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ORIGINAL ARTICLE

Young patients with type 1 diabetes poorly controlled and poorly compliant with self-monitoring of blood glucose: can technology help? Results of the i-NewTrend randomized clinical trial

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Abstract

Aims To compare iBGStar™ + DMApp (experimental meter + telemedicine system) (iBGStar) with a traditional glucose meter (Control) in type 1 diabetes adolescents/young adults.

Methods i-NewTrend was a multicenter, open-label, randomized trial involving subjects aged 14–24 years, on basal–bolus insulin, HbA1c $\geq$ 8.0%, and poorly compliant with SMBG (i.e., <30% of the recommended frequency). Primary end points were change in HbA1c and achievement of compliance with SMBG ($\geq$30% of the recommended frequency) after 6 months. Quality of life was also evaluated. A post-trial observational phase was conducted, where both groups used the experimental device.

Results Of 182 randomized patients (51.1% male; age 17.7 ± 3.0 years; diabetes duration 8.8 ± 4.7 years; HbA1c levels 10.0% ± 1.4), 92 were allocated to iBGStar and 90 to Control; 6.5% in iBGStar and 8.9% in Control dropped-out. After 6 months, HbA1c changes (±SE) were −0.44% ± 0.13 in iBGStar and −0.32% ± 0.13 in Control ($p = 0.51$). In the post-trial phase, HbA1c changes from 6 months (±SE) were −0.07% ± 0.14 in iBGStar and −0.31% ± 0.14 in Control ($p = 0.24$). Compliance end point was reached by 53.6% in iBGStar and 55.0% in Control ($p = 0.86$). Mean daily SMBG measurements increased from 1.1 to 2.3 in both groups without worsening quality of life. Compliant subjects showed a greater reduction in HbA1c levels (−0.60% ± 0.23 in iBGStar; −0.41% ± 0.21 in Control; $p = 0.31$). Within iBGStar group, telemedicine users (38.0%) reduced HbA1c by −0.58 ± 0.18.

Conclusions iBGStar was not superior to the traditional meter. Irrespective of the strategy, increasing from 1 to 2 SMBG tests/day was associated with HbA1c reduction in both groups, without pharmacologic interventions. Identifying new technologies effective and acceptable to patients is an option to improve adherence to diabetes care.

Trial registration The trial was registered at ClinicalTrials.gov (registration number NCT02073188).

Keywords Type 1 diabetes · Self-monitoring blood glucose · Compliance · Telemedicine

Managed by Massimo Porta.

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Introduction

Management of type 1 diabetes in adolescents and young adults represents a challenge for healthcare providers [1]. Poor metabolic control relates to physiological changes of puberty, poor adherence to treatment regimens, reduced attendance to outpatient visits, and psychological factors [2].

Furthermore, short-term complications, such as hypoglycemia and diabetic ketoacidosis, represent a barrier for achieving metabolic targets [3]. DCCT trial showed that 5–7 years of poor glycemic control, even during adolescence and young adulthood, is associated with an increased risk of microvascular and macrovascular complications in the subsequent 6–10 years [4, 5].

In the last two decades, the availability of new insulins, insulin pumps, and glucose monitors has improved the care of patients with type 1 diabetes. This has been translated into reduced mean HbA1c levels and reduced rates of severe hypoglycemia, as documented by studies on population-based cohorts of children and adolescents with type 1 diabetes [6, 7]. Nevertheless, the achievement of the recommended targets still represents a problem for many patients. Although American Diabetes Association (ADA) and International Society for Paediatric and Adolescent Diabetes (ISPAD) have established a target HbA1c of 7.5% (58 mmol/mol) for pediatric population with type 1 diabetes [1], HbA1c concentrations reported in large multinational and national databases remain mostly between 8 and 9% [8]. In regional or national registries worldwide relative to 324,501 people with type 1 diabetes, the proportions of individuals with HbA1c <7.5% (58 mmol/mol) varied from 15.7% to 46.4% in the different areas among people aged <15 years, from 8.9% to 49.5% among people aged 15–24 years, and from 20.5% to 53.6% among people aged ≥ 25 years [9].

A recent study documented that more frequent SMBG measurements are associated with better metabolic control with a drop in HbA1c of 0.20% for each additional SMBG measurement per day [10]. Data from the DPV-Wiss database relative to 26,723 children and adolescents with type 1 diabetes showed that the frequency of SMBG decreases when age increases: an average of 6.0 measurements/day was found in children aged <6 years, versus 5.3 measurements/day in children aged 6–12 year, and 4.4/day in those aged >12 years [11]. However, effective self-management requires frequent and high levels of educational input and continuing support [12]. This requires an organizational model facilitating long-term relationships with adolescents and their families and facilitating multi-professional teamwork [13]. Nevertheless, time and facilities to implement structured self-management education are often suboptimal in diabetes centers.

