

An Unsafe/Safe Typology in People with Type 2 Diabetes: Bridging Patients' Expectations, Personality Traits, Medication Adherence, and Clinical Outcomes

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Background: Support programs are provided to people with diabetes to help them manage their disease. However, adherence to and persistence in support programs are often low, making it difficult to demonstrate their effectiveness.

Aim: To identify the determinants of patients' perceived interest in diabetes support programs because it may be a powerful determinant of effective participation in such programs.

Patients and Methods: An online study conducted in April 2021 in metropolitan France on 600 people with diabetes recruited from a consumer panel. A 64-item psychosocial questionnaire including a question asking to evaluate the helpfulness of a support program was used. Univariate, multivariate, and multiple correspondence analyses were performed.

Results: The existence of a typology, known as *Unsafe/Safe*, was discovered, in which patients with type 2 diabetes respond in two distinct ways. Type *U* (unsafe) patients, who believe that a support program would be helpful, are more likely to be nonadherent to their treatment, have high hemoglobin A1c levels, have at least one diabetic complication, lack information regarding their disease and treatment, rate the burden of their disease and impairment of their quality of life as high, worry about their future, and are pessimistic. Type *S* (safe) patients have the opposite characteristics. Type *U* patients can be dichotomized into two broad classes: one in which they lack information regarding disease and treatment and the other in which alterations in the quality of life and burden of the disease predominate. Insulin-treated patients give more importance to the lack of information, whereas noninsulin-treated patients complain primarily about the burden of the disease and impairment of quality of life.

Conclusion: This study describes this new *U/S* typology, proposes a simple method based on a nine-item questionnaire to identify type *U* patients by calculating a Program Helpfulness Score described herein, and clarifies the nature of the intervention to be provided to them. This novel approach could be applied to other chronic diseases.

Keywords: type 2 diabetes, adherence, support programs, typology, personality traits, clinical outcomes, patients' expectations

Introduction

People with diabetes often view their disease and its treatment as a major burden that impacts their quality of life.^{1–3} Support programs have been developed to help patients optimize self-care and cope with their disease over the long term.⁴ However, adherence to and persistence in support programs are often low. This may be due to the fact that they are sometimes provided without considering patient demand. The psychological factors that determine this demand are not yet clearly understood, as this question is rarely asked in the “Assess” phase of the patient education process,⁵ and, in general, studies evaluating chronic disease support programs have focused more on the determinants of effectiveness than on those of persistence.

Nonadherence is considered to be a major determinant of clinical outcomes of therapy. It concerns the three steps of implementation, correct completion, and continuation of medical prescriptions.⁶ There is extensive literature on the determinants of nonadherence, its frequency, and its consequences in terms of morbidity, mortality, and healthcare costs.^{7–11} Importantly, nonadherence can also be intentional,¹² highlighting the importance of considering patients' needs, preferences, and demands in shared medical decision making.¹³

A key element influencing this study is that adherence is not only about taking medication and implementing lifestyle change measures but also about following support programs. This is shown in Figure 1, which represents the theoretical model that forms the basis for this study. Determinants of adherence to this specific aspect of care may affect clinical outcomes such as controlling risk factors and the genesis of diabetic complications. Thus, the aim of this study was to clarify the demographic and psychosocial factors involved in patients' interest in support programs.

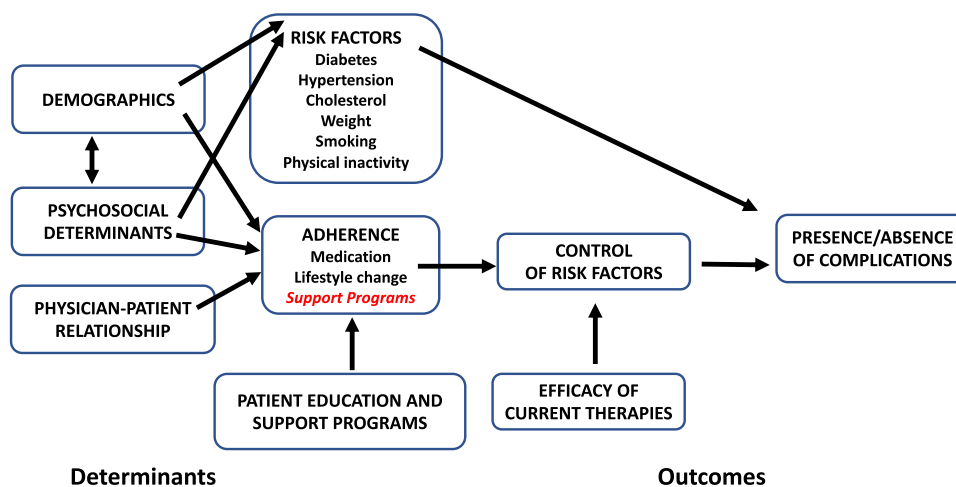


Figure 1 The theoretical model on which the study is grounded. Patients' demographic and psychosocial factors are involved in the genesis of risk factors such as diabetes, hypertension, hypercholesterolaemia, overweight and obesity, smoking, and physical inactivity. They are also determinants of adherence, with its three components: medication, lifestyle change, and participation in support programs. The quality of the physician–patient relationship and the use of patient education and support programs are also determinants of adherence. Adherence to the three aspects of care and the efficacy of current therapies are determinants of the control of risk factors. The quality of this control is a determinant of the presence or absence of diabetic complications. This study focuses on the determinants of adherence to support programs (in red in this figure).

