FEATURE ARTICLE

Effectiveness of an Interprofessional Program (Siscare) for Supporting Patients With Type 2 Diabetes

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OBJECTIVE | To assess the effectiveness of an interprofessional support program (Siscare) that includes motivational interviews (patient-pharmacist), electronic monitoring (EM) of medications, patient-reported and clinical outcomes monitoring, and interactions with physicians for patients with type 2 diabetes in French-speaking Switzerland.

METHODS | This was a prospective, multicenter, observational cohort study using a hybrid implementation-effectiveness design. Individual daily adherence to at least one oral antidiabetic medication was measured by EM. A global adherence score was estimated by the product of a model-estimated implementation and a nonparametric estimate of persistence over time. Clinical outcomes (A1C, blood glucose, BMI, blood pressure, heart rate, and cholesterol levels) and quality of life (QoL) were analyzed over time using linear mixed-effect models.

RESULTS | A total of 212 patients were included from 27 pharmacies; 120 patients (57%) were followed up for at least 15 months. In total, 140 patients (66%) were male, the mean age was 64 ± 11 years, and the mean number of chronic medications per patient at baseline was 5 ± 3. Of 178 patients who used EM, 95% (95% CI 92–99%) remained persistent at the end of the follow-up period. The percentage of persistent patients taking their medications appropriately (implementation) was stable during follow-up and was estimated to be 90% (95% CI 87–92%) at baseline and 88% (95% CI 84–91%) at month 15. At baseline, the mean A1C and BMI were 7.5% and 31 kg/m^2, respectively, which decreased by 0.5% ($P = 0.012$) and 0.6 kg/m^2 ($P = 0.017$), respectively, after 15 months. QoL remained stable during follow-up.

CONCLUSION | The program supports medication adherence and improves clinical outcomes, illustrating the overall preventive effect of coordinated care.

Worldwide, 9% of the adult population lives with diabetes, which affects 463 million people and causes 4 million deaths each year (1). Medication is the preferred adjunct therapy to control diabetes and reduce negative clinical outcomes and mortality when lifestyle changes are not sufficient (2). Despite proper diagnosis and medical care, only half of patients take their medications as prescribed; the other half do not receive optimal clinical benefits from therapy (3). According to a literature review, medication adherence rates range from 39 to 93% (4) in patients taking diabetes medications.

Medication adherence is defined as the process by which patients take their medications as prescribed by health care professionals (HCPs) (3). It is a dynamic and complex process characterized by the daily intake of a medication and management of a drug regimen and covers three dimensions: initiation, implementation, and persistence (5). Medication adherence can vary over time depending on a very large number of factors, of which more than 700 have been identified (6).

Medication nonadherence leads to disease progression, poor disease management and clinical outcomes, reduced quality of life (QoL), and increased use of health resources and mortality (7). Improved medication adherence is associated with a reduction in diabetes complications (e.g.,

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ulcers, retinopathy, acute myocardial infarction, neuropathy, and amputations) and a reduction in the number of short-term disability days (7). Adherent patients with diabetes had 37% fewer emergency room visits and 30% fewer hospitalizations than nonadherent patients (8). Medication nonadherence affects health care systems significantly because of the resulting wasted resources, costly and preventable adverse events, and hospitalizations (9). A 2005 study found that the total cost of diabetes decreased by 50% (from $8,867 to $4,570 per person) with higher levels of medication adherence despite increases in diabetes medication use and costs (10).

To reduce these negative outcomes, interventions from HCPs are needed to support medication adherence and improve health outcomes. A recent meta-analysis of pharmacist-led interventions to improve medication adherence in adults with diabetes showed that a combined intervention strategy that included both educational and behavioral components improved outcomes such as medication adherence and A1C (11). Another meta-analysis examining the impact of medication adherence interventions in adults with any clinical condition identified an additive effect of interventions with longer follow-up (≥10 months) (12). Thus, the aim of this study was to assess the effectiveness of a long-term interprofessional support program called Siscare, delivered by community pharmacists and physicians, for patients with type 2 diabetes in a primary care setting.

Research Design and Methods

Study Design

This research is part of a larger study that used a hybrid implementation-effectiveness design based on data from a prospective, multicenter, observational study (13). This article focuses on the effectiveness results.

Intervention

Siscare is an interprofessional patient support program that includes *1*) regular motivational semistructured interviews (conducted by a community pharmacist) at least every 3 months; *2*) electronic monitoring (EM) of medication adherence, feedback to patients (MEMS and MEMS AS, AARDEX Group, Switzerland), and monitoring of patient-reported and clinical outcomes; and *3*) feedback reports to the referring physician (i.e., the general practitioner or specialist responsible for coordinating the patient's care) to ensure information-sharing and provide a starting point for collaborative patient care. The program aims to help patients reach their individual therapeutic goals to improve their general health, support medication adherence, and strengthen continuity of care among the different HCPs involved in the patient care pathway.

