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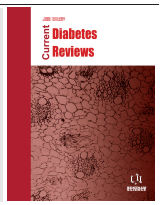

A Prospective Study for Introducing Insulin Pens and Safety Needles in a Hospital Setting. The SANITHY Study.

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Abstract: ***Background*:** to assess costs and safety of insulin pen devices and safety needles as compared to vial/syringes in hospitalized patients requiring insulin therapy in a General Hospital in Northern Italy.

***Materials and Methods*:** in a prospective 9-month study, consecutive patients admitted to three Hospital Units received insulin therapy through either a traditional disposable syringe method, or pen/safety needles with dual-ended protection, or disposable safety syringes. We compared the median direct (insulin and devices) and indirect (insulin supply at discharge, insulin wastage) costs of a 10-day in-hospital insulin treatment in the 3 study groups, additionally accounting for the costs related to the observed needlestick injury rate. Patients' safety during in-hospital stay (hypo- and hyperglycemia episodes) and satisfaction were also assessed.

***Results*:** N=360 patients (55% men, mean age 75.6 years, 57% with DM since ≥10 years) were recruited in the study. Insulin pens had higher median direct cost than both traditional syringes (43 vs. 18 €/patient, p<.0001) and safety syringes (21.5 €/patient, p<.0001). However, when also indirect and injuries costs were taken into account, the estimated savings for using pens over traditional syringes were as high as 32 €/patient (45.8 vs. 77.6 €/patient, p-value <.0001). No differences in patients' safety were observed. 74% and 12% of patients using pens and syringes would like to continue the method at home, respectively (p<0.0001).

***Discussion*:** A selective use of individual pre-filled pens/safety needles for patients who are likely to continue insulin therapy at home may strongly reduce hospital diabetes treatment related costs.

Keywords: Inpatients insulin therapy, insulin pens, safety needles, customer satisfaction, safety devices, insulin therapy costs.

1. INTRODUCTION

For decades, the classical method for subcutaneous insulin administration was represented by the vial/syringe system. The first insulin pen injector was introduced in the 1980s and was conceived combining insulin vial and syringe into a single component [1]. Advantages of insulin pens over syringes for outpatient care have been confirmed by numerous studies and are represented by ease of use, discretion of employ in public, ease in transport, reduction of time of therapy administration, reduction in fear of injection, greater accuracy in insulin dosage [2-6]. These benefits are associated with patient preference, treatment satisfaction, better-quality of life so as to improve adherence to insulin treatment and achieve better glycemic control [7-12]. Despite these arguments and the wide availability of pen devices, vial/syringe for subcutaneous insulin injection is still the preferred system for in-hospital insulin delivery, mainly due to direct costs [13] and safety concerns both on the patients [14, 15] and on the healthcare professionals [16] sides.

In the light of the recent introduction on the market of more advanced safety features for pen devices, potentially reducing needlestick injury rates among healthcare professionals, new researches are needed to investigate the potential of insulin pens in the hospital setting.

2. MATERIALS AND METHODS

The SANITHY (SAfety Needles and Insulin pens at Treviglio Hospital - ItalY) prospective study was designed to compare the use of prefilled insulin pens and novel safety needles with disposable traditional or safety syringes and