Therefore, the specific needs of young people with type 1 diabetes necessitate innovative management strategies, among which telemedicine, i.e., the use of medical information exchanged from one site to another via electronic communications to improve a patient's clinical health status, is recognized as one of the most relevant [14]. Telemedicine includes a growing variety of applications and services using two-way video, e-mail, smart phones, wireless tools, and other forms of telecommunications technology. In particular, with the availability of internet and smart phone applications (apps) there is a hope that such technology could provide a mean to encourage treatment adherence in this group of patients [15]. At present, there are significant information gaps regarding the long-term effects, acceptability, costs, and risks of innovative telemedicine interventions, and further research into these issues is needed [16].

In the last few years, a new device has been developed to help patient in self-managing diabetes and achieve the desired target through an increase in the adherence to SMBG. The device is represented by the iBGStar™ glucose meter to be associated with the iBGStar™ Diabetes Manager Application installed on the iPod touch or iPhone OS. It has been developed to conjugate the features of the iBGStar™ products with the appealing Apple products. Hypothesizing that this advanced telemedicine system could improve metabolic control and compliance with SMBG in the complex population of adolescents and young adults with type 1 diabetes, we conducted a randomized controlled trial to compare iBGStar™ with a traditional self-monitoring blood glucose strategy.

Research design and methods

Detailed description of the experimental telemedicine system and the study protocol has been published elsewhere [17].

Briefly, the "i-NewTrend" study is an open-label, randomized (1:1) trial involving type 1 diabetes subjects aged 14–24 years, treated with basal–bolus insulin regimen, with HbA1c ≥ 8.0%, and poorly compliant with SMBG (i.e., performance of <30% of the recommended SMBG measurements). Compliance was assessed based on the measurements recorded in the glucose meter versus the number of tests prescribed by the physician.

Participants were randomized by 21 diabetes clinics in Italy to two different SMBG strategies:

- Group A: experimental glucose meter and telemedicine system (iBGStar™ + DMApp) (iBGStar);
- Group B: traditional glucose meter (Accu-Check Aviva™) (Control) (Supplemental Figure S1).

Patients in the iBGStar group received training on the use of the system. Both groups were instructed on the study procedures. No other intervention was implemented in the two groups other than standard clinical care. Patients in both groups were allowed to contact the center through SMS, e-mails, or telephone calls, if needed. In addition to the pre-planned study visits, extra visits were also allowed, based on clinical judgement.

After randomization, data were collected after 3 and 6 months (experimental phase) and after 12 months (post-trial observational phase). In the post-trial observational phase, all subjects used iBGStar^{TM} + DMApp, and the impact of initiating the experimental device also in Control group was assessed.

The objective of this study was to demonstrate the superiority of iBGStar^{TM} + DMApp as a component of the diabetes management versus traditional blood glucose self-monitoring system in:

- Reducing HbA1c levels after 6 months of follow-up;
- Improving the compliance to SMBG after 6 months.

Additionally, the study aimed to evaluate the impact of iBGStar^{TM} + DMApp versus traditional SMBG on patient quality of life and satisfaction, contacts between patient and physician, and safety.

Compliance with SMBG was assessed based on the measurements recorded in the glucose meter during the 2 weeks before the randomization visit and then during the whole follow-up of the randomized phase. Afterward, until visit V2, patients sent their glycemic test values and notes by mail monthly, nine reports in total. In both groups, all data recorded in the meters were collected and reported. Compliance was defined in three different ways: as dichotomous variable (i.e., frequency of SMBG $\geq$30% vs. $<$30% of the recommended frequency); average number of SMBG performed/week; and "percent compliance" (i.e., proportion of SMBG tests performed vs. number prescribed by the physician).

Changes in HbA1c levels and percentage of patients compliant with SMBG (i.e., performance of at least 30% of the recommended SMBG tests/week) after 6 months represented the study primary end points.

Secondary efficacy end points after 6 months were:

- Additional measures of metabolic control: percentage of patients with HbA1c $\leq$7.5%;
- Additional measures of compliance with SMBG: average number of SMBG/week; percent compliance;
- Quality of life and patient satisfaction: changes after 6 months in the scores of selected questionnaires;
- Number and type (extra visit, call, SMS, e-mail) of overall contacts between patient and center.

Safety end points were:

- Incidence of grade 1 and grade 2 hypoglycemia. Grade 1 was defined as symptoms of hypoglycemia: adrenergic symptoms (e.g., tachycardia, palpitations, shakiness), cholinergic symptoms (e.g., sweating), or neurologic symptoms (e.g., inability to concentrate, dizziness, hunger, blurred vision, obvious impairment of motor function, confusion, or inappropriate behavior) associated with a SMBG confirmed blood glucose value $<$60 with the patient still alert enough to seek self-treatment. Grade 2 was any episode resulting in coma, seizure, or significant neurologic impairment so that the subject is unable to initiate self-treatment or requires the assistance of another person;
- Adverse events, i.e., any untoward medical occurrence in a patient administered an experimental product and which does not necessarily have to have a causal relationship with this treatment;
- Serious adverse events, defined as any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect;
- Incidents, i.e., any malfunction or deterioration in the characteristics and/or performance of a device which, directly or indirectly, might lead to or might have led to death or to a serious deterioration in their state of health of a patient.