Materials and Methods

Type of Study and Patient Inclusion

The Timkl-1 Study, a cross-sectional online study conducted in metropolitan France, was the first step of the development of Timkl, a program aimed at developing a support program for the care optimization of people with type 2 diabetes. Patients were recruited from the Norstat panel. Norstat is one of the leading data collectors for market research in Europe. It has a panel network of over 2 million consumers across 19 countries. In France, it has access to 54,000 consumers (response rate: 40%), generally responding to marketing/media studies but also (8% of the studies) to questions concerning their health.¹⁴

The survey began with questions to identify patients suffering from type 2 diabetes. Those identified were given a login code to complete an online questionnaire. Participants were aware of NORSTAT's extensive quality controls, including not allowing the same person to register under more than one account or email address and analysing participants' response times.¹⁵

Responses to the questionnaire were collected between April 14 and 30, 2021, with the recruitment being stopped when 600 patients had completed the questionnaire. This sample size, decided a priori, was the one that could be expected within 15 days of the survey opening, given the size of the panel and the response rate. In a previous study using the same panel,¹⁶ it was possible to identify 3001 people with hypertension, hypercholesterolemia, or diabetes; 774 people with diabetes; and 318 people in the subpopulation of people with diabetes only. This number of participants had the power to demonstrate statistical relationships between different aspects of intentionality and adherence (unpublished results). There were no missing data. There were less than 10 implausibilities regarding BMI and age.

Questionnaire ([Appendix 1](#))

Participants completed a 64-item questionnaire, shown in [Appendix 1](#), including demographic information, a 6-item adherence questionnaire, used in France to screen nonadherent patients,¹⁷ such as “do you ever find you have too much medication to take,” a psychological questionnaire constructed from the literature including studies from the first author,^{13,16,18–21} and eight questions supposed a priori to identify patients in need of a support program. This part of the questionnaire included the question “We can offer you a diabetes support program. Do you think it would be helpful?” They were asked to rate their answer on a scale from 1 (not helpful) to 10 (extremely helpful). The entire questionnaire was discussed by the Timkl Study Group, a board of experts in diabetes care including a person with diabetes, himself being responsible for a regional section of the French association of people with diabetes. The feasibility of the questionnaire was evaluated in a pilot study of 10 patients who asked for changes to improve the intelligibility of some questions.

Answers were dichotomized as follows. In case of a Likert scale with four possible answers, eg, never, rarely, often, and always, the first two and last two answers were combined. One question concerned trust in the doctor, in which patients were dichotomized into those who answered “completely” and those who answered something else. For questions with an analog response of 0 or 1 to 10 (people were instructed to never answer 5 to avoid the tendency to choose a neutral value), the dichotomy was performed on the median. Adherence was also dichotomized on the median of the number of positive responses (0–1 vs 2–6 positive responses to the 6-item adherence questionnaire).

Construction of a Program Helpfulness Score

A univariate analysis of responses to the helpfulness question (below or above the median response) identified nine statistically significant determinants. Discriminant analysis was used to assign coefficients describing the weight of each of these determinants, the sum of which would be equal to 100. This enabled calculating a “Program Helpfulness Score” (PHS) for a given patient, ranging from 0 to 100. This procedure was performed on the whole population (n = 600) and on patients treated with insulin (n = 142) or those who were untreated (n = 458).

Statistics

Analyses were based on univariate and multivariate studies using determinants with probability $P < 0.10$ in the univariate study. For multivariate analyses, the question on the number of blood glucose measurements was not included in the model because several patients did not practice glucose monitoring. As a large number of patients were analysed for a large number of characteristics with different modalities, we also used multiple correspondence analysis (MCA). Briefly, this method allows the respective Euclidean coordinates of these modalities, such as being adherent or nonadherent, having complications or not having complications, and being happy or sad, to be represented on a two-axis plane. The proximity of the modalities on the graph makes it possible to visualize their associations. The MCA thus allows a holistic analysis of the characteristics of a population, allowing the discovery of relationships that would not be detected by separate classical univariate analyses. For this reason, this method, initially used in marketing studies, is now widely used in the social sciences.²² MCA was applied to the two groups of insulin-treated ($n = 142$) and noninsulin-treated ($n = 458$) patients involved in this study. A simplified MCA was also performed on the entire population of patients ($n = 600$) on the following four categories: adherence, control of HbA1c, presence of complications, and various ranges of the PHS, whose calculation is described earlier.