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insulin vials for the administration of insulin therapy in hospitalized patients with diabetes, in terms of costs, safety and satisfaction. In this paper, we report on economic outcomes, differentiating direct and indirect costs, as well as on patients' safety and satisfaction. Patients on multiple daily injections according to "Basal Bolus" (which includes an injection of long-acting insulin and a rapid-acting analogue at each meal, to roughly emulate how a non-diabetic person's body delivers insulin) [17] or "Basal Plus" (*i.e.* an injection of long-acting analogue and correction with one pre-meal short-acting insulin) [18] were consecutively enrolled from three medical Units at medium/high level of care (*i.e.*: from standard to highly specialized intensity of medical care being provided by the physician or health care facility), Department of Internal Medicine, Treviglio General Hospital, Northern Italy, from October 2012 to April 2013, and from October to December 2013. All the enrolled patients received their personalized insulin treatment according to the study period, as follows. During the first three-month period (Phase I), conventional disposable syringes and 10mL insulin vials were used. Lyspro (Humalog®) was the rapid acting analogue, while Glargine (Lantus®) was the basal one. In the successive three months (Phase II), prefilled insulin pens (Humalog KwikPen® and Lantus SoloSTAR®) and novel needlestick prevention devices (safety needles BD Auto-Shield Duo®) were introduced. Finally, from October to December 2013 (Phase III) the same rapid acting or basal analogues were used with disposable safety-engineered insulin syringes with permanently attached needle (BD-Safety Glide Insulin® TNT: Tiny Needle Technology, 1 mL, 29 Gx1/2), recently introduced in Italy, in accordance with European Legislation 2010/32/UE [19]. At the beginning of the study the involved nurses received a specific training which included three theoretical-practical meetings, with interactive sessions, related to the use of the pen and the safety needle, with individual "mastery" testing of novel devices. The study was conducted according to the Declaration of Helsinki principles, was approved by the Independent Ethical Committee of the Treviglio Hospital, and informed consent was obtained from every patient.

2.1. Outcome Measures

Economic Outcomes

We collected information on direct and indirect costs related to in-hospital insulin treatment for each inpatient enrolled in the study. Direct costs included insulin, insulin administration devices (traditional syringes, pens with safety needles or safety syringes, according to the study phase), and blood glucose self-monitoring costs (test strips and lancets). Indirect costs included the costs of 4 days of insulin treatment supply at discharge, according to current Regional law which aims to ensure the continuity of care between hospital and territory [*Delibera Regione Lombardia, DGR n° 5/12317 del 30/7/1991*]. For each patient discharged alive, costs of discharge were referred to insulin vials (10mL; 1,000 insulin units each; 1 bran new vial of rapid acting analogue, and 1 of basal insulin) with 16 traditional disposable syringes for patients discharged in Phase I and III (in order to allow a maximum of 4 injection a day, at least for 4 days), and pre-filled pens (3mL; 300 insulin units each; pens were already individually "in use" during hospital stay; in few occasions, bran new pens were supplied: 1 of rapid acting analogue, and 1 of basal insulin), with 16 standard needles in Phase II (coverage of 4 days insulin treatment, as above indicated). Insulin wastage costs were estimated from the number of insulin units each patient was not likely to use at home, due to change in insulin delivery method or discontinuation of insulin treatment, before insulin expiration date (28 days). Given the lack of a European standardized price list, direct and indirect costs were taken from the official price list of the study Hospital. Finally, we added indirect costs related to nurses' injuries. During the study period, we observed two needle-stick injuries, both in Phase I, corresponding to an injury rate of 0.31 per 1,000 injections with traditional syringes. Injury cost was fixed at € 850 from Italian available literature [20]. The total cost was the sum of direct, indirect, and injury costs.

Patient Safety

Patients safety was defined in terms of mistakes in insulin administration (any error associated with insulin therapy, such as wrong dose, or wrong patient, or wrong insulin, or missing doses), and frequency of hypoglycemic (glucose <70 mg/dl) and hyperglycemic (glucose >300 mg/dl) events occurred during the 3 study periods. These episodes were defined on the basis of fingerstick blood glucose monitoring, confirmed by plasma assay and reported on the nursing diary.

Patient Satisfaction

Patient satisfaction degree to therapy was assessed through a questionnaire delivered to each patient (or caregiver) at discharge. For this purpose, the Italian version of the Diabetes Treatment Satisfaction Questionnaire (DTSQ) [21] was used. The questionnaire included 8 questions about the degree of satisfaction to insulin treatment performed during hospitalization, treatment safety in terms of correctness of the administered dose, injection aching, convenience of the used device, satisfaction in continuing at home with the device used during hospitalization.