HbA1c levels, SMBG frequency, and quality of life score changes were also assessed during the observational phase of the study, i.e., after 12 months from randomization.

Socio-demographic and clinical information was collected on electronic clinical record forms (eCRFs). HbA1c levels were measured in a centralized laboratory (Centro Diagnostico EXACTA, Verona, Italy) and measured through high-performance liquid chromatography—National Glycohemoglobin Standardization Program (HPLC—NGSP). SMBG data were downloaded by the glucose meters on the physician's computer during the office visit and recorded on eCRF. Hypoglycemia episodes were assessed by reviewing patient diaries and reported on eCRF.

At baseline, after 6 months, and after 12 months, patients filled in a questionnaire including the following instruments:

- Audit of diabetes-dependent quality of life (ADDQoL-19) [18] to measure a diabetes impact rating, weighted by importance for 19 potentially applicable domains of life. The average weighted impact is a composite score of all applicable domains indicating individualized impact of diabetes on quality of life. Scores for single domains and average weighted impact can range from -9 (maximum negative impact of diabetes) to $+3$ (maximum positive impact of diabetes). The questionnaire also includes two single items measuring "present quality of life" and "impact of diabetes on quality of life" with scores ranging from -3 (extremely bad) to

+3 (excellent). ADDQoL was used in patients aged between 18 and 24 years;

- Diabetes Quality of Life for Youth (DQOLY) [19]: this tool consists of 52 items, divided into 4 sections: impact of diabetes (23 items); worries about diabetes (11 items); satisfaction with treatment (10 items); and satisfaction with life (7 items); one single item on health perception is also included. Questions are scored using a 5-point Likert scale, with the exception of health perception, which is measured using a 4-point Likert scale. Lower scores indicate poorer quality of life. For ease of comparisons across subscales, items on all subscales are scored in the same directions. DQOLY was used in adolescents aged between 14 and 17 years;
- Visual analogue scale (VAS): patient satisfaction with glucose meter was assessed through a visual analogue scale.

The protocol was approved by all the Ethics Committees of all participating centers, in accordance with the local legal requirements. The trial was registered at ClinicalTrials.gov (registration number NCT02073188).

Statistical analysis

Assuming a standard deviation of HbA1c of 0.9% and considering as clinically relevant a minimum between-group difference in HbA1c levels of 0.4%, the number of patients to be enrolled to ensure a power of 80% (alpha = 0.05) was 81 patients per arm. Assuming a dropout rate of 10%, 178 patients were needed. The same sample size ensured a statistical power of over 90% to detect a difference of 25% in the proportion of patients compliant with SMBG schedule (i.e., at least 30% of recommended measurements).

Randomization was performed through sealed envelopes. Random lists were computer generated and stratified by center. To ensure equal allocation rates within centers, permuted block randomization was used.

Baseline characteristics are summarized as mean and standard deviation (continuous, normally distributed variables), median and interquartile range (continuous, not normally distributed variables and ordinal variables), or percentage (categorical variables). Patient characteristics have been compared between study arms using the unpaired t test, the Mann–Whitney U test, or the Chi-squared test, as appropriate.

A mixed model analysis of covariance (ANCOVA) using an auto-regressive correlation structure, with intervention groups and visits as fixed factors and patients as a random factor, was used to analyze the changes from randomization to month 6 in the continuous efficacy variables. This analysis was followed by the between-group comparison and the within-group pre-post comparison, using the appropriate contrasts. Mixed models allow to account for missingness at random in a much more efficient way than multiple imputation methods, since it is not necessary to exclude any patient. For all the remaining secondary end points, the same methods were applied. The number of contacts and safety end points have been analyzed as incidence rates expressed as number of events per person-month. Incidence rate ratios (IRRs and 95% CI) have been estimated through Poisson regression analysis, and between-group differences in the number of adverse events were analyzed through exact Poisson regression analysis. Two-tailed p values <0.05 have been considered statistically significant.

In accordance with the study protocol, all analyses were also stratified by age (14–17 and 18–24 years) and gender. Additional analyses were conducted to measure the impact of higher compliance with SMBG and use of telemedicine features on HbA1c reduction adopting the same methods. Patients in the experimental groups with at least one e-mail, SMS, or telephone contact exchanged with the diabetes center through the experimental device during the 6-month follow-up were defined as "telemedicine users."

Results

From June 2012 to September 2014, 182 subjects were randomized by 21 centers in Italy. Baseline patient's characteristics are shown in Table 1. After randomization, study arms were balanced for all the examined characteristics. Figure 1 shows the study flowchart. Out of 182 patients randomized, 168 completed the experimental phase of the study (92.3%).