Participants and Setting

Eligible patients were adults (≥18 years of age) who were diagnosed with type 2 diabetes and taking at least one oral antidiabetic medication (OAD). The exclusion criteria were a diagnosis of type 1 diabetes, an obvious cognitive impairment, or an insufficient speaking fluency in French. Patients were recruited from community pharmacies belonging to a network implementing patient-centered services in the French-speaking part of Switzerland who volunteered to participate in the study.

The advisory board estimated a target sample size of 200 patients. This value was calculated based on the estimated number of participating pharmacies (n = 20) and the target number of patients to be recruited (10 per pharmacy).

The study protocol was approved by the Cantonal Ethics Committee of Research on Human Beings of the Canton of Vaud (protocol no. 2016-00110). Data were kept in a coded form. Written consent was obtained from patients through the pharmacists.

Outcomes and Measurements

Sociodemographic characteristics were collected using a self-report questionnaire at baseline. Patients' types and number of medications taken, clinical outcomes (A1C, blood glucose, BMI, systolic and diastolic blood pressure, heart rate, and cholesterol levels), and smoking status were documented by the pharmacist on a web-based platform at each interview during the 15-month study period. Clinical outcomes were obtained from measurements taken at the pharmacy, from the patient (self-reported or laboratory results), and/or from the physician. The primary outcomes were medication adherence to OADs and the clinical outcomes; all of the other outcomes were considered secondary.

Medication adherence to at least one OAD was monitored by EM for 15 months. The pharmacist was responsible for defining the number and types of medications to monitor by EM according to each patient's needs. A pillbox was equipped with a cap containing an electronic chip that records the date and time of each opening and allows the data to be uploaded to a web-based platform at each patient visit (14).

Medication adherence covered three dimensions: implementation, persistence, and adherence (5,15). Implementation was defined as the percentage of patients who correctly took all prescribed doses of their monitored medication on one day among all patients who were still persistent on that day.

Persistence was defined as the survival function associated with the individual time differences between the initiation and discontinuation of treatment, and persistence ended when the next dose to be taken was omitted and no further dose was subsequently taken. Unilateral discontinuation of a drug occurred when a patient discontinued the treatment on his or her own initiative, and clinically appropriate discontinuation occurred when the patient discontinued the treatment in agreement with the physician (e.g., because of adverse events or toxicity of the treatment). Any other reason for stopping the program and/or treatment was considered censoring (e.g., patients stopped using the electronic pillbox but continued using the medication). Adherence was defined as the percentage of patients taking all prescribed doses of their monitored medications based on the prescribed regimen among all patients initially included in the study (i.e., adherence was defined as "all" [i.e., taking 100% of prescribed doses] or "nothing" [i.e., taking less than 100% of prescribed doses] for each day). No secondary method was used to validate the medication adherence data.

At the end of the inclusion period, some patients were recruited for and included in the study with the pharmacist monitoring but without EM, to increase the number of patients. The clinical outcomes, except the medication adherence, of these patients were considered in the analysis.

General and specific QoL were assessed using two self-report questionnaires at baseline and at 6- and 12-month follow-ups. The Short Form-12 Health Survey (SF-12), v. 2, includes 12 items covering eight health domains and provides a physical component summary (PCS) and a mental component summary (MCS) (16). Scores range from 0 to 100, with 0 being worst and 100 being best QoL. The Audit of Diabetes Dependent Quality of Life 19 (ADDQoL) includes three parts: global questions, diabetes-specific questions, and questions related to 19 life domains measuring the impact of diabetes on patient QoL (17,18). The weighted score ranges from −9 (maximum negative impact) to +3 (maximum positive impact), and the average gives an overall score for each time point.

Patient satisfaction with the program was assessed using a self-report questionnaire at the end of the study (i.e., at the 15-month follow-up) or earlier if patient follow-up was stopped before the end of the study. The research team developed the questionnaire based on earlier works (19–21) to cover topics on motivational interviews, EM, and interprofessional collaboration in addition to reasons for participation, willingness to continue with the program, and open comments, including space to suggest improvements. Auto-administered questionnaires were distributed to patients by the pharmacists and returned to the research team in pre-stamped envelopes. Qualitative interviews with patients were planned but not conducted because of time constraints.

Statistical Analyses

Descriptive statistics were used to describe patients' sociodemographic and clinical characteristics at baseline (closest to time point ± 3 months), QoL, and patient satisfaction.