Statistical Analysis

The distribution of main demographic and clinical features of patients at hospital admission, and the length of in-hospital insulin treatment (in days) was summarized by means of descriptive statistics. We tested the null hypothesis of no difference among patients enrolled in the three study periods using F-tests, chi-square test, or non-parametric Kruskal-Wallis rank test, for mean, prevalence and median values, respectively [22]. Direct costs are reported as median (25^{th}-75^{th} percentile) cost per patient (€/patient) for a 10-day in-hospital insulin treatment (median length). A common length was chosen since it differed among the three study periods (see Table **1**). Differences between insulin pens and traditional or safety syringes were tested using the Wilcoxon rank test. A total median cost for 10-day insulin treatment was the sum of direct, indirect and injuries costs. Patient safety was defined as the prevalence of patients reporting episodes of hypo- or hyperglycemia; differences in the three study phases were tested using a chi-square test. The patient satisfaction questionnaire was distributed to all enrolled patients in a given study period, only once in case of repeated admission in the same study phase (n=12 patients). N=5

Table 1. Demographic and clinical characteristics of patients at hospital admission.

	SANITHY Study All Patients	Phase I Vial/Traditional Syringe	Phase II Pen/Safety Needle	Phase III Vial/Safety Syringe	p-value
N	360	120	111	129	-
Age	75.6 (11.8)	75 (10.7)	76 (11.6)	75.6 (13.0)	0.8
Men (%)	198 (55.0%)	71 (59.2%)	52 (46.8%)	75 (58.1%)	0.1
Duration of diabetes (%)					
Newly diagnosed	32 (8.9%)	10 (8.3%)	11 (10.1%)	11 (8.5%)	0.4
Less than 10 years	123 (34.4%)	42 (35%)	30 (27.5%)	51 (39.5%)	
More than 10 years	203 (56.7%)	68 (56.7%)	68 (62.4%)	67 (51.9%)	
Diabetes treatment at admission (%)					
Diet alone	39 (10.9%)	12 (10%)	13 (11.8%)	14 (10.9%)	0.6
Oral Antidiabetic Drugs	106 (29.5%)	35 (29.2%)	27 (24.5%)	44 (34.1%)	
Insulin (vial/syringe)	12 (3.3%)	3 (2.5%)	3 (2.7%)	6 (4.7%)	
Insulin pen	202 (56.3%)	70 (58.3%)	67 (60.9%)	65 (50.4%)	
HbA1c (%) at admission	8.05 (1.68)	8.15 (1.82)	8.49 (1.81)	7.58 (1.24)	<.0001
HbA1c (mmol/mol) at admission	64.5 (18.3)	65.6 (20.0)	69.3 (19.8)	59.3 (13.6)	<.0001
FPG at admission (mg/dL)	218.7 (138.3)	231.5 (168.1)	243.7 (142.2)	185.2 (90.5)	0.002
In-hospital days on insulin therapy*	9 (6, 17)	12 (7, 20)	8 (4, 16)	9 (6, 17)	0.01
In-hospital death (%)	25 (6.9%)	6 (5%)	9 (8.1%)	10 (7.8%)	0.3
Hospital Unit at discharge (%)					
Neurology/Stroke Unit	90 (25%)	45 (37.5%)	35 (31.5%)	10 (7.8%)	<.0001
Internal Medicine/Urgent Care	207 (57.5%)	57 (47.5%)	51 (45.9%)	99 (76.7%)	
Cardiology/Coronary Unit	63 (17.5%)	18 (15%)	25 (22.5%)	20 (15.5%)	

Numbers are mean (SD) or n (%), unless otherwise stated. *: median (25^{th}-75^{th} percentiles); FPG: Fasting Plasma Glucose

patients were lost at discharge, while n=40 patients did not complete the questionnaire due to either medical conditions (Alzheimer's, dementia, encephalopathy, stroke or coma; n=37), or to poor Italian knowledge (n=3). For this analysis, phase I and III patients were considered together, as both received insulin via syringes. The Cronbach's alpha metric [23] was 0.76 and 0.82 in the syringe and pen groups respectively, suggesting a satisfactory internal consistency of compilation. For each item, we compared the prevalence of patients answering "satisfied" or "very satisfied" in the syringe/insulin pen groups, by means of a chi-square test adjusting for age, sex and diabetes duration. In a sensitivity analysis, we replicated the analysis by considering only those patients who did not use syringes or pens at hospital admission. All the analyses were conducted using the SAS software, 9.2 release.