Primary end points

After 6 months, in both groups HbA1c levels were reduced ($-0.44 \pm 0.13\%$ in iBGStar and $-0.33 \pm 0.13\%$ in Control), and no significant between-group difference in HbA1c levels change was found ($p = 0.51$).

Furthermore, after 6 months, 53.6% of patients in the iBGStar group and 55.0% in the Control group became compliant to SMBG, without a statistically significant difference between groups ($p = 0.85$) (Supplemental Figure S1).

Secondary end points

Metabolic control

Results relative to HbA1c changes during the experimental phase are reported in Table 2. After 6 months, one patient

Table 1 Patients' characteristics by study arm

Characteristics		IBGStar	Control	*p* value*
N		92	90	
Age (years)		17.6 ± 3.1	17.8 ± 3.0	0.56
Age (%)	14–17	58.7	52.2	0.38
	18–24	41.3	47.7	
Gender (%)	Women	48.9	48. 9	1.00
	Men	51.1	51.1	
Living status (%)	Lives alone	3.3	3.3	0.6
	Lives with family	96.7	95.6	
	Other	0	1.1	
Occupational status (%)	Employed	9.8	15.6	0.44
	Unemployed	13.1	14.4	
	Student	77.1	70.0	
School level (%)	Primary or middle school	32.6	33.3	0.94
	High school	60.8	58.9	
	Graduate/postgraduate	5.4	5.6	
	Other	1.2	2.2	
Diabetes duration (years)		8.6 ± 4.5	9.0 ± 4.7	0.65
HbA1c (%)		9.9 ± 1.3	10.2 ± 1.5	0.18
Number of HbA1c measurements collected in the previous 12 months		3.6 ± 0.9	3.7 ± 1.2	0.48
% patients with at least one severe hypoglycemic episode (grade 2) in the previous 12 months		17.4	14.4	0.59
Number of severe hypoglycemic episodes (grade 2) in the previous 12 months		2.0 ± 7.6	1.1 ± 5.6	0.51
% patients with at least one episode of ketoacidosis in the previous 12 months		5.4	6.7	0.73
Number of episodes of ketoacidosis in the previous 12 months		0.1 ± 0.4	0.2 ± 1.2	0.7
Education to carbohydrate counting (%)		41.3	40.0	0.21
HbA1c (%)		9.9 ± 1.3	10.2 ± 1.5	0.18
BMI (Kg/m^2)		23.1 ± 3.7	23.1 ± 3.7	0.87
Diabetes complications (%)**		1.1	1.1	0.99
Any relevant condition ongoing at study entry (%)		20.0	17.0	0.61
Audit of diabetes-dependent quality of life (ADDQoL) (age class 18–24 years)	Average weighted score	−1.5 ± 1.1	−1.7 ± 1.6	0.84
	Present quality of life	0.8 ± 1.0	0.8 ± 0.8	0.98
	Impact of diabetes on quality of life	−1.1 ± 0.9	−1.2 ± 0.9	0.74
Diabetes Quality of Life for Youth (DQOLY) (age class 14–17 years)	Average score	26.8 ± 12.4	27.9 ± 10.5	0.47
	Impact of diabetes (23 items)	28.0 ± 12.3	25.3 ± 9.9	0.32
	Worries about diabetes (11 items)	20.1 ± 15.7	20.7 ± 15.1	0.83
	Satisfaction with treatment (10 items)	25.1 ± 15.5	29.8 ± 19.6	0.37
	Satisfaction with life (7 items)	35.8 ± 16.4	41.0 ± 16.3	0.19
	Health perception (1 item)	2.2 ± 0.8	2.3 ± 0.6	0.37
Visual analogue scale (VAS)		63.6 ± 21.6	63.5 ± 24.5	0.62

Data are mean and standard deviation or percentages

* Mann–Whitney *U* test or Chi-squared test

** Presence of at least one complication among: heart disease, cerebral vascular disease, diabetic neuropathy, diabetic retinopathy, kidney disease, or peripheral vascular disease

