Systolic and diastolic blood pressure (mmHg) (numerical)
- o Blood glucose (mg/dL) (numerical)
- o Glycated hemoglobin(%) (numerical)

All the abovementioned variables were measured or registered by the PCU team during the PTF. Therefore, they were present in the records used by the researchers as the source of data.

Additionally, the following rates of clinical outcomes were considered in the present study to assess the effectiveness of the service. They were calculated by the researchers after the data collection and organization in a database.

- o Rate of patients who reached the therapeutic goal for blood pressure (numerical)
- o Rate of patients who reached the therapeutic target for blood glucose (numerical)
- o Rate of patients with a decrease in the category of cardiovascular risk (numerical)

To calculate the clinical outcomes involving the therapeutic goals (e.g., the rate of patients in the systolic pressure goal, the rate of patients in the blood glucose goal, etc.), it was necessary to define the goals and classify patients categorically according to the level of the parameter associated with the goal (systolic and diastolic pressure and blood glucose, Table 1). We used general therapeutic goals recognized in Brazilian national guidelines.

Table 1. Therapeutic goal values used for systolic and diastolic blood pressure, blood glucose and lipid profile.

<i>Parameter</i>	<i>Therapeutic goal used</i>
Systolic blood pressure	<140 mmHg
Diastolic blood pressure	<90 mmHg
Capillary blood glucose	<140 mg/dL
Glycated hemoglobin	<7%
Total cholesterol	<200 mg/dL
LDL cholesterol	<100 mg/dL
HDL cholesterol	>45 mg/dL
Triglycerides	<150 mg/dL

Source: Brazilian Guidelines on Hypertension (2020)¹⁴; Brazilian Guideline on Dyslipidemia and Prevention of Atherosclerosis (2017)¹²; Guidelines of the Brazilian Society of Diabetes 2019-2020 (2019)¹⁵.

Data analysis

The total number of patients seen by the PCU was initially analyzed as a group only to allow the effect of the clinical pharmaceutical service could be evaluated, even in the case of patients who received a single pharmaceutical orientation session. This analysis was carried out by comparing the data for the variables of interest as presented at the first meeting with these patients and the last one according to the records.

To allow detailed analyses of the effectiveness of complete PTF and to increase the significance of the findings in the study involving PTF time, clinical outcomes, and other variables linked to the clinical pharmaceutical service performed, two groups were formed (complete PTF and Control). The complete PTF group comprised the patients that attended all planned visits with the PCU team. As described before, the patients considered the “control” group were those who attended just the first meeting and opted not to continue the PTF. The Control group patients were invited to return to the PCU once more for data collection for comparison purposes. These groups were compared on the basis of the data regarding the variables of interest and clinical outcomes previously described.

The comparison between the study groups was carried out in two ways: PTF end results and post-PTF results. The results at the end of PTF included data on PTF onset/entry into the PCU service and those at the end of the PTF period, the last interview in the complete PTF group, and the last equivalent data collection from the control group. The post-PTF results were composed of the data collected during the interviews with patients who were previously enrolled as described earlier, and the possible maintenance of the beneficial effects (maintenance of controlled blood pressure and glycemic parameters) of the pharmaceutical service was analyzed.

The analysis of the results was performed after data processing using IBM SPSS Statistics 22 for Windows and included the following procedures:

According to the study of variables, the data were presented in a descriptive way, represented by tables and/or graphs. Numerical variables were described as mean±SD and categorical variables in the form of proportions. McNemar tests for categorical variables and paired t-tests were used and Wilcoxon (when the normality of data distribution could not be assumed) and Friedman tests for the numerical variables when intra-group comparisons were made. For comparisons between different groups, t-tests were applied for the numerical variables (assuming normality of data distribution and equality of variance in standard deviation) considering mean values and the chi-square test for the categorical variables and comparisons between proportions. For outcomes that reflected therapeutic goals, prevalence ratios (PR) were generated.

A significance level was set at 5% for all comparisons.

Ethical aspects

This study was carried out in accordance with the regulatory directives and norms involving humans (Resolution 466/12) and was previously approved by the Research Ethics Committee of the Federal University of Ceará (protocol No 329.717/CAAE No. 05925513.2.1001.5054).

RESULTS

A total of 224 patients were registered in the PCU. Of these, 109 followed the minimum PTF time to reach the expected results (complete PTF group). The control group had 115 patients.

Afterward, 109 out of 224 patients were contacted and responded to the contact regarding a post-PTF new data collection for long-term benefit analysis, being included in the specific sample for post-PTF analysis. Of these, 46 were patients who completed PTF, and 63 were patients from the control group.