3. RESULTS

A total of 363 patients were enrolled: 122, in Phase I (usual treatment group, receiving vial/traditional syringe system); 112, in Phase II (prefilled pen/safety needle group); and 129, in Phase III (vial/safety syringe system). Three patients were dropped out either in Phase I (use of insulin pens, n=2) or in Phase II (pen refusal, n=1), leaving a total size of 360 patients for the analyses. Table **1** shows the demographic and clinical characteristics of the enrolled patients, according to the study phase. Age (mean 75.6 years), gender (55% men), duration of diabetes (57% more than 10 years) and treatment at admission (60% insulin users, only 3% on traditional syringes) did not differ among the study periods (all p-values >0.1). However, patients enrolled in Phase III had a better glycometabolic control at admission (lower HbA1c, p-value <0.0001, and reduced fasting plasma glucose, p=0.002); 75% of them were enrolled in the internal medicine unit, vs. 48% and 46% in Phase I and II, respectively (p-value<0.0001). Nevertheless, in-hospital death prevalence did not change significantly in the three periods (p=0.3), nor did the distribution of the Diagnostic Related Groups (DRGs), a proxy of comorbidities (data not shown). Finally, the median length of in-hospital insulin treatment was 12 days in Phase I, significantly longer than in the remaining two periods (p=0.01).

Table 2. Median direct and indirect costs of 10-day in-hospital insulin treatment per patient, according to insulin delivery group.

	Phase I Vial/Traditional Syringe	Phase II Pen/safety Needle	Phase III Vial/Safety Syringe	p-value[1]	p-value[2]
Direct costs of 10-day in-hospital treatment (Euro)*					
Insulin	6.5 (4.6, 7.8)	20.1 (12.6, 36.7)	5.1 (3.3, 8.4)	<.0001	<.0001
Devices	11.5 (10.6, 12.9)	22.9 (20.5, 24.3)	16.4 (13.6, 17.4)	<.0001	<.0001
Costs of insulin supply at discharge (Euro)^	50.9 (19.9, 50.9)	0.8 (0.6, 0.8)	50.9 (0.0, 50.9)	<.0001	<.0001
*Of which: estimated costs of wasted supply (Euro)^*	26.8 (4.8, 33.8)	0.0 (0.0, 0.6)	21.6 (0.0, 38.2)	-	-
Total cost of 10-day in-hospital treatment and supply at discharge (Euro)^	68.2 (40.5, 71.1)	45.8 (36.9, 63.9)	71.4 (22.3, 75.8)	0.02	0.08
Additional costs related to nurses' injuries (Euro)**	9.9 (8.8, 10.5)	-	-	-	-
Total costs, including nurses' injuries (Euro)^	77.6 (46.5, 81.1)	45.8 (36.9, 63.9)	71.4 (22.3, 75.8)	<.0001	0.08

*: Direct costs of in-hospital treatment are expressed as median value per patient (25°-75° percentile), considering a length of insulin treatment equal to 10 days (observed median length)
^: among n=335 discharged alive (93%)
**: Considering the observed injury rate (per 1.000 injections) during the study, a median insulin treatment of 10 days, and a direct cost of 850 euros per injury (14).
p-value comparing median costs. 1: pen/safety needle vs. vial/traditional syringe; 2: pen/safety needle vs. vial/safety syringe.

Table 3. Prevalence of patients presenting >1 episode of either hypoglycemia or hyperglycemia during the hospital stay.

	Phase I Vial/traditional Syringe	Phase II Pen/Safety Needle	Phase III Vial/Safety Syringe	p-value
N	120	111	129	
Patients presenting >1 in-hospital hypoglycemic event (%)	12 (10%)	15 (13.5%)	9 (7%)	0.3
Patients presenting >1 in-hospital hyperglycemic event (%)	38 (31.7%)	30 (27.0%)	30 (23.3%)	0.3

p-value testing the difference in the prevalence of episodes of hypo- or hyperglycemia among the three groups, adjusted for age, sex and diabetes duration.