Receiver operating characteristic (ROC) curves were used to define the PHS thresholds that best distinguish between patients who find a support program useless and those who find it helpful. In patients with a score above the helpfulness threshold, an unsupervised ascending hierarchical analysis was performed on all the dimensions of the first MCA. This analysis, working “bottom-up” through a series of iterations by starting from each individual, groups together individuals that share most similarities using the Ward’s criterion that seeks to minimize the intraclass variance and maximize the interclass variance. The result is represented in the form of a tree or dendrogram. Classes are defined by cutting branches off the dendrogram where the distance between two branch formations is maximal.²² All statistical analyses were conducted using the SPAD 9.2 software (Coheris).

Ethics and Conformity to Publication Reporting Guidelines

This study complied with the Declaration of Helsinki. *A priori* IRB approval was obtained (Comité Local d’Éthique Avicenne-2021-180, March 5, 2021). The Norstat panel complies with the ESOMAR²³ and RGDP standards that ensure data confidentiality. The following sentence was part of the document submitted to the Ethics Committee for approval: “Completing the questionnaire implies provision of consent. Indeed, as mentioned above, Norstat specifies the conditions of consent for consumers” (patients who were contacted as part of this consumer panel were included). This study conforms to STROBE guidelines.

Patient Involvement in the Study

One patient, regional director of a patient association, is the vice president of the Timkl scientific board. He was therefore involved in the development of the questionnaire used in this study. Furthermore, he submitted the questionnaire to 10 patients as a pilot study to improve its comprehensibility. He also participated in the discussion of the study results.

Results

Characteristics of Included Patients ([Appendix 1](#))

[Appendix 1](#) also shows all the responses to the auto-questionnaire. In particular, there were as many men as women, the median age was 61.3 years, the median body mass index was 29.5 kg/m², the median duration of diabetes was 9.2 years, and 23% of patients were treated with insulin. In 60% of the cases, the HbA1c level was within the target, and 22% of patients had at least one diabetic complication. Regarding the last professional activity (socioprofessional category), 53.2% were or had been farmers, employees, workers, and others without activity, grouped under the term SPC.2, and 46.8% were or had been craftsmen, shopkeepers, executives, and intermediate professionals (SPC.1). Among the respondents, 35% had higher education.

In total, 366 (61%) of patients were defined as adherent. Another 12% of patients stated that they sometimes deliberately did not take their medication. Moreover, 40% of them reported experiencing adverse effects due to their

medication, and 21% and 26% of patients considered that they did not have enough information about their disease and treatment, respectively. On a scale of 1–10 (intolerable), regarding tolerability in terms of burden and impairment of quality of life, the median was 6. Regarding the potential helpfulness of a support program, the median of responses ranging from useless to helpful was 6. Only 57% of patients reported they had complete trust in their doctor.

Determinants of Patients' Views on the Helpfulness of a Support Program

In univariate analysis, the following nine determinants were found to be associated with patients finding a support program rather helpful: 1. lack of information about the treatment ($P < 0.001$) and 2. the disease ($P < 0.001$), 3. feeling a heavy disease burden ($P < 0.001$) and 4. a strong alteration in quality of life ($P < 0.001$), 5. being sometimes depressed ($P < 0.001$), 6. thinking that preparing the future is very important ($P < 0.001$), 7. that they will have physically changed a lot in 10 years ($P < 0.001$), 8. that they are bothered by hypoglycaemia ($P = 0.003$), and 9. that they engage in physical activity ($P = 0.004$).

In multivariate analysis ($n = 535$), the following five criteria emerged as independent determinants of finding a support program helpful: 1. finding the disease burden intolerable ($P = 0.019$), 2. being obedient ($P = 0.021$), 3. feeling sometimes depressed ($P = 0.022$), 4. finding the preparation of future important ($P = 0.024$), and 5. sticking to habits ($P = 0.019$). This logistic regression model identified patients finding a support program helpful with a sensitivity of 53.2% and a specificity of 79.3%, yielding an Area Under the Curve (AUC) of the ROC curve of 0.713.

Discovery of an Unsafe/Safe Typology Through Multiple Correspondence Analysis (MCA)

Table 1 shows the responses to the questions associated with being adherent to medication, having the HbA1c level within target, and having no complications. For adherence, the determinants are presented in the descending order of significance. In these three univariate analyses, some of these determinants are shared by the three variables. Figure 2 shows in a MCA all the elements that appeared to be significantly associated in these analyses (Box 1). Two clusters of characteristics emerged from this MCA; the

Table 1 Determinants of Adherence, Diabetes Control, and Absence of Diabetic Complications

Question	Answer	Adherence	HbA1c in Target	No Complication
		n = 366	n = 373	n = 470
		61.00%	62.17%	78.33%
		P	P	P
Adherent (0 or only 1 positive answer to the 6-item adherence questionnaire)	Yes		0.02	0.000
Do you ever deliberately not take your medication	No	0.000		
Have you ever experienced any adverse effects from your medication?	No	0.000		0.013
Age	≥ 61	0.000	0.001	
Do you feel you have enough information about your treatment	Yes	0.000	0.000	
Are you particularly bothered by your hypoglycaemia?	No	0.000		0.000
Do you ever feel depressed?	No	0.000		0.000
Do you have any complications from diabetes	No one	0.000		
Do you consider on this scale from 1 to 10 that your diabetes impairs your quality of life (10 intolerable):	< median	0.000	0.001	0.000
Do you consider on this scale from 1 to 10 that your diabetes is a burden (10 intolerable)	< median	0.000	0.000	0.008

(Continued)

Table I (Continued).