Medication adherence was assessed through implementation, persistence, and adherence. On each day, patients' behavior regarding their treatment was dichotomized as "adequate" when they opened their electronic pillbox at least the prescribed number of times for each single monitored OAD or as "inadequate" when they opened their electronic pillbox less than the number of times prescribed for at least one monitored OAD. Generalized estimating equation (GEE) models with an auto-regressive correlation structure were adopted to estimate the population implementation trend over time; the GEE entered the model using natural cubic splines. Persistence was estimated using the Kaplan-Meier survival function. Adherence was estimated empirically as the product between implementation and persistence at each follow-up time (15). To estimate population adherence over time, GEE models were applied to observed adherence data that were weighted to correct for bias induced by censoring generated missingness (22).

Changes over time in clinical outcomes and QoL (PCS, MCS, and overall ADDQoL scores) were estimated by three-level (time, patient, and pharmacy) mixed-effect linear regression models. These models took into account that the data were measured repeatedly for the same patient and that patients within a pharmacy are not independent. In the analysis, the pharmacy cluster effect was negligible (i.e., no difference observed); thus, only time and patient were considered in the reported results. These analyses were performed for clinical data if ≥25% of the patients had a value at baseline. For clinical outcomes, locally weighted scatterplot smoothing (lowess) was also performed to graphically illustrate trends over time. For QoL, time was treated as an ordinal variable with three categories (baseline, 6 months, and 12 months), with the reference category being the baseline score. When evaluating group-level results, the proposed minimally important difference for the PCS and MCS scores was 3 points (23).

Descriptive statistics were calculated with Microsoft Excel 2016, regression and lowess analyses were performed with StataIC 16 (StataCorp, College Station, TX), and medication adherence analysis was performed with *R*-3.6.2 (The R Foundation for Statistical Computing, Vienna, Austria). The statistical significance level was set at two-sided $\alpha = 0.05$.

Results

Characteristics of the Study Patients

Two hundred and twelve patients from 27 pharmacies were included in the study between April 2016 and June 2017, with a mean number of 8 (SD 5, range 1–29) patients per pharmacy. The baseline characteristics of the study population are shown in Table 1. The mean age of the patients was 63.9 years (range 32–93 years).

The mean number of medications per patient was 5.1 (range 1–19). Patients were primarily treated with an A class (digestive system and metabolism) medication according to the Anatomical Therapeutic Chemical (ATC) classification system, with an average of 2.1 medications per patient, followed by ATC C class medication (cardiovascular system), with an average of 1.5 medications per patient. Most patients had one OAD (Figure 1), with metformin being used most commonly (n = 137 of 194), followed by gliclazide (n = 32 of 194) and a combination of metformin and sitagliptin (n = 29 of 194).

Although 72% of respondents rated their general QoL as good, very good, or excellent, 68% also reported that their QoL would be better if they did not have diabetes.

Of the patients who began the follow-up, 59% (120 of 205) were monitored for at least 15 months, for a median of 456 days (interquartile range 298–456). Supplementary Figure S1 provides details on follow-up duration. Of the 205 patients, 186 (91%) had at least one electronic pillbox, and 19 (9%) had only a weekly pillbox. Eight patients (4%) had no EM data and were considered lost to follow-up (i.e., they started monitoring with the pillbox but never returned to the pharmacy and/or never used the pillbox). Finally, 178 patients (87%) provided EM data.

The pharmacists reported 250 reasons for participation for 199 patients. The most common reasons were therapeutic complexity (n = 70 of 199 patients [35%]), participation in a study (n = 39 [20%]), introduction of a new treatment (n = 28 [14%]), medication adherence issues exposed by the patient (n = 27 [14%]), failure to achieve therapeutic objectives (n = 22 [11%]), suspicion of nonadherence by the HCP (n = 15 [8%]), and treatment intensification (n = 13 [7%]). Among the patients who stopped the follow-up before 15 months (n = 77), the pharmacists reported 86 reasons for 62 patients: no longer wanted to continue with the follow-up (n = 25 [40%]), refused to use EM (n = 20 [32%]), achieved their therapeutic objectives (n = 8 [13%]), changed pharmacies or moved (n = 7 [11%]), and stopped treatment (n = 7 [11%]). Of note, patients who failed to use the EM were using a weekly pillbox for other medication.

Medication Trends

Of the patients with complete data at 15 months, 28 of 117 (24%) had a change (i.e., addition or withdrawal) in OADs, including 14 patients (12%) with an addition of one or two OADs. The mean number of OADs per day was constant over the study period. Supplementary Figure S2 shows the evolution of the average number of medications over time.

Medication Adherence

The mean monitoring time was 372 days (SD 137 days, range 26–456 days). Implementation was globally stable with low and constant variability over time (Figure 2). The implementation rate was estimated at 90.1% (95% CI 87.3–92.3%) at the beginning of monitoring, 86.9% (95% CI 83.6–89.6%) at day 100, and 87.6% (95% CI 83.6–90.7%) at day 400 (GEE model). Seven patients discontinued their OAD, including six for an appropriate clinical reason and one on his or her own initiative. Figure 3 depicts the Kaplan-Meier persistence and adherence estimates. The persistence rate (percentage of subjects who did not stop their treatment) at the end of follow-up (i.e., 365 days) was 95.2% (95% CI 91.7–98.7%).