Socio-demographic data

A total of 224 patients showed a predominance of female patients (n=162, 72.3%). The group had an average age of 60.74 years. More than half (n=134; 59.8%) of the patients did not complete high school, including 11 (4.9%) who were illiterate. The majority reported not having a caregiver (n=175; 78.1%) and receiving up to two times the minimum salary (n=160; 71.4%), also referring to being able to purchase needed medications at drugstores (n=149, 66.5%).

The main disease of the patients was hypertension (n=215, 96%), followed by type II diabetes mellitus (n=109, 48.7%) and dyslipidemia (n=103, 46%).

Table 2 presents the general population data of the stratified study according to the defined groups: the PTF group and the control group. The differences observed between the study groups were not statistically significant, except for the variables "dyslipidemia" and "presence of the caregiver."

Despite the statistically significant difference observed between the groups in relation to the frequency of dyslipidemia and caregiver, the subsequent analyses demonstrated that the two variables did not imply inter-group differences in any of the clinical outcomes addressed.

The difference in the presence of individuals with hypertension and associated diabetes between the analyzed groups showed borderline statistical significance (close to $p < 0.05$). However, as in the case of the above variables, it was not a factor associated with the inter-group differences observed in the results to be reported in this section.

Table 2. General characteristics of study groups (total n=224) (Fortaleza, Ceará/November 2008 – May 2016)

Variable	Control (n=115) n (%)	Complete PTF (n=109) n (%)	p-value
Females	82 (71.3)	80 (73.4)	0.73
Males	33 (28.7)	29 (26.6)	0.73
Mean age (years)	60.22	61.29	0.44
Hypertension	67 (58.3)	49 (45)	0.06
Diabetes mellitus	4 (3.5)	6 (5.5)	0.46
Hypertension + diabetes	45 (39.1)	54 (49.5)	0.12
Dyslipidemia¹	44 (38.3)	59 (54.1)	0.02
No. of alcohol drinkers	27 (23.5)	17 (15.6)	0.23
No. of smokers	9 (7.8)	4 (3.7)	0.55
Follows diet*	64 (55.7)	69 (63.3)	0.24
Health complication# (n=215)	31 (28.7)	39 (36.4)	0.23
Regular physical activity	48 (41.7)	50 (45.9)	0.20
Presence of caretaker¹	16 (14)	32 (29.4)	0.01
Illiterate	4 (3.48)	7 (6.42)	0.15
Elementary school not completed	41 (35.65)	35 (32.11)	0.15
Elementary school completed	14 (12.17)	12 (11.01)	0.15
Middle school not completed	6 (5.22)	15 (13.76)	0.15
Middle school completed	42 (36.52)	32 (29.36)	0.15
High school completed	8 (6.96)	8 (7.34)	0.15
Income \leq 2 m.s.	79 (68.7)	81 (74.3)	0.28
Ability to buy medications (n=210)	75 (70.8)	74 (71.2)	0.95

¹ $p < 0.05$, according to chi-square test; *diet from dietician or dietary standard according to the underlying disease advised by another health professional (self-reported by patient); #infarct, cerebral vascular accident, retinopathy, nephropathy, diabetic foot or other condition related to hypertension, diabetes and dyslipidemia (n=215).

Results related to clinical outcomes

Blood pressure

Regarding the systolic pressure levels of the population of patients on PTF from the PCU, the mean was 139.17 ± 20.6 mmHg at the time of entry into the service, while at the end, it fell to 130.77 ± 16.03 mmHg, a decrease of 8.4 mmHg ($t=5.18, df=143, p=0.00$).

After stratification of the patients followed according to PTF closure status (complete or control), a different behavior was observed in the systolic blood pressure variation between the groups. The mean control group varied from 138.42 ± 25.1 to 137.63 ± 22.47 mmHg in the last contact with the PCU team ($t=0.25, df=37, p=0.80$). On the other hand, the mean of the complete PTF group was from 139.43 ± 18.86 to 128.31 ± 12.2 mmHg at the end of PTF ($t=6.1, df=105; p=0.00$) (Table 3). When comparing the final inter-group means, the statistical test showed that their difference was statistically significant ($t=2.43, df=45.06, p=0.02$).

Diastolic pressure levels also showed a reduction in mean value. At the beginning of PTF, the mean was 81.59 ± 11.44 mmHg, and after the pharmaceutical service, it decreased to 79.05 ± 9.21 mmHg. The difference between the means, in this case, was 2.54 mmHg, which was statistically significant ($t=2.48, df=143, p=0.01$).

When stratifying according to complete PTF or control, there was a difference in the variation of mean diastolic levels. The control group had a mean increase, going from 79.21 ± 12.6 to 82.89 ± 11.13 mmHg ($t=-1.86, df=37, p=0.07$). The complete PTF group, on the other hand, had a mean decrease of 4.77 mmHg (from 82.45 ± 10.93 to 77.68 ± 8.03 mmHg), which was found to be a statistically significant difference ($t=4.24, df=105, p=0.00$) (Table 3). The inter-group difference was also considered statistically significant when the means related to the patient's exit time from the PCU service were compared ($t=2.65, df=51.49, p=0.01$).