Question	Answer	Adherence	HbA1c in Target	No Complication
		n = 366	n = 373	n = 470
		61.00%	62.17%	78.33%
		P	P	P
Do you feel you have enough information about your disease?	Yes	0.001	0.000	
Do you trust your doctor	Completely	0.001	0.006	
Smoking: Never/Has stopped/Active smoker	Never	0.001		0.008
Generally speaking, when you are in the habit of doing something, do you stick to it	Yes	0.003		
Are you rather Cheerful/Sad?	Cheerful	0.005	0.005	0.000
Are you a natural Optimist/Pessimist?	Optimist	0.010	0.016	
BMI	< 30	0.015	0.014	
Are you naturally Cautious/At risk	Cautious	0.017		
Is your current HbA1c (glycosylated haemoglobin) in the target range?	Yes	0.020		
Are you rather obedient to recommendations (Obedient/Disobedient?)	Obedient	0.021		
CSP.1 = Craftsmen, shopkeepers, managers, intermediate professions SCP.2= Farmers, employees, workers, other, not active	CSP.1	0.021	0.001	
Have you seen a diabetes specialist in the last 18 months	No	0.021		
In 10 years, your physical appearance will probably have changed to some extent. Do you think you will have changed not at all or very much? Scale 0 10 extremely changed median 6	< median			0.003
Have you seen a diabetes specialist in the last 18 months?	No			0.004
Physical activity Sedentary (nothing)/ Occasionally/Daily/Sport	Some			0.008
Do you have grandchildren?	No			0.012
Have you seen your GP for less than 1 year	Yes		0.003	
In your opinion, does your future depend on you?	Yes		0.022	

first, which we propose to call *Unsafe* (right-hand side of the two figures), gathers the following characteristics: Q31.1: Support helpful; A2: Nonadherent; Q27.2: HbA1c level not in target; Q23.2: At least one complication; Q57.1: Deliberate nonadherence: yes; Q24.2: Intolerable burden; Q26.2: Quality of life intolerable; Q65.1: Presence of adverse effects of treatment; Q30.2: bothered by hypoglycaemia; Q58.2: not enough information about the disease; Q59.2: not enough information about treatment; BMI ≥ 30 kg/m²; Q50.1: depressed; Q51.2: pessimistic; Q53.2: sad; Q54.2: disobedient; Q55.2: not completely trusting the doctor; Q56.2: not sticking to habits; Age < 61 years; SPC.2; Q47.2: feeling that he/she will change a lot in the next 10 years; and Q48.1: preparing the future very important. The *Safe* type (left-hand side of the figures) has the opposite characteristics.

Comparison between the insulin-treated patients (left side of the figure) and noninsulin-treated patients (right side of the figure) revealed only two discordances, viz., Type *U* was associated with smoking (Q14.2) and absence of physical activity (Q20.2) in people not treated with insulin, whereas in patients treated with insulin, it was associated with nonsmoking (Q14.1) and physical activity (Q20.1).