Clinical Outcomes

Mean A1C decreased by an average of 0.032 units per month (95% CI −0.056 to −0.007 units, P = 0.012) (Figure 4), which represents a decrease of 0.473 units over the 15-month monitored period. Without considering the extreme value documented for one patient at the beginning of follow-up (A1C 15%), the effect of time remained significant, corresponding to a mean decrease of 0.022 units per month (95% CI −0.039 to −0.006 units, P = 0.008, n = 292 observations for 118 patients) and thus a cumulative decrease of 0.336 units over 15 months.

BMI significantly decreased by 0.043 units per month (95% CI −0.077 to −0.008 units, P = 0.017) (Supplementary Figure S3) or 0.641 units over 15 months. After removing the highest BMI value (BMI = 54 kg/m^2), the decrease was 0.042 units per month (95% CI −0.076 to −0.007 units, P = 0.018, n = 226 observations for 84 patients) and 0.622 units over 15 months.

Regarding the other clinical data (blood glucose, blood pressure, and heart rate), the results did not change significantly over time (Supplementary Figure S3 and Supplementary Table S1).

Quality of Life

The numbers of questionnaires completed at baseline, 6 months, and 12 months were 163, 103, and 69, respectively.

TABLE 1 Baseline Characteristics of Study Participants

Characteristic	Value
Sociodemographic characteristics	
Age, years (n = 212)	63.9 ± 11.3
<65	99 (47)
65–74	80 (38)
≥75	33 (15)
Women (n = 212)	72 (34)
Education level (n = 156)	
Primary	68 (44)
Secondary	57 (36)
Tertiary	28 (18)
Other	3 (2)
Employment status (n = 159)	
Retired	85 (54)
Employee	43 (27)
Independent or family business	7 (4)
Looking for a job	8 (5)
Unable to work	8 (5)
Other	8 (5)
Participation in another support program diabetes patient association (n = 157)	10 (6)
Smoking status (n = 99)	
Nonsmoker	74 (75)
Current smoker	24 (25)
Medication	
Total number of medications per patient (n = 194)	5.1 ± 3.3
Number of antidiabetic medications per patient (n = 194)	
1	104 (54)
2	52 (27)
3	28 (14)
4	10 (5)
Type of antidiabetic medication (n = 194)	
Oral and injectable medication	153 (79)
Oral medication only	41 (21)
Clinical characteristics	
A1C, % (n = 82)	7.5 ± 1.6
A1C categories, %	
≤7.0	41 (50)
>7.0 and ≤8.0	22 (27)
>8.0 and ≤9.0	9 (11)
>9.0	10 (12)
Blood glucose, mmol/L (n = 90)	8.2 ± 3.2
BMI, kg/m^2 (n = 76)	30.8 ± 5.3
Systolic blood pressure, mmHg (n = 99)	136 ± 16
Diastolic blood pressure, mmHg (n = 74)	83 ± 9
Heart rate, bpm (n = 49)	76 ± 12
Cholesterol, mmol/L	
Total (n = 18)	5.0 ± 1.2
LDL cholesterol (n = 21)	3.0 ± 1.1
HDL cholesterol (n = 17)	1.3 ± 0.6
Triglycerides (n = 18)	2.3 ± 1.5
Quality of life	
SF-12	
SF-12 PCS score (n = 156)	46.34 ± 8.72
SF-12 MCS score (n = 157)	45.61 ± 10.51

Data are mean ± SD or n (%).