Blood glucose and glycated hemoglobin

Regarding blood glucose, a mean difference of 25.16 mg/dL was observed, going from a mean value of 145.72 ± 75.8 to 120.56 ± 47.56 mg/dL after the pharmaceutical care process. This observed drop in mean blood glucose showed statistical significance according to a paired t-test ($t=3.98, df=98, p=0.00$).

The initial mean glycated hemoglobin was around $8.06\% \pm 1.75$ at the beginning of clinical and care actions of the PCU to $7.22\% \pm 1.42$ after their application. However, this observed decrease was not considered statistically significant ($t=2.05, df=11, p=0.09$).

In the stratified analysis, it was observed that the initial mean blood glucose of the control group was 118.5 ± 57.99 mg/dL while that of the complete PTF group was higher (151.78 ± 78.22 mg/dL). Both groups had a mean decrease after start of PTF, with a fall to 116.83 ± 46.27 mg/dL ($t=0.126, df=17, p=0.90$) in the control group and a statistically significant reduction ($t=4.32, df=80, p=0.00$) in patients who completed PTF (Table 3).

The final mean blood glucose did not differ significantly between the study groups ($t=-0.366, df=97; p=0.71$); however, it should be noted that the initial mean of the group that had PTF up to the end with the PCU team was higher than that in patients who did not complete the care plan.

It was not possible to perform the stratified analysis for glycated hemoglobin, since the number of patients with glycated hemoglobin tests was too low to make the comparison ($n=12$), and practically all patients who had that test were patients in the complete PTF group.

Lipid profile

The initial mean total cholesterol in the study group was 201.26 ± 74.18 mg/dL, which decreased to 191.95 ± 61.7 mg/dL at the last sampling by the PCU team. The LDL fraction had an initial mean of 115.44 ± 43.01 mg/dL and the final mean was 115.1 ± 58.15 mg/dL, while the HDL fraction had means of 42.86 ± 11.47 and 43.8 ± 10.08 mg/dL, respectively. The initial mean

triglyceride level was 177.46 ± 102.71 mg/dL while the final mean level was 169.12 ± 92.97 mg/dL for the patients seen in the PCU with laboratory tests. In these cases, there was no statistically significant difference ($p > 0.05$).

Stratified analysis by study group did not reveal significant differences between groups. In both, the final mean total cholesterol was below the initial mean, but the other components of the lipid profile differed between times. The control group showed a decrease in mean LDL, while in the complete PTF group there was a slight increase. The final mean HDL of the PTF group showed an increase compared to the initial mean, while there was no change in the control. Finally, the PTF group had a reduction in mean triglycerides, with the opposite occurring in the control group. The detailed results are seen in Table 3. Similar to the analysis of the groups combined, none of the differences described above were statistically significant ($p > 0.05$).

Cardiovascular risk

The patients considered in this analysis had a mean global risk score of 16.36 ± 4.31 points upon entry into PTF and a mean of 15.62 ± 4.03 points at the PTF exit time, and the difference was statistically significant ($t = 2.32$, $df = 63$, $p = 0.03$).

Regarding the cardiovascular risk rate, a mean of $20.05 \pm 9.42\%$ was determined before the introduction of the pharmaceutical service for the patient. After this process, there was a significant decrease in the mean rate to $18.47 \pm 9.06\%$ ($t = 2.32$, $df = 63$, $p = 0.04$).

In the control group, the initial mean global risk score was 14.47 ± 3.9 points. The final mean was 15.47 ± 3.4 points. Considering the cardiovascular risk rate measured, the initial mean rate was found to be $15.04 \pm 8.78\%$ and the final $16.93 \pm 8.67\%$. The difference in global risk score ($t = -2.35$, $df = 14$, $p = 0.04$) was statistically significant, while the difference in cardiovascular risk ratio ($t = -1.93$; $p = 0.07$) was not for this group.

In the complete PTF group, in contrast, there was a decrease in the mean global risk score (16.94 ± 4.3 to 15.67 ± 4.24 points) and cardiovascular risk rate (21.59 ± 9.2 to $18.95 \pm 9.22\%$). The difference was considered statistically significant in both cases (respectively $t = 3.51$, $df = 48$, $p = 0.00$ and $t = 3.37$, $df = 48$, $p = 0.00$) (Table 3). The inter-group analysis of the final means did not show a statistically significant difference between the variables.

Table 3: Comparison of clinical outcomes (means) of groups analyzed at end of study (Fortaleza, Ceará/November 2008 – May 2016).