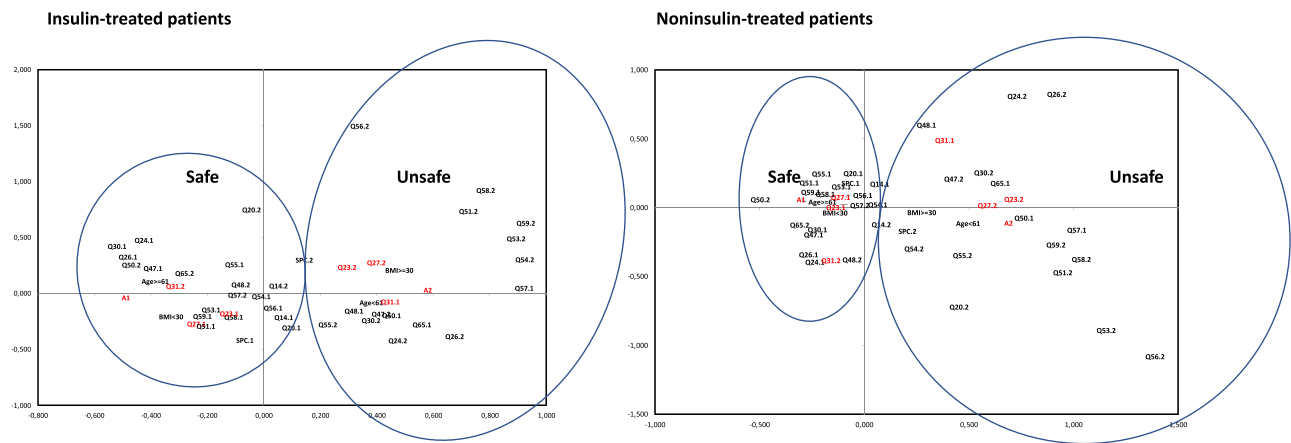


Figure 2 Multiple correspondence analysis of insulin-treated patients and noninsulin-treated patients. A1: Adherence/A2: Nonadherence; Q31.1: Support found helpful/Q31.2 nonhelpful; Q27.1: HbA1c in target/Q27.2 not in target; Q23.1: No complication/Q23.2: At least one complication; Q57.1: Deliberate nonadherence: yes/Q57.2: no; Q24.1: Disease burden tolerable/Q24.2: intolerable; Q26.1: Quality of life tolerable/Q26.2: intolerable; Q65.1: Absence of adverse effects of treatment/Q65.2: Presence; Q30.1: Bothered by hypoglycaemia No/Q30.2 Yes; Q58.1: Enough information about the disease/Q58.2: Not enough; Q59.1: information about treatment = Enough/Q59.2: Not enough; BMI <30/≥30 kg/m²; Q50.1: Not depressed/Q50.2: Depressed; Q51.1: Optimistic/Q51.2 = Pessimistic; Q53.1: Cheerful/Q53.2: Sad; Q54.1: Obedient/Q54.2: Disobedient; Q55.1 trusting completely the doctor/Q55.2: Not completely; Q56.1: sticking to habits/Q56.2: not sticking to habits; Age <61/≥61 years; Socioprofessional category SPC.1: craftsmen, shopkeepers, executives, intermediate professionals/SPC.2: farmers, employees, workers, others without activity); Q47.1: Feeling that he/she will not change a lot in the next 10 years/Q47.2: a lot; Q48.1: Preparing the future very important/Q48.2 not very important; Q14.1: never smoked/ Q14.2 smoker: Q20.1: physical activity/Q20.2 Sedentarity. This type of analysis allows a visualization of the respective proximities between categories, for instance, the responses to questions on adequacy or insufficiency of information about the disease and treatment (Q58, Q59), burden and quality of life (Q24, Q26), lot of change in the next 10 years, and preparation of future important (Q47, Q48). The general explanation of this MCA representation is given in the Methods section.

Construction of a Program Helpfulness Score (PHS) and Relationship with Patient Characteristics

This score was constructed using a discriminant analysis of the nine determinants of the answer to the question (Q31) concerning the feeling by patients that a support program would be useful. This analysis enabled determining the

Box 1 Categories Used in the Multiple Correspondence Analysis

Adherence/Nonadherence
 Support found helpful/nonhelpful
 HbA1c in target/not in target; No complication/At least one complication
 Deliberate nonadherence: yes/no
 Disease burden tolerable/intolerable
 Quality of life tolerable/intolerable
 Absence/Presence of adverse effects of treatment
 Bothered by hypoglycemia yes/no
 Enough/Not enough information about the disease
 Enough/Not enough information about treatment
 BMI <30/≥30 kg/m²
 Not depressed/Depressed
 Optimistic/Pessimistic
 Sad (yes/no)
 Obedient/ Disobedient
 Completely/Not completely trusting the doctor
 Sticking/not sticking to habits
 Age <61/≥61 years
 Socioprofessional category SPC.1/SPC.2 (craftsmen, shopkeepers, executives, intermediate professions/farmers, employees, workers, others without activity);
 Feeling that he/she will change a lot in the next 10 years/Not a lot
 Preparing the future very important/not very important
 Smoking/Not smoking
 Sedentarity/Physical activity.

respective weights of these criteria to arrive at a PHS ranging from 0 to 100 (useless to helpful). Table 2 shows these coefficients for the overall population of 600 patients and for insulin-treated and noninsulin-treated patients. In general, insulin-treated patients gave more weight to the lack of information about the treatment and the disease, while the noninsulin-treated patients gave more weight to the impairment of their quality of life and the burden of the disease. In noninsulin-treated patients, sedentary lifestyle was a determinant of the feeling that a support program could be helpful.

These coefficients were used to calculate the PHS by adding their value in the case of a positive response (as shown in Table 2, in noninsulin-treated patients, the 1.555 coefficient is added if the answer to the physical activity question is *sedentary*). The calculation is described in Box 2.