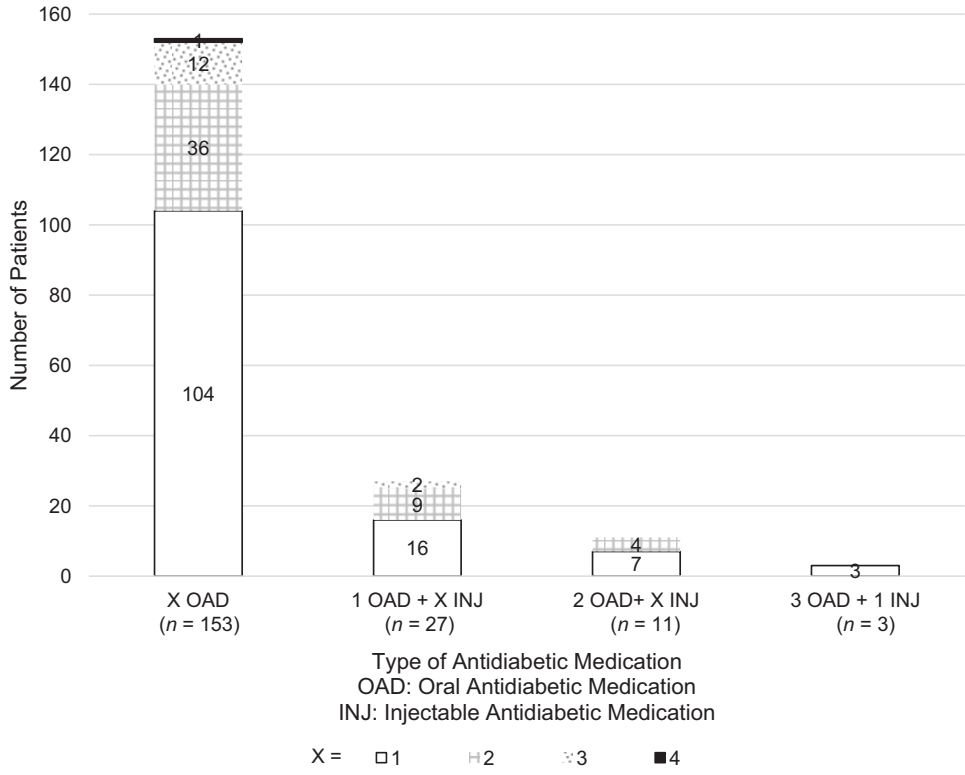

FIGURE 1 Patients stratified by type and number of antidiabetic medications at baseline ($n = 194$). Number of patients is presented on the vertical axis according to the antidiabetic treatment regimen: oral antidiabetics alone or with injectable antidiabetic medications. OAD, oral antidiabetic medication; INJ, injectable antidiabetic medication.

According to the regression model, the mean PCS score at 6 months was 0.34 units higher than at baseline (95% CI −0.85 to −1.52, $P = 0.577$). Between baseline and 12 months, there was a decrease of 1.64 units (95% CI −3.02 to −0.25, $P = 0.020$). The estimated mean decrease between 6 and 12 months was 2.00 units (95% CI −3.43 to −0.51, $P = 0.008$). The mixed-effect regression model showed that the mean MCS score increased significantly by 0.17 units per month (95% CI 0.01–0.32 units, $P = 0.032$). Detailed PCS and MCS values and each dimension of the SF-12 at baseline, 6 months, and 12 months are presented in Supplementary Figure S4.

The mean overall ADDQoL score decreased over the short term but increased over the long term without significance (−0.060 units at 6 months [95% CI −0.287 to 0.166], $P = 0.602$ and 0.004 units at 12 months [95% CI −0.261 to 0.269], $P = 0.978$). Supplementary Figures S5 and S6 show the weighted impact scores and responses, respectively, for the 19 domains at each time point.

Patient Satisfaction

Sixty-eight patients (33%) responded to the patient satisfaction questionnaire. Thirty-five respondents (51%) joined the study to help research efforts, 21 (31%) enrolled for support in their daily treatment, 16 (25%) participated to please their pharmacist, and 6 (9%) joined because they had to start a new treatment.

Most patients ($n = 65$ [96%]) reported that the length and frequency of the interviews were adequate, rated the interviews as somewhat to very helpful ($n = 54$ [79%]), and felt that the interviews allowed them to express problems they encountered while taking their medications ($n = 53$ [78%]). A minority of patients ($n = 13$ [19%]) felt that they were being controlled. Supplementary Figure S7 provides detailed patient opinions about the interviews. Fifty-seven patients (84%) found the EM pillbox easy to use, useful, and space saving. For 50 patients (74%), the collaboration between their pharmacist and referring physician was considered to be relatively present to very present, and 30 patients (44%) stated that the collaboration improved their management. Finally, 16 patients (24%) said they definitely wanted to continue the program, 15 (22%) said they were most likely going to continue, 17 (25%) preferred to stop, and 13 (19%) reported that they no longer wanted to continue at all. Three-fourths of the patients ($n = 51$ [75%]) said they would recommend the program to another person with diabetes.