Variable	Control (total n=115)			Complete PTF (total n=109)		
	Start	End	p	Start	End	P
SBP (mmHg)	138.42	137.63	0.80	139.43	128.31	0.00
DBP (mmHg)	79.21	82.89	0.07	82.45	77.68	0.00
BG (mg/dL)	118.5	116.83	0.90	151.78	121.39	0.00
Hb _{A1c} (%)	-	-	-	8.06	7.22	0.09
TC (mg/dL)	196	185.6	0.43	202.87	193.9	0.4
LDL (mg/dL)	120.6	109	0.34	113.78	117.04	0.7
HDL (mg/dL)	44.6	44.33	0.9	42.33	43.63	0.42
TGL (mg/dL)	153.67	161.73	0.57	184.89	171.42	0.25
GRS (points)	14.47	15.47	0.04	16.94	15.67	0.00
CVR (%)	15.04	16.93	0.07	21.59	18.95	0.00

SBP - Systolic blood pressure; DBP - Diastolic blood pressure; BG - Blood glucose; Hb_{A1c} - Glycated hemoglobin; TC - Total cholesterol; TGL - Triglycerides; GRS - Global risk score; CVR - Cardiovascular risk level.

Clinical outcomes

The influence of PTF status (complete or control) was also considered in the analyses of these data. The systolic goal was reached in 55.3% of patients in the control group (total n=38; n=21), while 74.5% of the complete PTF group reached the goal (total n=106; n=79) (PR=2.369,

$p=0.027$). The diastolic goal in the control group was achieved by 60.5% (total $n=38$, $n=23$), while 85.8% of the complete PTF group achieved it (total $n=106$; $n=91$) ($PR=3.957$; $p=0.001$). The results for the blood glucose goal did not show a statistically significant difference between the control patients and those of the complete PTF ($PR=0.753$; $p=1.00$), with proportions of 83.3% (total $n=18$; $n=15$) and 79.9% (total $n=81$; $n=64$), respectively. The results described above are represented graphically below (Figure 1).

The inter-group differences for the lipid profile outcomes were inconclusive since there was no statistical significance. The proportion of patients in the control group ($n=15$) reaching the goal for each parameter was: total cholesterol - 73.3%, LDL - 40%, HDL - 53.3% and triglycerides - 53.3%. The proportion in the PTF group ($n=50$) was: total cholesterol - 52%, LDL - 46%, HDL-38% and triglycerides - 48% (Figure 1).

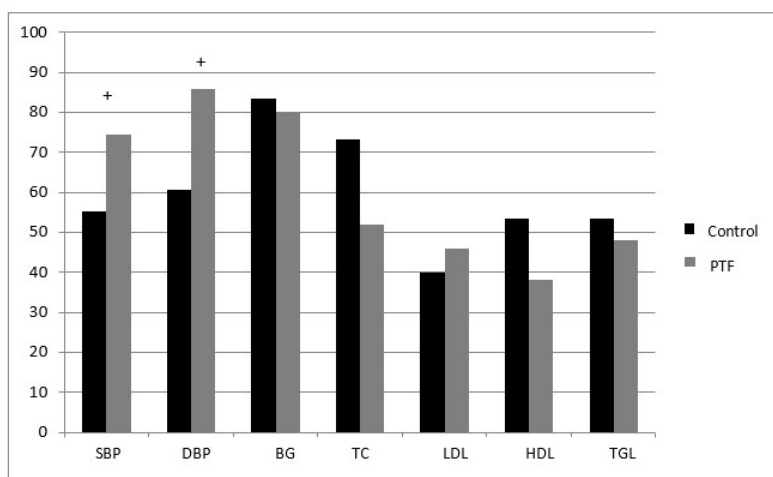


Figure 1: Difference between study groups in the proportion of patients (%) reaching the therapeutic goals chosen for clinical outcomes (Fortaleza, Ceará/November 2008 – May 2016; PTF $n=109$ and Control $n=115$). SBP–systolic blood pressure; DBP - diastolic blood pressure; BG–blood glucose; TC - total cholesterol; TGL - triglycerides. + $p<0.05$. Y-axis – percentage.

In 64 cases, it was possible to evaluate the change in cardiovascular risk in an ordinal fashion (improved or worse after PTF), although it was not possible to categorize the data according to a therapeutic goal. Thus, an improvement in the cardiovascular risk rate was observed in only 1 case (6.67%; total $n=15$), with a predominance of worsening cardiovascular risk rate ($n=8$; $n=15$; 53.33%; $p=0.039$) among the control patients. On the other hand, in the group with complete PTF, there was a decrease in the risk rate in 27 cases (55.1%; total $n=49$) and an increase in cardiovascular risk in 7 cases (14.28%; total $n=49$), and this difference was statistically significant according to the Wilcoxon test ($p=0.001$).