Economic Outcomes

Table **2** reports the median direct and indirect costs per patient of 10-day in-hospital insulin treatment, according to insulin delivery device, as well as two p-values testing the difference in median costs between pen devices with traditional and safety syringes, respectively. Direct insulin costs were higher in the group of pens (20.1 €/patient) compared to the groups treated with syringes (traditional syringe: 6.5€/patient; safety syringe: 5.1€/patient; both p-values <.0001). Direct costs of insulin pen devices were 22.9€/patient, higher than both costs of traditional syringe (11.5€/patient, p<.0001) and safety syringe (16.4€/patient, p<.0001). In contrast, indirect costs at discharge were higher in the two syringe groups, with a median cost of 50.9€/patient vs. 0.8€/patient in the insulin pen group (both p-values<0.0001). Of note, the estimated costs of insulin wasting cover about 50% of the supply in the syringe groups. Total costs (direct + indirect) for 10-days of in-hospital treatment were significantly lower for insulin pens vs. traditional syringes (45.8€/patient vs. 68.2€/patient, p=0.02), while the difference in median costs with safety syringes was not significant (45.8€/patient vs. 71.4€/patient, p=0.08). Finally, when injury costs were taken into account for the traditional syringe group, the median saving for 10-days insulin treatment with insulin pens was as high as 31.8€/patient (p<.0001).

Patient Safety

No insulin-related medication errors, no "missing doses" or "near-miss" events were reported in all groups, during observational study time. A total number of 36 patients (10%) reported at least one episode of hypoglycemia during hospital stay, with no significant differences according to the treatment group (p-value 0.3; Table **3**). The prevalence of patients with at least one episode of hyperglycemia was 27% (98/360), but no significant differences were reported among the three study phases (p=0.3; Table **3**).

Table 4. Patients' satisfaction for the received in-hospital treatment.

Questionnaire Items	Phase I and III Vial/Syringe*		Phase II Pen/Safety Needle		p-value
	N	% Very Satisfied	N	% Very Satisfied	
The method used to give me my insulin in the hospital was convenient.	209	61.7	94	94.7	<.0001
I was confident I was given the correct dose of insulin during my hospital stay.	209	72.7	93	83.0	0.1
The method used to give me my insulin in the hospital was not aching.	208	72.1	93	77.4	0.3
The method used to give me my insulin in the hospital was simple and easy.	209	40.7	93	85.0	<.0001
The method used to give me my insulin in the hospital was able to help in obtaining a good glycemic control.	208	53.8	93	87.2	<.0001
Overall, I was satisfied with my knowledge on diabetes and on my diabetes awareness.	206	40.8	94	74.5	<.0001
I would recommend to other people with diabetes to use insulin by the method I used during my hospital stay.	208	38.9	93	89.3	<.0001
I would like to continue taking insulin at home by the method used during my hospital stay.	209	12.4	93	74.2	<.0001

*: including both traditional and safety syringes.
p-value testing the difference in the prevalence of "satisfied" or "very satisfied" answers in each item of the Italian version of the Diabetes Treatment Satisfaction Questionnaire, among the different in-hospital insulin administration groups, adjusted for age, sex and diabetes duration.

Patient Satisfaction

Table **4** reports the prevalence of "satisfied" or "very satisfied" answers to each of the 8 items of the satisfaction questionnaire, according to insulin treatment device. After adjustment for age, gender and diabetes duration, statistically significant differences emerged for almost all of the answers given by patients between the 2 groups. In particular, patients in the pen group were more satisfied with the treatment received (94.7% vs 61.7%, p<.0001), considering the method used for insulin therapy easier/comfortable (85% vs 40.7%, p<.0001); they were more satisfied to continue at home with the devices used in hospital (74.2% vs 12.4% p<.0001), and would recommend the insulin administration method used during hospitalization to other patients with diabetes (89.3% vs 38.9%, p<.0001). There were no significant differences between the 2 groups with regard to the answers to question about the correctness of the administered dose (p=0.1) or aching at the injection's site (p=0.3). These findings were largely confirmed also in the subgroup of newly insulin users: satisfaction for insulin pens was still as high as 92%, and 56% of patients would likely continue using pens at home, vs. 7% in the vial/syringe group (p-value <0.0001).