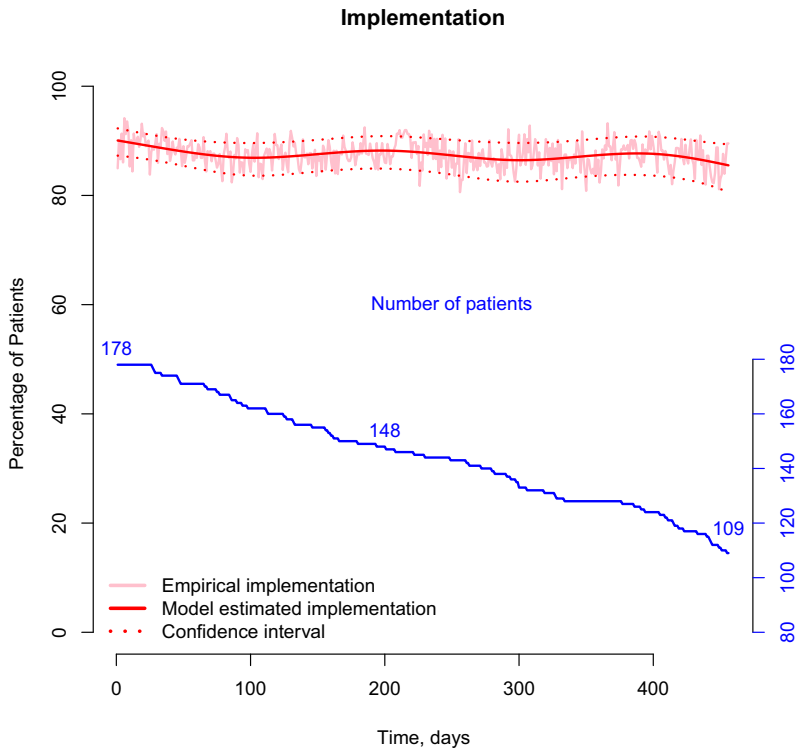

FIGURE 2 Implementation results with the GEE exchangeable model (auto-regressive). The pink curve represents the proportion of patients with the correct number of daily pillbox openings among patients still under observation over time (empirical implementation); the continuous red curve represents the model-estimated implementation rate with 95% CI (dotted red curves); and the blue curve represents the number of patients over time.

Discussion

This study assessed the 15-month effectiveness of the Siscare program for patients with type 2 diabetes in a primary care setting in Switzerland. The results show stable and high medication adherence over time (primary outcome). The only other Swiss study based on health insurance data for patients with diabetes taking OADs showed a medication adherence rate of 42% (percentage of days covered ≥80%) over 12 months (n = 26,713 patients) (24), which is in contrast with the very high medication adherence rate in the current study. No recommendations to pharmacists were made regarding which patients should be included (e.g., based on medication adherence level) outside the specified inclusion criteria. According to the focus group results (25), pharmacists mostly selected patients based on the likelihood that they would accept the program. However, the study population was comparable to that of two other studies conducted in Switzerland (24,26). Moreover, the age categories and education levels of the patients corresponded to Swiss epidemiological data, since the prevalence of the disease increases beyond the age of 55 years, and people with a low education level were twice as likely to have diabetes as those with a higher education level (8 vs. 4%) (27). The higher proportion of men taking part in the study also reflects the reality that 5% of men versus 3% of women had diabetes in 2017 (27). Data on the representativeness of the patients allowed us to reduce potential selection bias in the study population. Hence, the very high level of medication adherence in the first few months seems to have been more influenced by the novelty of the electronic pillbox than by patient characteristics.

For primary clinical outcomes, only A1C and BMI significantly decreased over time. Baseline A1C (other primary outcome) averaged 7.5% and decreased by 0.3–0.5 units after 15 months, while the effect on A1C of adding an OAD ranged from 0.5 to 1.0% after 3–6 months in the literature (28). In addition, a subanalysis of our data conducted among patients with a baseline A1C ≥7.5% showed a significant decrease in A1C of 0.082 units per month (95% CI −0.147 to −0.018 units, P = 0.012, n = 99 observations for 33 patients) and a cumulative decrease of 1.2 units over 15 months. As other studies have shown, patients with higher A1C levels at baseline are likely to benefit more from interventions (29–31). Particular efforts should be made by community pharmacists to screen for such patients.