Long-term clinical outcomes

Table 4 shows the results obtained for numerical variables in post-PTF interviews. This table relates, together with the means obtained at the post-PTF time, the results previously obtained at the beginning of PTF and at the time of exit from PTF (closure for the complete PTF group and last meeting for the control group) for each study group. For inter-group comparison of the central tendency measures of the variables of interest related to the post-PTF interview, we found that there was no statistically significant difference in any of the cases.

Intra-group analysis showed that the diastolic blood pressure of the control group differed significantly as seen in the aforementioned table, with its mean level first increasing (during the PTF-equivalent period) and then decreasing (months after the PTF period/post-PTF). The

PTF group also showed a significant difference, namely in the main systolic level, decreasing with time and continuing to do so in the post-PTF period.

Table 4: Comparison of clinical outcomes (mean) post-PTF* of the groups analyzed at end of study (Fortaleza, Ceará/November 2008 – May 2016).

Variable	Complete PTF (total n=46)				Control (total n=63)			
	Start	End	Post	p	Start	End	Post	P
SBP ¹ (mmHg)	135.22	126.59	125.31	0.032	133.63	136.36	130.60	0.171
DBP ¹ (mmHg)	81.59	78.18	78.68	0.409	78.78	83.33	79.39	0.008
Blood glucose ² (mg/dL)	115.57	107.23	117.42	0.051	126.06	133.18	157.93	0.055

*post-PTF was defined as a moment at least six months after the end of the PTF or the last meeting (in the case of the control group). Systolic blood pressure (SBP), diastolic blood pressure (DBP), p value according to Friedman test; ¹complete PTF n=44 and control n=33; ²complete PTF n=26 and control n=16.

DISCUSSION

The group of patients seen by the PCU analyzed showed general socio-demographic characteristics usually observed in other studies on the assessment of healthcare services focused on diseases of interest in this study. The mean age of age 60, the prevalence of female patients, low level of schooling (more than half not finishing high school), and limited monthly income were also reported in studies concerning this area of the country¹⁶⁻¹⁸. The comparison of the general characteristics of the study groups after stratification shows that, except the presence of caregiver and dyslipidemia, the study groups were similar, and none of the other differences were considered statistically significant.

The greater presence of dyslipidemic patients in the complete PTF group, although not a factor related to the achievement of the main goals of the study, might have contributed to the difficulty of reaching the lipid profile goals, since there tended to be fewer patients in the lipid goal among the participants of this group. The higher cardiovascular risk ratio in the complete PTF group was also possibly due to this fact since total cholesterol and HDL levels were considered in the determination of this parameter.

The results related to the clinical parameters demonstrated the effectiveness of the clinical pharmaceutical service provided by the PCU. The non-stratified analysis showed statistically significant achievement of the primary goals outlined in the initial PTF plan for the enrolled patients, i.e., reductions in mean systolic and diastolic blood pressure, blood glucose, and cardiovascular risk ratio. It should be noted that in this case, mean blood glucose after PCU intervention was lowered to within the general therapeutic goal adopted (<140 mg/dL). These results corroborate the findings of other studies carried out in Brazil in a similar setting (primary healthcare), in which there were better results regarding the achievement of therapeutic goals by the patients and solving drug-related problems^{19,20}.

The stratified analysis allowed the comparison when the participants were divided according to the final status of the PTF (complete or control), making it possible to discern with more precision the influence of continued service by the PCU studied. This analysis showed that patients with at least 6 months of continuous and systematic care achieved more positive results than those who only received orientations at specific moments (control group). The mean blood pressures were reduced to levels that would guarantee to reach a more demanding therapeutic goal for systolic arterial hypertension (<130x80 mmHg), adopted for hypertensive patients with high cardiovascular risk according to the latest guidelines¹⁴. Considering that the global cardiovascular risk rate of patients treated can be considered indicative of high risk, this is relevant for the population in question. The control group did not show such decreases in means of clinical parameters as did the complete PTF group, and there was no statistically significant difference between the two sampling times. This, according to our interpretation, demonstrated the potential benefit of systematic and continuous PTF.

Similar results were observed in previous studies in Brazil and in Europe^{4,16,18,21,22}, but not always with a comparison group, which provides better evidence of the positive effects of the inclusion of the pharmaceutical services aimed at the patient, the family and the community in the healthcare of hypertensive and diabetic patients. In addition, an earlier study performed at the PCU studied had already shown positive PTF results compared to traditional patient care, but with a smaller 'n'⁶. The current study corroborated previous results, and the positive results argue for a continuous PTF process since the control group used in this study was composed of patients who were also seen at this PCU, but were limited to punctual pharmaceutical guidance.

One of the differentials of the present study was the analysis considering the achievement of the therapeutic goals, categorizing the patients according to their achievement at the different times of data collection (service entry and exit). Few studies in Brazil have analyzed results in this way, with a recent study presenting results portrayed in this way¹⁶, yet without a comparison group.