4. DISCUSSION

In the SANITHY study, the direct costs of in-hospital insulin therapy with the innovative needlestick prevention devices (pre-filled pens/safety needles, and vial/disposable safety syringes) were higher than with the traditional system (vials/disposable syringes). Both safety needles and insulin pens impacted the direct costs quite equally. Conversely, the vial system (either with or without safety syringes) allows the use of a single vial for multiple patients (in accordance with Italian legislation), with a considerably saving of costs. In addition, pens not completely used (and not given to patients at discharge) may be considered a cause of a relative "wastage" of insulin during hospitalization which, although small, should be taken into account: this is true for all those patients who discontinue brief insulin treatment (therapeutic choice, deaths, etc.). In contrast, the use of vial system does not always involve any waste, if we consider departments with a high turnover of diabetic patients. In a similar study, conducted by Davis in 2008 [24], which aimed to compare the use of insulin pens to syringes in a hospital setting, it was found a savings of $ 36 per patient using pens compared to syringes, but it should be noted that in their experience, risk

management did not allow the use of the same vial for more than one patient. Insulin pens had considerably lower costs at discharge, leading to an overall saving of 20 €/patient if these were taken into account. At discharge, the use of vials and syringes is not reasonable because of higher costs (for the Hospital) in supplying bran new vials to released patients, in accordance to local Regional laws. In contrast, in-hospital pen utilization provides the greatest savings at discharge, because each subject received his own pen, with no additional costs for the hospital.

Thus our findings suggest that a selective use of insulin pens for diabetic patients who are likely to continue insulin treatment at home may lead to a reduction of in-hospital costs. These patients were as frequent as more than 75% of our diabetic in-patients, in medical Units at medium/high level of care, but differences may be considered in other Units, depending on the percentage of "critically" or "non-critically" ill patients.

In-hospital use of pen/safety needle devices resulted in a greater satisfaction for patients (Table **4**), confirming the findings from the out-patient setting [5, 7]. In particular, patients in the pen group were more satisfied with the treatment received, considered the method easier/more comfortable, retained the injections less aching, would recommend other diabetic patients to receive the same treatment, and were more satisfied to continue at home with the devices used in the hospital. These findings were largely confirmed in the subgroup of newly insulin users, *i.e.* with no previous familiarity with the insulin delivery method, and could therefore be generalized to different contexts where the prevalence of insulin pen users in the out-of-hospital setting is lower than in our study population. Since satisfaction is related to compliance [11], the use of pens at discharge may enhance adherence to treatment.

Safety is a major concern for insulin pens in hospital. The use of pens/safety needles in hospital setting was found to be safe, avoiding the risk of needlestick injury, allowing workers' health safeguard, being cost saving without any related adverse event. In fact, in case of accidental injury with a contaminated sharp, even in the case in which the injured operator did not contract any disease, the management cost of each individual injury is valued about € 850 (analysis on the source patient, monitoring of the operator, any prophylaxis, etc..) for a total costs, in Italy, of € 72 million a year: resources that could be reasonably invested in preventing needlestick injuries rather than groped to limit damage [20]. This issue is clearly of great interest in diabetes: both patients and care-givers are exposed daily and several times a day to the risk of unexpected needlestick injury with contaminated needles, and therefore potentially infectious. A relatively higher risk of needlestick injuries, for example, was reported among acute care nurses caring for diabetic patients and injecting insulin with a disposable syringe; additionally, it was revealed a significant derived emotional distress, suggesting possible under-reporting of needlestick injuries to hospital officials, so demonstrating the need for a more effective needle safety device [16]. In the UK, the economic burden of needlestick injuries costs the National Health System approximately £ 600,000 per annum; many of these injuries and associated costs could be avoided through increased adoption of safety devices [25]. According to an Italian study, in 2006 with the adoption of appropriate prevention plans, training and introduction of secure devices could have saved up to 53,000 accidents in biohazard, up to 550,000 hours and nearly 16,000 lost work days of illness [26]. Regarding diabetes related safety devices, pen needles should be equipped with a double interlock, one that covers the portion of needle in contact with the patient (patient end), and the other that covers the back of the needle (cartridge end). Non safety pen needles, indeed, may cause needlestick injuries, and insulin pens were considered the major instrument involved with unsafe needle-handling practices in nursing homes [27]. Moreover, to fully protect patients and health workers, adequate nurses training is essential to eliminate the risk of transmission of infectious diseases associated with pens misuse. In fact, more than 700 patients in New York hospitals may have been exposed inadvertently to human immunodeficiency virus (HIV), hepatitis B or hepatitis C because of reuse of insulin pens on multiple patients after changing the disposable needle [28]. Patient notification events resulting from multipatient use of insulin pens in U.S. health care settings were recently summarized [29]. It is unquestionable that each pen is absolutely for personal usage only, and it must be labeled with the name of the patient; in fact, in the final phase of insulin delivery, an aspiration of material occurs: this may contaminate the pen, as shown by several observations, and also in a recent study who demonstrated trace of biological contamination (hemoglobin, squamous epithelial cells, macrophages and RBC) in the pen after use [28]. As recommended by the Institute for Safe Medication Practices, all the study nurses performed a training period before using pens, which also included a hands-on individual testing of devices. Even a low number of un-trained nurses is enough to generate serious damage [29].