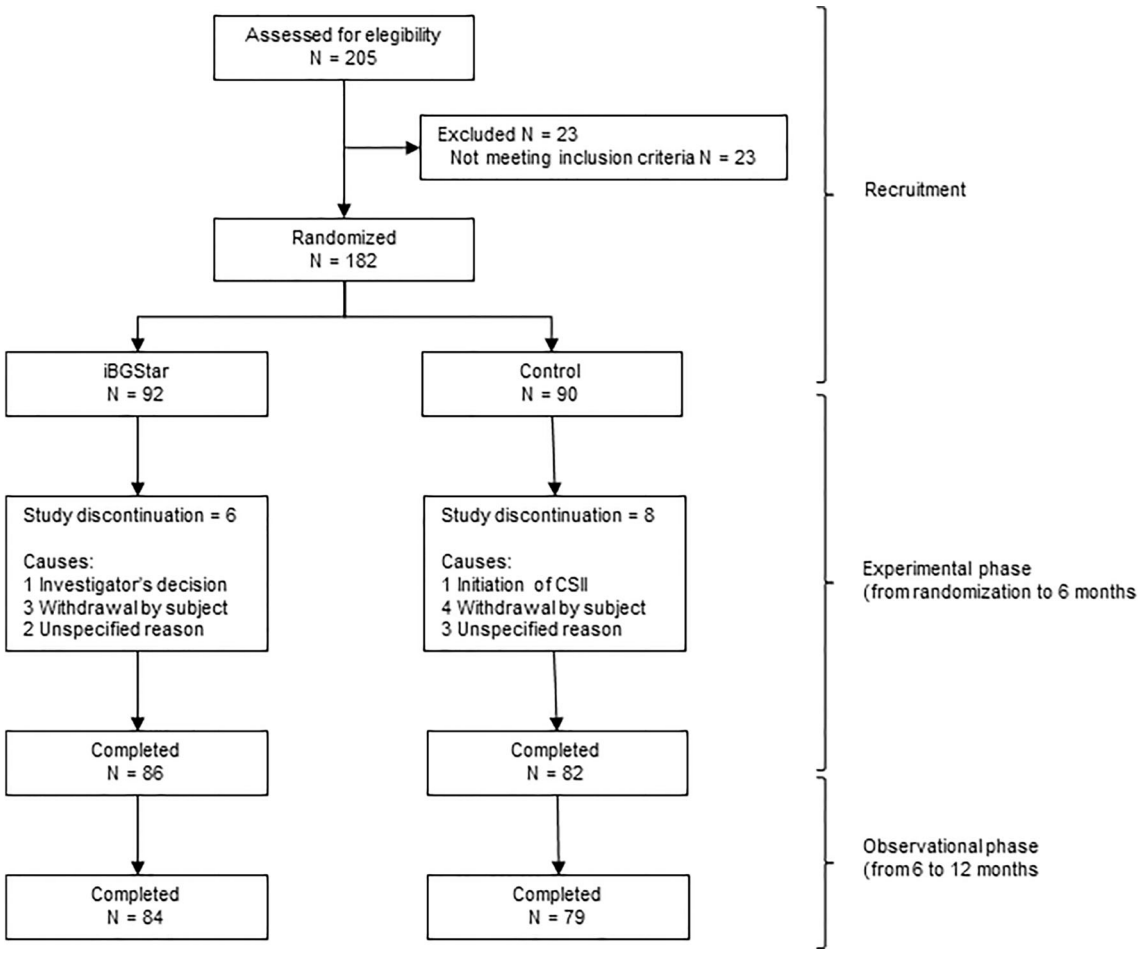

Fig. 1 Study flowchart

(1.1%) in the iBGStar group and three patients (3.6%) in the Control group reached the HbA1c target ≤7.5%.

Two additional analyses documented that:

1. After 6 months, HbA1c levels decreased by about 0.6% in patients who became compliant with SMBG, irrespective of the glucose meter used, while no or only minor changes in HbA1c levels were documented in patients who remained not compliant with SMBG during the study (Table 2).
2. After 6 months, within the iBGStar group, telemedicine users represented 38.0% of the sample and reduced their HbA1c levels by $-0.58 \pm 0.18\%$; patients who did not use the telemedicine features reduced HbA1c by $-0.26 \pm 0.21\%$ ($p = 0.25$).

From 6 to 12 months, HbA1c levels remained stable in the iBGStar group ($-0.07 \pm 0.14\%$), while they further decreased by $-0.31 \pm 0.14\%$ in the Control group after switching to the experimental meter ($p = 0.24$). The HbA1c change from 0 to 12 months was $-0.50 \pm 0.14\%$ in iBGStar and $-0.63 \pm 0.14\%$ in Control ($p = 0.64$).

At 12 months, one patient (1.2%) in the iBGStar group and six patients (7.7%) in the Control group had HbA1c ≤7.5%.

Compliance with SMBG

After 6 months, over 50% of patients in both study arms became compliant with SMBG (Supplemental Figure S2). The mean weekly number of SMBG increased from 8.8 ± 0.9 to 16.0 ± 0.9 in the iBGStar group and from 8.5 ± 0.9 to 16.2 ± 0.9 in the Control group. Compliance was reached more frequently in women than in men in both groups, while the two age classes did not substantially differ in terms of compliance (Supplemental Figure S2).

At 12 months (observational phase), the proportion of patients compliant to SMBG slightly decreased to 46.2% and 49.3% without differences between the study arms ($p = 0.70$).