The effectiveness of the PCU service was also attested in this analysis, with the proportion of patients meeting the goals set for blood pressure and blood glucose levels increased significantly after pharmaceutical care measures. The complete PTF status once again proved to be differential for reaching blood pressure goals, where patients with PTF continued to have at least twice as much chance of achieving the goals compared to the other patients.

There was no association between complete PTF status and blood glucose goal achievement as expected, as it was associated with a reduction in mean blood glucose as previously demonstrated. Possibly, the fact that the complete PTF group was composed of a larger proportion of diabetic patients with associated hypertension influenced this finding. Notably, the guidelines for these diseases indicate that their association represents a complicating factor for health and treatment, which can lead to difficulty in reaching goals^{14,15}.

Different from the study conducted in Divinópolis, MG¹⁶, our results did not show a significant increase in the proportion of individuals meeting goals for dyslipidemia. However, it is important to note that the goals adopted in the above-cited work were less demanding than those adopted in our study, considering a positive result in a 30% higher LDL range. In addition, although the results regarding the lipid profile were not conclusive or indicative of the effectiveness of PCU, the reduction in the cardiovascular risk ratio was still statistically significant, as previously observed in smaller groups of patients seen in the PCU studied^{5,6} and in similar studies in other states^{4,18}. Moreover, this was a predominant observation, mainly in the complete PTF group (with more than half of this group having a final reduction in cardiovascular risk rate).

During the analysis of the long-term clinical outcomes of the study, the focus of observation was the health situation, according to the variables of interest adopted, of the patients after at least 6 months of leaving the PTF of the PCU to see if the benefits were maintained obtained after the end of the service. The PTF group did indeed have results that supported the initial hypothesis that patients could maintain the goals achieved during PTF in general since none of the parameters determined during post-PTF showed a statistically significant difference between the endpoint of PTF and after at least six months with the exception of the diastolic blood pressure levels for the control group, which could have been associated with the initially increased blood pressure levels observed in this group at the time corresponding to the "end of PTF". As the diastolic variable range is much narrower than the systolic, changes in the mean values could have a considerably greater impact on its statistics. Notwithstanding, in the study by Balisa-Rocha et al. (2014)⁸, it was similarly observed that the benefits for blood pressure control and quality of life achieved during the pharmaceutical service were maintained even 12 months after withdrawal from PTF.

The difference in the glycemetic control of diabetics was not statistically significant between the beginning and the end of PTF, as previously described; however, it is emphasized that, even after months without PCU guidance to stimulate adherence and self-care, these patients did not show worsening in glycemetic control, maintaining a mean level within the goal adopted. These data can be considered relevant since there is a concern in guaranteeing the long-term

effectiveness of interventions to prevent the reversal of results achieved caused by factors inherent to the disease and other external factors such as diet and lifestyle changes²³.

On comparing the final results, we found that the results at the post-PTF time were not statistically different between the groups, and at some points, the results pointed to an improvement in the health of patients in the control group. A more in-depth analysis²⁴ of the patients in question showed that patients who did not follow the PTF actually reached goals and had lower blood pressure means after a certain time exiting the PCU, around 36 months, possibly equaling the benefits gained with PTF. It can be suggested that traditional healthcare can provide better treatment among patients who continue to attend medical appointments and seek healthcare services offered over time, thus better meeting the needs of each patient. However, it is worth noting that the same results were achieved by PTF patients in approximately 6 months, thus a considerably shorter time.

As a final proposition, it is important to consider outcomes, whether clinical, humanistic or economical, in the analysis of the effectiveness of pharmaceutical services. Its use allows assessing if the improvement of clinical parameters (e.g., blood pressure levels and glycemia) provided by most of these services facilitates the achievement of therapeutic goals planned for the patients. The proportion of patients achieving therapeutic goals or improving a specific condition/situation, such as cardiovascular risk, could be used as shown in this study. Other outcomes that were not included in this analysis could be considered as well, such as the proportion of patients improving treatment adherence or quality of life, number of drug-related problems solved by the service, or acceptance of the pharmacist's intervention by the patient or healthcare team, among other possibilities.

Despite the findings reported in this paper, some limitations should be considered. First, it is possible that some patients might have benefitted from a different therapeutic goal based on age, as most guidelines suggest more flexible goals depending on age. As the study did not consider therapeutic goals in such an individualized manner, some results related to their achievement could have been underrated.

Another limitation to be considered is the lack of multivariate and regression analysis in the present study. Therefore, some bias related to the influence of some variables, such as socio-demographic characteristics, on the results cannot be totally disregarded. Future studies should include a more robust statistical analysis presenting effect size of all tests on their method to better explore these issues.

Additionally, the present study was carried out at a single center, and therefore, the results might be limited to its particularities and regional characteristics of its population. Thus, the possibility of a multicenter study should be considered for future research. Notwithstanding, even though the findings reflect only a single center, it is encouraging for the duplication of the service in other PHC in the same city.