Finally, dosing accuracy, in particular at low-doses, is another point to be taken into account [30]. About 77% of the study nurses felt more confident about correct dose using pens than using syringes, and several aspects of dose preparation and administration were a key factor for nurses' satisfaction [31].

Among the points of weakness of our study, we underline that only Internal Medicine Units were involved, and we recognize that a larger portion of patients from Phase III were discharged from Internal Medicine/Urgent Care group. It would be interesting to extend such an experience to other Emergency Units as well as to Surgical Units, where diabetic patients usually have a shorter length of hospitalization. Besides, we performed short observational periods (a quarter each Phase). Finally, this study findings (related to Lombardia Region) are difficult to be generalized, even in Italy and, moreover, in other Countries. However, as points of strengths, we performed, first in Italy, a complete study of a model for introducing prefilled pens in hospital settings, with a complete study organization and design, based on education and training for all the involved nurses. We were also able to record a full customer satisfaction (both for nurses and for patients), and we took into account a complete

costs description (direct costs: in-hospital and at-discharge insulin utilization and wastage, treatment and blood glucose monitoring devices; indirect costs: needlestick injuries). Finally, we were aware of errors in insulin therapy and near miss events, which should have importance (if any) in total cost evaluation.

In conclusion, in our study the use of insulin pens with dual-ended safety needles was found to be safe for both nurses and patients. In-hospital use of vial/syringes with safety needles in diabetic patients who are likely to discontinue treatment at home should be preferred, as it does not involve wastage during hospitalization. These represented about 25% of hospitalized patients in the investigated hospital units. For the remaining patients, the use of insulin pens may reduce total hospital costs. Finally, the use of insulin pens at discharge for all insulin-treated patients involves considerable savings, increases compliance and satisfaction, enhancing adherence to treatment.

CONFLICT OF INTEREST

Declaration of Funding: the SANITHY study was funded by the Treviglio Hospital Management.

Declaration of Financial/other Relationship: GV obtained sponsorship from Eli Lilly. ACB received research grants from Eli Lilly, Novo Nordisk, and consultant/advisor honoraria from Johnson & Johnson, Boehringer Ingelheim. Other Authors do not have to disclose any conflict of interest.

Author contributions: CSP, ACB and GV planned the study design, enrolled patients and nurses, reviewed and interpreted the questionnaires' obtained responses, wrote and edited the manuscript. CSP, AB, SM, MD, BF, and PS were investigators and they participated in the interpretation of data. LG, and EMD participated in editing of the manuscript. GV performed the statistical analyses and, finally, ACB, GV and EMD reviewed the manuscript.

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Preliminary findings were presented (as poster presentation) at the National Annual Meeting of the Italian Society of Hospital Pharmacy (Turin, October 2013) and at the XXV SID (Italian Society of Diabetes) National Annual Meeting (Bologna, May 2014).

SUPPLEMENTARY MATERIAL

Supplementary material is available on the publishers Web site along with the published article.

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