Quality of life

After 6 months, no changes occurred in ADDQOL average scores in young adults aged 18–24 years and no changes

Table 2 Changes in HbA1c levels from 0 to 6 months by study arm overall and in specific subgroups

	IBGStar ($N = 92$)				Control ($N = 90$)				iBGStar versus Control	p value[§]
	Baseline*	3 Months*	6 Months*	Mean change 0–6**	Baseline*	3 Months*	6 Months*	Mean change 0–6**	Mean difference 0–6**	iBGStar versus Control
All patients	9.9 (1.3)	9.3 (1.6)	9.5 (1.4)	−0.44 (0.13)	10.2 (1.5)	9.9 (1.7)	9.8 (1.6)	−0.32 (0.13)	−0.12 (0.18)	0.51
Age 14–17	10.1 (1.3)	9.6 (1.9)	9.8 (1.6)	−0.39 (0.17)	10.3 (1.3)	9.9 (1.5)	9.8 (1.4)	−0.45 (0.18)	+0.06 (0.25)	0.82
Age 18–24	9.6 (1.2)	9.0 (1.1)	9.1 (1.0)	−0.50 (0.19)	10.1 (1.7)	9.9 (2.0)	9.9 (1.9)	−0.16 (0.19)	−0.34 (0.27)	0.21
Men	9.9 (1.1)	9.4 (1.5)	9.6 (1.5)	−0.32 (0.16)	10.2 (1.5)	9.9 (1.6)	10.1 (1.6)	−0.16 (0.16)	−0.16 (0.22)	0.48
Women	10.0 (1.5)	9.3 (1.7)	9.4 (1.4)	−0.55 (0.20)	10.2 (1.5)	9.9 (1.9)	9.6 (1.7)	−0.49 (0.21)	−0.06 (0.29)	0.83
Compliant with SMBG at 6 months[#]	9.7 (1.3)	8.9 (0.8)	9.1 (0.9)	−0.60 (0.18)	9.8 (1.2)	9.4 (1.3)	9.2 (1.3)	−0.58 (0.18)	−0.02 (0.25)	0.93
Not compliant with SMBG after 6 months[##]	10.3 (1.3)	10.0 (2.1)	10.1 (1.7)	−0.22 (0.20)	10.7 (1.6)	10.5 (1.7)	10.8 (1.8)	0.03 (0.22)	−0.25 (0.29)	0.40

[#] Compliant with SMBG = patient with a frequency of self-monitoring blood glucose (SMBG) at 6 months ≥30% the prescribed frequency

[##] Not compliant with SMBG = = patient with a frequency of SMBG at 6 months <30% the prescribed frequency

* Mean and standard deviation

** Estimated mean change and standard error

[§] Between-group comparison for each parameter (iBGStar vs. Control); p values <0.05 are considered statistically significant

occurred in DQOLY scores in adolescents aged 14–17 years (Table 3). Some subscales of DQOLY deserve consideration: during the experimental phase, "satisfaction with treatment" changed in favor of the iBGStar group (+4.5 ± 2.9 vs. −3.8 ± 2.9; $p = 0.05$) and "satisfaction with life" remained stable in the iBGStar group (−0.2 ± 2.7) while it decreased in the Control group (−5.8 ± 2.9) ($p = 0.05$), but the differences did not reach statistical significance. No other relevant differences emerged in quality of life dimensions.

Improvements in the VAS score were found in both study groups after 6 months, but they were more marked in the iBGStar group (+12.4 ± 2.5 vs. +5.7 ± 2.9; $p = 0.05$), even if statistical significance was not reached (Table 3). At 12 months, quality of life was generally unchanged.

Contacts between patient and diabetes center

Distributions of contacts between patient and diabetes clinics were markedly skewed, with a few patients accounting for many contacts. Contact rates (telephone calls, SMS, or e-mails) were significantly higher in the iBGStar group (via telemedicine features of the experimental device) than in the Control group (via traditional systems), while no differences between study arms were found in face-to-face visits (Table 4).

Safety

No relevant adverse events (AEs) occurred during the experimental phase of the study. Overall, 9 patients (5.1%) had 14 AEs, of whom 6 patients (6.8%) with 11 AEs in the iBGStar group and 3 patients (3.4%) with 3 AEs in the Control group ($p = 0.41$). All AEs were classified as "not related" to the study products.

No statistically significant between-group differences in the incidence per person-month of grade 1 and grade 2 hypoglycemia were found [Grade 1 IR and 95%CI: 8.37; 4.61–15.21 in the iBGStar group and 8.85; 4.98–15.71 in the Control group ($p = 0.89$); Grade 2 IR and 95%CI: 0.48; 0.23–0.98 in iBGStar vs. 0.36; 0.15–0.83 in Control ($p = 0.60$)].

No incidents occurred.

Conclusions

The study could not demonstrate the superiority of the experimental glucose monitoring strategy versus the traditional approach in improving metabolic control and compliance with SMBG in this population of poorly adherent adolescents and young adults with type 1 diabetes.