Furthermore, some data could not be collected as planned because of some reasons related to the service routine. For example, the test results containing lipid and glycemic parameters could not be found on every patient's record because, according to the PCU team, the patient did not present it (lost it or did not appear for the scheduled visit) or the PHC team did not provide it to the PCU team. Therefore, some analyses were limited. Future studies in the same or similar scenario should consider this potential obstacle during the planning stages so it would not impact the results.

A final limiting factor that should be considered in the analysis of long-term results is the fact that many post-PTF data collections were telephoned because many respondents were unable to visit the unit on scheduled days. Therefore, the post-PTF results of many participants were self-reported, which might have been subject to the respondent's memory shortcomings or incomplete information given in a deliberate manner.

Further studies should be carried out to define time points where new intervention is necessary for these patients and to extend these long-term results.

In conclusion, our findings indicated that the target population for PCU clinical measures, in fact, lacks information on medications and has many problems related to the achievement

of therapeutic goals, implying the need for a service focused on optimizing and monitoring the prescribed treatments.

The clinical outcomes showed that the PTF provided by the PCU evaluated is able to improve blood pressure control in hypertensive patients and to avoid uncontrolled blood glucose in the diabetic patients followed-up, in addition to reducing cardiovascular risk in these patients. The increase in patient rates achieving the therapeutic goals outlined corroborates these results and the failure to observe the same benefits in the control group enhances the evidence about these benefits.

The results also demonstrate that the benefits gained during the PCU care period can be maintained even after months of service closure, provided the patient completes the PTF plan. This suggests that a process of re-education and promotion of patient self-care may have occurred.

Finally, the patient enrolled in the PHC who was seen by the PCU and completed the planned PTF, in general, had a greater probability of achieving and maintaining the therapeutic goals commonly adopted, which was observed especially in patients with hypertension. Therefore, an established pharmaceutical service operating according to pharmaceutical care practice can be considered strategic for improving the healthcare of users of Brazil's Unified Health System.

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REFERENCES

1. Aguiar PM, Balisa-Rocha BJ, Brito GC, da Silva WB, Machado M, Lyra DP Jr. Pharmaceutical care in hypertensive patients: A systematic literature review. *Res Social Adm Pharm.* 2012;8(5):383-96. <http://dx.doi.org/10.1016/j.sapharm.2011.10.001>
2. Eizerik DP, Manfroi WC. Eficácia da atenção farmacêutica em dislipidemia: revisão sistemática. *Rev HCPA.* 2008;28(1):37-40.
3. Collins C, Limone BL, Scholle JM, Coleman CI. Effect of pharmacist intervention on glycemic control in diabetes. *Diabetes Res Clin Pract.* 2011;92(2):145-52. <http://dx.doi.org/10.1016/j.diabres.2010.09.023>. PMID:20961643.
4. Obreli PR No, Marusic S, Lyra DP Jr, Pilger D, Cruciol-Souza JM, Gaeti WP, Cuman RKN. Effect of a 36-month Pharmaceutical Care program on coronary heart disease risk in elderly diabetics and hypertensive patients. *J Pharm Pharm Sci.* 2011;14(2):249-63. <http://dx.doi.org/10.18433/J3259Q>. PMID:21733413.
5. Firmino PYM, Martins BCC, Alves SCF, Vasconcelos TO, Lima LF, Oliveira BE, Vieira VMSF, Ponciano AMS, Silva LMM, Fonteles MMF. Avaliação do risco cardiovascular em pacientes hipertensos sob acompanhamento farmacoterapêutico em atenção primária à saúde. *Rev Bras Farm Hosp Serv Saúde.* 2012;3(2):42-6.
6. Firmino PYM, Vasconcelos TO, Ferreira CC, Moreira LM, Romero NR, Dias LA, Queiroz MGR, Lopes MVO, Fonteles MMF. Cardiovascular risk rate in hypertensive patients attended in primary health care units: the influence of pharmaceutical care. *Braz J Pharm Sci.* 2015;51(3):617-27. <http://dx.doi.org/10.1590/S1984-82502015000300013>.
7. Machado M, Bajcar J, Guzzo GC, Einarson TR. Sensitivity of patient outcomes to pharmacist interventions. Part I: systematic review and meta-analysis in diabetes management. *Ann Pharmacother.* 2007;41(10):1770-81. <http://dx.doi.org/10.1345/aph.1K311>. PMID:17712043.
8. Balisa-Rocha BJ, Aguiar PM, Cerqueira KS, Novaes MB, Alcântara TS, Lyra DP Jr. Evaluation of the effects of long-term of pharmacotherapeutic follow-up intervention on clinical and humanistic outcomes in diabetes mellitus patients. *Afr J Pharm Pharmacol.* 2014;8(14):372-8.