Table 2 Respective Weights of the Nine Criteria for the Overall Population, Insulin-Treated Patients, and Noninsulin-Treated Patients

Question	Answer	A	B	C
		Overall Population (n = 600)	Insulin-Treated (n = 142)	Noninsulin-Treated (n = 458)
Do you feel you have enough information about your disease?	No	14.844 C	21.548 C	9.623
Do you feel you have enough information about your treatment?	No	14.282 C	22.078 AC	10.363
Do you consider on this scale from 1 to 10 that your diabetes is a burden (10 intolerable); Median of answers: 6	Intolerable (> 6)	14.408	11.488	19.989 AB
Do you consider on this scale from 1 to 10 that your diabetes impairs your quality of life? (10 intolerable); Median of answers: 6	Intolerable (> 6)	12.234	10.397	18.098 AB
Is preparing for your future important to you? Scale of 0 to 10; Median: 7	Important (>7)	12.363 C	10.588	8.345
Physical activity: Sedentary (nothing), other answer	Other answer	8.840 C	8.922 C	1.555 if sedentary
Do you ever feel depressed?	Yes	8.138	5.604	11.104 B
Are you particularly bothered by your hypoglycaemia? Scale from 0 to 10, extremely bothered; Median: 2	Yes (> 2)	7.780	6.255	10.550 B
Do you think you will have changed not at all or very much? Scale from 0 to 10, extremely changed; Median: 6.	Changed (>6)	7.111 B	3.120	10.374 B
Total		100	100	100

Note: A,B,C: P < 0.05.

Box 2 Calculation of the Program Helpfulness Score (PHS)

Add coefficient shown in Table 2 (middle and right columns, corresponding to insulin- and noninsulin-treated patients, respectively)

1. Do you consider your diabetes to be a burden (10 intolerable) on a scale of 1 to 10? **If answer is >6**
2. Do you consider on a scale of 1 to 10 that your diabetes impairs your quality of life (10 intolerable)? **If answer is >6**
3. Are you particularly bothered by your hypoglycaemia? Scale from 0 to 10; **If answer is > 2**
4. Physical activity: **Insulin-treated patients: if answer is at least some activity; noninsulin-treated patients: if answer is sedentary**
5. In 10 years' time, your physical appearance will probably have changed to some extent. Do you think you will have changed not at all or very much? Scale of 0 to 10 extremely changed; **If answer is >6**
6. Is preparing for your future important to you? Scale from 0 to 10; **If answer is >7**
7. Do you ever feel depressed? **If answer is Yes**
8. Do you feel that you have enough information about your illness? **If answer is No**
9. Do you feel that you have enough information about your treatment? **If answer is No**

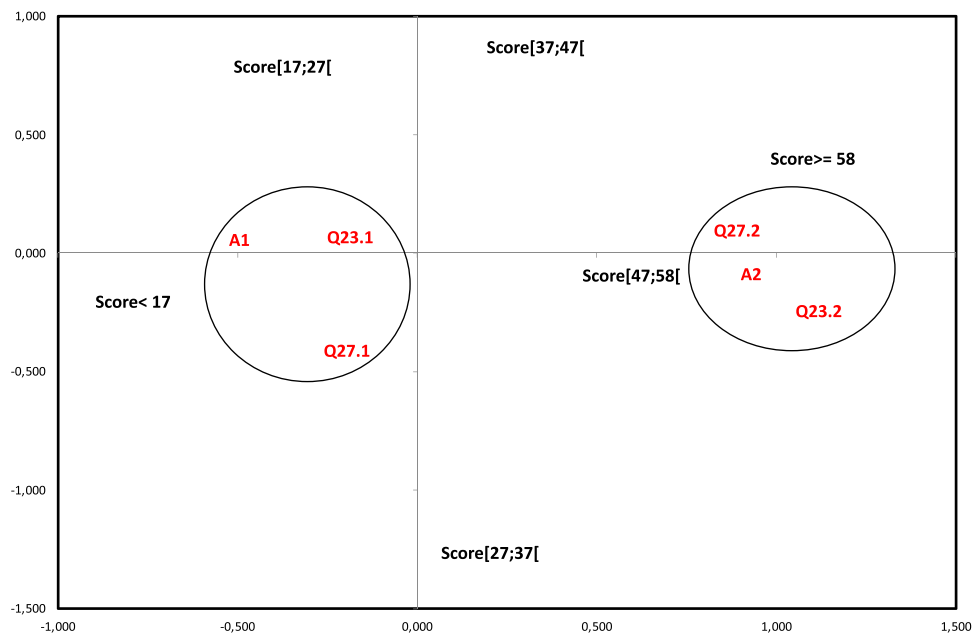


Figure 3 Ranges of Program Helpfulness Scores (PHS) and Clinical Outcomes (n = 600). A High PHS means that the program can be considered helpful. Q27.1: HbA1c in target/Q27.2: HbA1c not in target; Q23.1: No complications/Q23.2: At least one complication; A1: adherent/A2: nonadherent.

Figure 3 shows the MCA results of the entire population (n = 600), linking different ranges of PHS to the control of HbA1c level, the presence of complications, and adherence to medication. ROC curve analyses were used to determine the best PHS thresholds defining the uselessness and helpfulness of a support program. Data representing these thresholds, the percentages of patients below the uselessness and above the helpfulness thresholds, respectively, and the AUC of the ROC curves are shown in Table 3, and Table 4 shows the results of the univariate analysis of the entire population data comparing participants above and below the 58 PHS threshold, the determinants being given in the descending order of importance, shown by the test value.