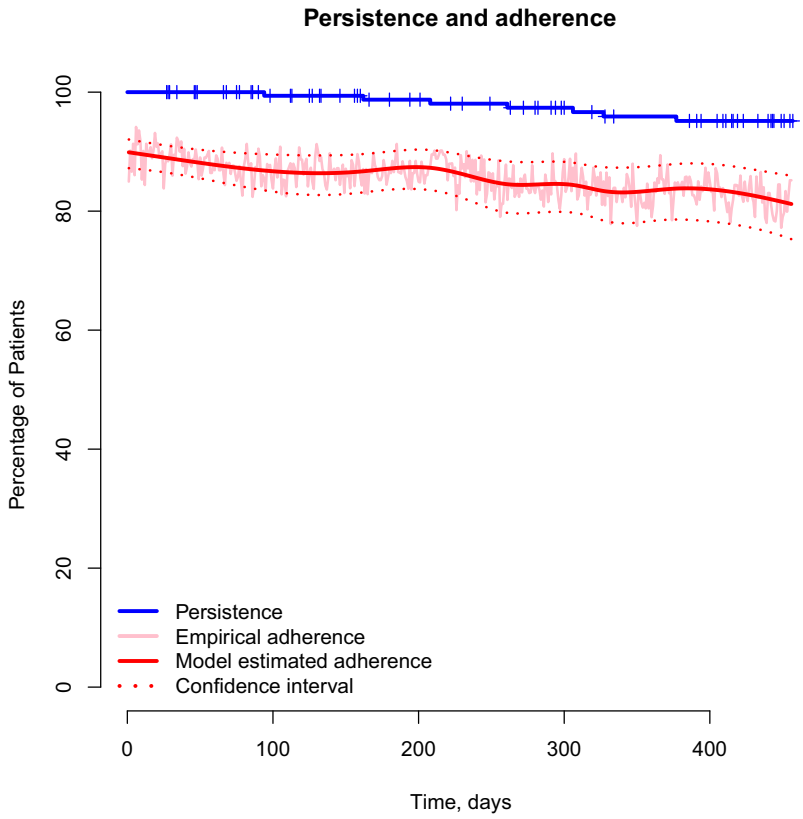

FIGURE 3 Persistence and medication adherence results. The pink curve represents the proportion of patients with the correct number of daily pillbox openings among all patients over time (empirical adherence), the red curves represent model-estimated adherence with 95% CI, the blue curve represents the number of patients still under treatment using the Kaplan-Meier survival estimate (persistence), the vertical blue bars represent the censored patients, and the downward jumps in the blue curve represent discontinuation.

Thus, the program resulted in a clinically significant reduction in A1C equivalent to the addition of an OAD, with no change in the number of antidiabetic treatments for these patients, while BMI decreased significantly by 0.6 units over 15 months. The 2% decrease in BMI (weight data were not available) was not considered as clinically significant because a 5% weight loss is generally considered clinically significant, and our study indicates a 2% decrease.

Most of the included patients had regular contact with their pharmacist at least every 12 weeks during the study, although the frequency of physician visits was unknown. Regular meetings with HCPs are essential to allow patients to play a more active role in the management of their disease (32). Medication use partly relies on patients' trust in their HCPs. The key to improving the quality of chronic patient care seems to be dependent on patient-tailored monitoring to achieve therapeutic objectives and maintain stability over time. In addition, a large majority of patients with type 2 diabetes have comorbidities such as hypertension and dyslipidemia and are prescribed more medications (mainly cardiovascular medications) (33). These factors may result in a complex treatment plan, more adverse events, and medication adherence issues, particularly for conditions that are mostly asymptomatic, such as diabetes, dyslipidemia, and hypertension (34).

In this study, 20 patients stopped the program because of failure to use the EM, notably when the patients were using a weekly pillbox for other medications. An electronic weekly pillbox system may seem easier for patients taking multiple medications (35), but we still lack data on the best device to satisfy the needs of patients, HCPs, and researchers. Research is needed on the appropriate device to integrate into patients' daily lives.

QoL was assessed through general (SF-12 PCS and MCS) and specific (ADDQoL) questionnaires for patients with diabetes. In Switzerland, the PCS and MCS scores were 49.8 and 46.3 in a representative sample of residents (36), whereas in patients with diabetes, the scores were 43.1 and 46.7, respectively (37). The ADDQoL score was estimated to be −1.6 in a cohort of Swiss people with diabetes (37). The current study found baseline PCS and MCS scores of 46.3 and 45.6, respectively, and an ADDQoL score of −1.6, indicating values similar to

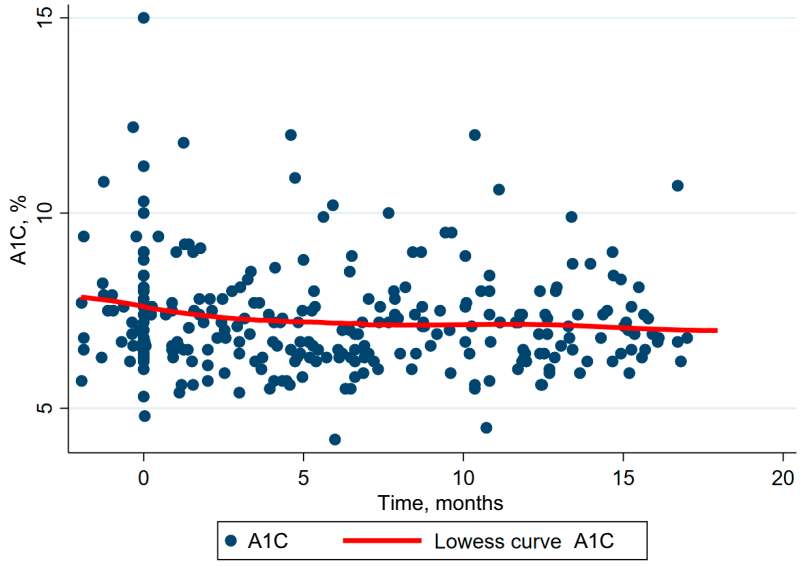

FIGURE 4 Distribution of patient A1C over time (n = 289 observations for 118 patients) and lowess nonparametric regression. The red line represents lowess, which is a set of simple regressions applied to subsets of data. Dots represent patients' A1C values.