Table 3 Changes in quality of life dimensions and satisfaction with glucose meter after 6 months by arm

	IBGStar ($N = 92$)			Control ($N = 90$)			iBGStar versus Control	p value[§]
	Baseline*	6 Months*	Mean change 0–6**	Baseline*	6 Months*	Mean change 0–6**	Mean difference 0–6**	iBGStar versus Control
ADDQoL (18–24 years)								
Average weighted score	−1.5 (1.1)	−1.6 (1.5)	−0.15 (0.17)	−1.7 (1.6)	−1.6 (1.5)	+0.14 (0.17)	−0.29 (0.24)	0.23
Present quality of life	0.8 (1.0)	1.0 (0.8)	+0.1 (0.1)	0.8 (0.8)	0.9 (1.0)	+0.1 (0.1)	+0.05 (0.2)	0.81
Impact of diabetes on quality of life	−1.1 (0.9)	−1.1 (0.9)	−0.03 (0.2)	−1.2 (0.9)	−1.2 (0.9)	−0.02 (0.2)	−0.01 (0.2)	0.95
DQOLY (14–17 years)								
Average score	26.8 (12.4)	25.8 (12.1)	+0.4 (1.6)	27.9 (10.5)	25.9 (9.8)	−0.8 (1.6)	+1.2 (2.3)	0.60
Impact of diabetes	28.0 (12.3)	27.3 (13.9)	−0.5 (1.5)	25.3 (9.9)	25.1 (10.1)	+1.0 (1.6)	−1.4 (2.2)	0.52
Worries about diabetes	20.1 (15.7)	21.9 (17.3)	+0.8 (2.2)	20.7 (15.1)	20.1 (13.6)	+2.0 (2.2)	+1.1 (3.1)	0.72
Satisfaction with treatment	25.1 (15.5)	27.3 (15.1)	+4.5 (2.9)	29.8 (19.6)	26.7 (15.5)	−3.8 (2.9)	+8.3 (4.1)	0.05
Satisfaction with life	35.8 (16.4)	35.1 (17.7)	−0.2 (2.7)	41.0 (16.3)	34.9 (15.5)	−5.8 (2.9)	+5.6 (4.0)	0.17
Health perception	2.2 (0.8)	2.2 (0.8)	0.0 (0.1)	2.3 (0.6)	2.3 (0.8)	0.0 (0.1)	0.0 (0.2)	0.90
VAS								
Overall population	63.6 (21.6)	75.8 (17.4)	+12.4 (2.5)	63.5 (24.5)	69.6 (18.9)	+5.7 (2.5)	+6.7 (3.5)	0.05
14–17 years	60.6 (21.7)	75.6 (20.2)	+15.0 (3.4)	60.1 (25.0)	68.8 (18.2)	+7.2 (3.6)	+7.8 (4.9)	0.12
18–24 years	67.9 (21.0)	76.1 (13.0)	+8.7 (3.5)	67.1 (23.6)	70.4 (19.9)	+4.3 (3.3)	+4.4 (4.8)	0.37
Men	59.0 (21.6)	73.9 (19.4)	+15.1 (3.4)	63.5 (25.2)	66.0 (19.8)	+2.1 (3.4)	+13.0 (4.8)	**0.009**
Women	68.3 (20.7)	77.8 (15.1)	+9.7 (3.5)	63.5 (24.0)	73.6 (17.2)	+9.6 (3.5)	0.0 (4.9)	1.00

Bold value indicates statistically significant

* Mean and standard deviation

** Estimated mean change and standard error

§ Between-group comparison for each parameter (iBGStar vs. Control); p values <0.05 are considered statistically significant

The lack of difference was due to similar improvements in both groups, consisting of a small but not trivial reduction in HbA1c levels and a substantial increase in compliance with SMBG. A trial effect may explain the improvements emerged both in the experimental and in control group of this study [20].

Several important issues emerge from the study. First, good metabolic control is difficult to achieve in this challenging population. The recommended target of HbA1c $\leq$7.5% in our study was reached by only a few participants. Nevertheless, it is possible to increase the compliance with SMBG in this population, and performing at least 30% of measurements prescribed translates into a significant HbA1c reduction. In both study arms, improvements in HbA1c were obtained and maintained in the long run in association with a small increase in the frequency of SMBG tests from around 8 to 16 measurements/week (i.e., from 1.1 to 2.3 measurements/day). Telemedicine (i.e., a technologically advanced system facilitating the health communication between patient and physician), if used, can further increase the compliance with SMBG.

The association between frequency of SMBG and mean levels of HbA1c has been previously documented from diabetes registries [10, 11, 21]. However, due to the observational nature of these data, a clear cause–effect relationship cannot be established. Furthermore, a high compliance with SMBG can represent a proxy for greater adherence to medical recommendations, rather than a true effect of SMBG frequency on metabolic control. Our study suggests that increasing the frequency of SMBG also in this challenging population of poorly controlled and poorly compliant adolescents/young adults may have an impact on HbA1c levels.