Typologies of Insulin- and Noninsulin-Treated Patients with High PHS

As shown in Table 3, the PHS thresholds were 50 and 54 for insulin- and noninsulin-treated patients, respectively. An ascending hierarchical analysis was performed in patients having a score above these thresholds, representing 38 (26.7%) and 112 (24.4%) patients, respectively, of the patients. The dendrograms identified two major classes in both groups of patients (Figure 4). The drop from the two-cluster to the three-cluster solution was the largest, especially in noninsulin-treated patients. The first dichotomy leading to the formation of two classes separates patients according to the importance given either to the lack of information on the disease and treatment or to the impact of the disease as a burden and impairment of the quality of life. Patients who considered the burden of disease and impact on the quality of life to be intolerable (class 1 of insulin-treated patients and class 2 of noninsulin-treated patients) believed that they would have changed a lot in 10 years (insulin-treated patients) or that preparing for the future is very important (noninsulin-treated patients) (Table 5).

Table 3 Uselessness and Helpfulness PHS Thresholds

	Uselessness Threshold	% of Program Useless Below Uselessness Threshold	Helpfulness Threshold	% of Program Helpfulness Above Helpfulness Threshold	ROC Curve AUC
All patients n = 600	16.978	78.1	58.511	71.2	0.699
Insulin-treated n = 142	23.901	73.7	50.77	70.3	0.695
Noninsulin-treated n= 458	13.121	72.0	54.775	64.5	0.683

Abbreviations: PHS, Program Helpfulness Score ROC curve; AUC, area under the curve of the receiver operating characteristic curve.

Table 4 Determinants of Program Helpfulness Score ≥ 58 in Univariate Analysis, Entire Population, n = 600

Question	Answer	Test Value	Probability
Do you consider on this scale from 1 to 10 that your diabetes impairs your quality of life? (10 intolerable) Median of answers: 6	Intolerable (>6)	99.99	0.000
Do you consider on this scale from 1 to 10 that your diabetes is a burden (10 intolerable) Median of answers: 6	Intolerable (>6)	10.92	0.000
Are you particularly bothered by your hypoglycaemia? Scale from 0 to 10, extremely bothered Median of answers: 3	Bothered (>3)	8.06	0.000
Do you think you will have changed not at all or very much? Scale of 0 to 10, extremely changed; Median of answers: 6.	Changed (>6)	7.33	0.000
Is preparing for your future important to you? Scale of 0 to 10; Median of answers: 7	Important (>7)	7.29	0.000
We can offer you a diabetes support program. Do you think this would be helpful to you? Scale of 1 to 10, extremely helpful; Median of answers: 6	Helpful (>6)	6.41	0.000
Have you ever experienced any adverse effects from your medication?	Yes	5.09	0.000
Are you a natural Optimist/Pessimist?	Pessimist	4.55	0.000
Adherence	Nonadherence	4.01	0.000
Do you ever deliberately not take your medication?	Yes	3.80	0.000
Do you trust your doctor? Not at all, Not very much, Somewhat, Completely	No complete trust	3.66	0.000
Age	<61	2.95	0.002
Do you ever deliberately not take your medication?	Rarely	2.81	0.002
Are you rather Cheerful/Sad	Sad	2.62	0.004
Do you have any complications from diabetes?	At least one	2.60	0.005
Have you ever been late in taking your medication?	Yes	2.58	0.005
Is your current HbA1c (glycosylated haemoglobin) in the target range?	No	2.09	0.018
Have you seen a diabetes specialist in the last 18 months	Yes	1.97	0.024

Discussion

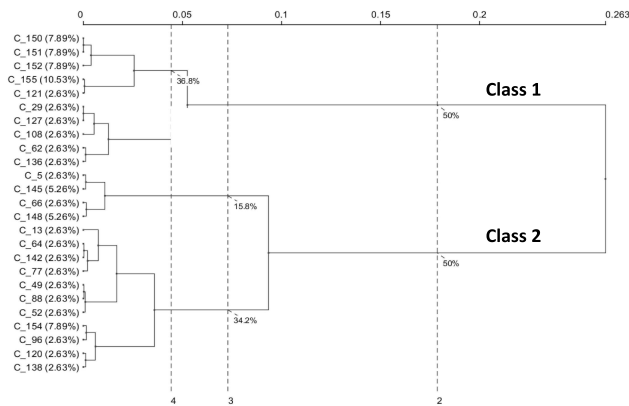
Main Findings

1. The MCA of data collected from 600 people with type 2 diabetes, on the basis of a holistic approach of patients' behaviours, revealed the presence of two clusters of characteristics linking the feeling that a support program would be useful to certain personality traits, nonadherence and two clinical outcomes: noncontrol of HbA1c level and presence of complications. Based on this discovery, it is proposed that the behaviour of individuals with a chronic disease can be described using the new typology of Unsafe/Safe (*U/S*).