those of the Swiss population. No significant differences were found over time, demonstrating that the program had no impact on QoL. Because the percentage of patients responding to the questionnaire decreased over time compared with patients still being followed (initial response rate 76% [157 of 205], 6-month response rate 51% [97 of 188], and 12-month response rate 39% [68 of 171]), caution should also be exercised when analyzing these data.

Regarding the satisfaction questionnaire, 75% of the responders indicated that they would recommend the program to another person with diabetes. The response rate to the satisfaction questionnaire was rather low (33%) and probably included those who were the most satisfied. The results on whether to continue the program were mixed, suggesting that patients were satisfied with the service and that its duration was sufficient. More research on the duration of such programs is needed.

The results of this study suggest that there is a major need for HCPs to support patients with chronic conditions by tailoring interventions to meet their needs. Newly diagnosed patients have a greater demand for knowledge than patients who have been living with diabetes for several years but still need support to improve the management of their disease (38). Pharmacists should also focus on patients with obvious medication adherence issues and high A1C values. This intervention can be adapted to patients' needs regarding the motivational approach (individual approach), the frequency of visits (which can be modulated over time), and the tools used to assist in medication intake.

The strength of this hybrid implementation-effectiveness study design lies in the electronic and longitudinal monitoring of medication adherence and patient-reported outcomes in a real-world setting over a long and representative period. Moreover, the implementation evaluation allowed us to monitor and collect data regarding the feasibility and acceptability of the program by community pharmacists (25). Collaboration primarily occurred through the unidirectional transmission of information from the pharmacist to the physician (level 1; 70% of pharmacists transmitted interview reports to physicians), bidirectional exchange of information sometimes occurred (level 2; 42% received physician responses), and concerted measures of treatment objectives took place occasionally (level 3; findings to be reported separately).

However, this study has limitations that need to be considered for future research. First, it did not include a control group; therefore, we cannot reach a conclusion on the direct cause of the decrease in A1C. This design was chosen because this intervention had already shown effectiveness in patients with HIV, which supported its applicability to this new study population (19,20). Randomization in routine care is quite difficult to implement, but other designs should be carefully considered in future research (39). Second, patients' self-reported QoL and satisfaction data may be subject to bias, but the use of stamped addressed envelopes, the recommendation to fill in the questionnaire outside of the pharmacy, and the fact that the research team was different from the field intervention team limited this bias. With regard to

clinical outcomes, no decrease in blood glucose levels was observed, which could be related to the different sources of these outcomes (e.g., self-reported without ensuring good clinical practice). Because food consumption influenced the results, the lack of measurement standardization led to a greater heterogeneity among these values than among A1C values. Access to a common database or platform should improve the quality of care by providing physicians with a continuously updated treatment plan and the pharmacist with access to the clinical data. Third, the real-world setting was chosen because of the hybrid effectiveness-implementation design of the study; this fact certainly contributed to the large amount of missing data. Nevertheless, the amount of missing data for A1C was consistent with that in another study (61% missing vs. 60% in our study at baseline) (40). Finally, it cannot be excluded that other factors such as dietary and lifestyle habits contributed to the decrease in A1C. It is assumed that this program itself has an impact not only on medication adherence but also on other daily behaviors such as food intake and exercise that pharmacists may have discussed with patients in a more structured way than is typical for usual care. This possibility needs further investigation.

Conclusion

Medication adherence was consistently high and stable during the 15-month intervention, and the A1C values improved, with no major changes in diabetes treatment or involvement of other support mechanisms. Pharmacists and physicians should tailor such support programs to patients with medication adherence problems and those who have not achieved their therapeutic goals to improve quality of care and prevent negative outcomes. It is also important that patients' needs, preferences, and perspectives be taken into account when choosing the method of measuring adherence. Research should focus on expanding the range of measurement tools and move toward tools that assess all medications to obtain an overview of all medications and to link adherence to clinical or other outcomes.

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DUALITY OF INTEREST

O.B. was a co-founder of Sispha SA and a member of the advisory board of Sispha SA. No other potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

N.B. researched data and wrote the manuscript. M.-P.S. contributed to the adherence data analysis and interpretation and reviewed/edited the manuscript. P.B. and I.L. contributed to the data analysis and interpretation and reviewed/edited the manuscript. O.B. researched data and reviewed/edited the manuscript first drafts. C.P. researched data and reviewed/edited the manuscript. N.B. and C.P. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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