9. Brasil. Conselho Federal de Farmácia. Resolução nº. 585, de 29 de agosto de 2013. Regulamenta as atribuições clínicas do farmacêutico e dá outras providências. Diário Oficial da União, Brasília, 25 set. 2013. Seção 1, p. 186-8.
10. Conselho Federal de Farmácia. Serviços farmacêuticos diretamente destinados ao paciente, à família e à comunidade contextualização e arcabouço conceitual. Brasília: Programa de Suporte ao Cuidado Farmacêutico na Atenção à Saúde; 2017.
11. Manzini F, Mendes SJ, Leite SN. O farmacêutico na assistência farmacêutica do SUS: diretrizes para ação. Brasília: Conselho Federal de Farmácia; 2015. Avaliação da assistência farmacêutica; p. 133-60.
12. Sociedade Brasileira de Cardiologia. Atualização da diretriz brasileira sobre dislipidemia e prevenção da aterosclerose. Arq Bras Cardiol. 2017;109(2, Supl. 1):1-76.
13. Sociedade Brasileira de Cardiologia. Atualização da diretriz brasileira de prevenção cardiovascular. Arq Bras Cardiol. 2019;113(4):787-891. PMID:31691761.
14. Sociedade Brasileira de Cardiologia. Diretrizes brasileiras de hipertensão arterial - 2020. Arq Bras Cardiol. 2021;116(3):516-658. <http://dx.doi.org/10.36660/abc.20201238>. PMID:33909761.
15. Sociedade Brasileira de Diabetes. Diretrizes da Sociedade Brasileira de Diabetes 2019-2020. São Paulo: Sociedade Brasileira de Diabetes; 2019.
16. Mendonça SAM, Melo AC, Pereira GCC, Santos DMSS, Grossi EB, Sousa MCVB, Oliveira DR, Soares AC. Clinical outcomes of medication therapy management services in primary health care. Braz J Pharm Sci. 2016;52(3):365-73. <http://dx.doi.org/10.1590/s1984-82502016000300002>.
17. Martins BCC, Souza TR, Luna ÂMPT, Fonteles MMF, Firmino PYM, Fernandes PFCBC, Garcia JHP, Oliveira CMC, Néri EDR. Pharmaceutical care in transplant patients in a university hospital: pharmaceutical interventions. Braz J Pharm Sci. 2013;49(4):659-68. <http://dx.doi.org/10.1590/S1984-82502013000400005>.
18. Plaster CP, Melo DT, Boldt V, Cassaro KOS, Lessa FCR, Boëchat GAP, Bissoli NS, Andrade TU. Reduction of cardiovascular risk in patients with metabolic syndrome in a community health center after a pharmaceutical care program of pharmacotherapy follow-up. Braz J Pharm Sci. 2012;48(3):435-46. <http://dx.doi.org/10.1590/S1984-82502012000300010>.
19. Santos BD, et al. Clinical impact of a comprehensive medication management service in primary health care. J Pharm Pract. 2021;34(2):265-71. <http://dx.doi.org/10.1177/0897190019866309>. PMID:31422732.
20. Neves CM, Nascimento MMG, Silva DÂM, Ramalho-de-Oliveira D. Clinical results of comprehensive medication management services in primary care in Belo Horizonte. Pharmacy. 2019;7(2):58. <http://dx.doi.org/10.3390/pharmacy7020058>.
21. Morgado MP, Morgado SR, Mendes LC, Pereira LJ, Castelo-Branco M. Pharmacist interventions to enhance blood pressure control and adherence to antihypertensive therapy: review and meta-analysis. Am J Health Syst Pharm. 2011;68(3):241-53. <http://dx.doi.org/10.2146/ajhp090656>. PMID:21258029.
22. Brajković A, Bosnar L, Nascimento MMGD, Prkačin I, Balenović A, Ramalho de Oliveira D, Mucalo I. Healthcare utilisation and clinical outcomes in older cardiovascular patients receiving comprehensive medication management services: a nonrandomised clinical study. Int J Environ Res Public Health. 2022;19(5):2781. <http://dx.doi.org/10.3390/ijerph19052781>. PMID:35270472.
23. American Diabetes Association. Standards of medical care in diabetes—2022. Diabetes Care. 2022;45(Suppl. 1):S1.
24. Carlos JO. Avaliação de Pacientes egressos de um serviço de cuidado farmacêutico para hipertensão e diabetes [monografia]. Fortaleza: Faculdade de Farmácia, Universidade Federal do Ceará; 2016.

Authors' contributions:

PYMF, JOC and JOL contributed to the the acquisition, analysis, interpretation of data and the draft of the work; PYM, NRR and MMFF contributed to the conception and design of the work, besides the revision of the draft.