Technologically advanced solutions can represent an option for motivating the patient to regularly monitor blood glucose [15, 22–24], but the choice of patients with the highest likelihood of benefitting from technology is a key aspect. We analyzed data by gender and age classes, and

Table 4 Distribution of contacts by study arm from 0 to 6 months. Results of the Poisson regression analysis

	Group	Overall number of contacts during 6 months	% of patients with at least 1 contact during 6 months	Distribution of contacts during 6 months (median and range)	Incidence rate of contacts per person-month and 95% confidence intervals	Incidence rate ratios (IRRs) and 95% confidence intervals
All contacts	iBGStar	292	53.4	1 (0–39)	0.55 (0.43–0.71)	**3.14 (1.89–5.20)**
	Control	92	54.0	1 (0–7)	0.18 (0.11–0.27)	1.0 (RC)*
Face-to-face visits	iBGStar	58	35.2	0 (0–5)	0.11 (0.08–0.15)	0.94 (0.61–1.45)
	Control	61	47.1	0 (0–5)	0.12 (0.09–0.16)	1.0 (RC)
e-Mails	iBGStar	90	21.6	0 (0–15)	0.17 (0.12–0.23)	**8.09 (3.06–21.40)**
	Control	11	3.4	0 (0–6)	0.02 (0.01–0.05)	1.0 (RC)
Telephone calls	iBGStar	96	33.0	0 (0–15)	0.18 (0.14–0.24)	**5.93 (2.76–12.77)**
	Control	16	8.0	0 (0–4)	0.03 (0.02–0.06)	1.0 (RC)
SMS	iBGStar	48	11.4	0 (0–15)	0.09 (0.06–0.13)	**11.86 (3.34–42.16)**
	Control	4	1.1	0 (0–4)	0.01 (0–0.03)	1.0 (RC)

RC reference class

IRRs in bold express the statistically significant differences in the rate of contacting the diabetes clinic (iBGStar group vs. Control group)

these variables influenced some results, but many other characteristics, needs, skills, attitudes can determine a different use of technology. In our study, only a small minority of patients allocated to the iBGStar group regularly used the device features and telemedicine contacts during the experimental phase, so the full potentiality of this technology remains unexploited. The suboptimal use of experimental technologies in studies represents a main limit to evaluate their maximum benefits. Innovative adaptive designs enabling the selection of patients more willing to exploit innovative devices may represent a new methodological frontier to formally test efficacy and safety of new technologies [25].

Furthermore, little is known about how the most advanced technology affects treatment satisfaction and health-related quality of life in people with diabetes. Besides impact on metabolic control and compliance with SMBG, our study took into consideration changes in quality of life; results suggested that doubling the frequency of SMBG did not negatively impact on quality of life in this population of adolescents/young adults with type 1 diabetes.

Finally, the study documented that the management of patients through telemedicine system can change number and type of contacts between patient and diabetes clinic, and this can have an impact on healthcare expenditure. We found (in an experimental setting) that distribution of contacts was very skewed in both study arms, with a few patients accounting for the majority of contacts. In the years to come, it will be important to improve the cost-effectiveness profile of telemedicine solutions through the identification of patients suitable for replacing face-to-face visits with telemedicine contacts.

The major strength of our study was the formal testing of the experimental device in this challenging population, taking into consideration clinical, person-centered, and resource utilization outcomes. In addition, we evaluated the long-term impact of the device also in a post-trial observational setting. The study also has limitations. First, the unexpected underutilization of the device features and telemedicine contacts may have diminished the efficacy of the technology. Second, the interpretation of our findings is made difficult by the possible presence of a trial effect.

In conclusion, we could not demonstrate the superiority of the experimental glucose meter versus the traditional one. Nevertheless, the study emphasizes the need to find new ways and adequately use old ones to manage diabetes in this difficult age group. Telemedicine can be an option to motivate young patients, although benefits depend on gender, age, and attitudes; an accurate identification of patients more likely to benefit from advanced technologies represents a high priority.

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Compliance with ethical standards

Conflict of interest Paolo Di Bartolo has been member of Advisory Panels of Novo Nordisk Inc., Eli Lilly and Company, Abbott, Novartis Corporation; he received Speaker's Bureau from Eli Lilly and Company, Novo Nordisk Inc., Merck Sharp & Dohme, Boehringer Ingelheim Pharmaceuticals, Inc., Medtronic, Inc.,Ypsomed, Menarini Group, Abbott, Novartis Corporation, Roche Diagnostics, AstraZeneca Pharmaceuticals LP, Bayer HealthCare, Sanofi Pasteur SA. Maria Chiara Rossi has been member of an Advisory Panel of Novo Nordisk. Valentino Cherubini and Marco Scardapane have no

conflict of interests. Dario Iafusco has been member of Advisory Panels of Eli Lilly and Company, Abbott and received Speaker's Bureau from Eli Lilly and Company, Boehringer Ingelheim Pharmaceuticals, Inc., Medtronic, Inc., Roche Diagnostics, Sanofi Pasteur SA. Antonio Nicolucci received Research Support from Sanofi Pasteur SA, Novo Nordisk Inc., Merck Sharp & Dohme, Bristol-Myers Squibb Company, ForaCare, Artsana, Sanofi, Novo Nordisk, Dexcom.

Ethical standard The study was conducted following accepted principles of ethical and professional conduct.

Human and animal rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed consent Informed consent was obtained from all patients for being included in the study.

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