2. We constructed a PHS from the nine determinants of the answer to a direct question of helpfulness that were found to be statistically significant in the univariate analysis of the answers. This PHS was found to be statistically related to adherence and clinical outcomes (HbA1c control, presence of diabetes complication). Importantly, the nine determinants used to construct the score did not include these variables, which gives this observation its full value.

3. We observed that patients with high PHS can be divided into two classes differing by their expectations from a support program, information on disease and treatment, or relief from burden and alteration of the quality of life. Insulin-treated patients

Insulin-treated patients, score ≥ 50 , n = 38



Noninsulin-treated patients, score ≥ 54 , n = 112

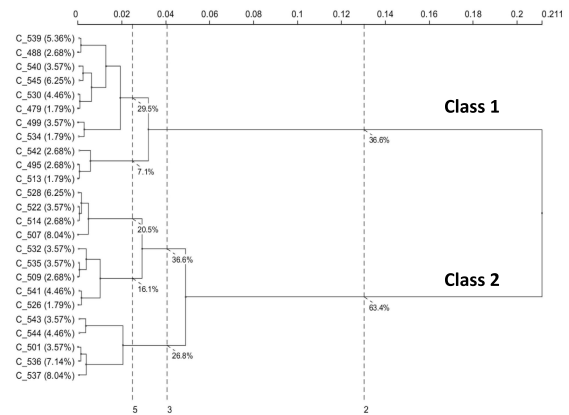


Figure 4 Dendrograms obtained by the ascending hierarchical cluster analysis in insulin- and noninsulin-treated patients. The explanation of this dendrogram representation is given in the Methods section.

gave more importance to the lack of information, whereas noninsulin-treated patients complained primarily about the disease burden and quality of life alteration.

Description of the *U/S* Typology

The complete set of characteristics associated with the *U* and *S* typologies, respectively, is shown in the MCA depicted in Figure 2, and the results of univariate analysis comparing participants below and above the PHS threshold are shown in Table 4. The ascending hierarchical analysis of type *U* patients (Table 5) showed that alteration in the quality of life and

Table 5 Characteristics of the Two Major Classes of Type *U* Patients

Insulin-Treated Patients (n = 38)			
Class 1/2 (n = 19, 50.00%)		Class 2/2 (n = 19, 50.00%)	
	Answer	Answer	P
Information on the disease	Sufficient	Insufficient	0.000
Information on the treatment	Sufficient	Insufficient	0.000
Disease's burden	Intolerable	Tolerable	0.002
Impact on quality of life	Intolerable	Tolerable	0.004
Similitude at 10 years	Changed	Little change	0.022
Noninsulin-treated patients (n = 112)			
Class 1/2 (n = 43, 38.39%)		Class 2/2 (n = 69, 61.61%)	
	Answer	Answer	P
Information on the disease	Insufficient	Sufficient	0.000
Information on the treatment	Insufficient	Sufficient	0.000
Disease's burden	Tolerable	Intolerable	0.001
Impact on quality of life	Tolerable	Intolerable	0.001
Preparing the future	Not very important	Very important	0.019

Note: The numbers of patients are obtained after consolidation of the algorithm, which explains that the percentages among noninsulin-treated patients are slightly different from those shown in Figure 4.

high disease burden were found in the same class as the importance of preparing for the future or thinking that one will have changed a lot in 10 years' time. Their association to the similitude question can be interpreted as a fear of change in the future. In fact, univariate analysis (Table 6) indicated that patients who said that they will have changed a lot in the future also said that they were sometimes depressed ($P < 0.001$), naturally pessimistic ($P < 0.001$), sad ($P=0.001$), had at least one diabetic complication ($P = 0.003$), and their future is important to them ($P = 0.001$). Interestingly, these patients who gave importance to the future and were afraid of the perspective to change physically were nevertheless nonadherent to medication. This may reflect all the ambivalence of nonadherence, which has been described as a case of weakness of will (*akrasia*),²⁴ one of the paradoxes of irrationality investigated by the philosopher Donald Davidson who linked them to a division of mind.²⁵

We also observed the presence of certain personality traits in type *U* patients, in particular not sticking to habits, disobedience, risk-taking, pessimism, and sadness, which have been observed in earlier studies by the first author to be associated with nonadherence.^{19–21}

There are studies on the role of habit in adherence,^{18,20,21,26,27} and an association between obedience and adherence has been reported elsewhere. In this study, a multivariate analysis revealed that obedience is an independent factor in finding a support program useful, confirming the role of this character trait in adherence to long-term therapies.^{19–21} Not fully trusting the doctor was also found in the *U* typology, consistently with several studies showing the relationship between trust in the doctor and adherence.^{13,20,21,28–32} Finally, the association between adherence and personality traits should imply that it represents a syndrome.²¹ As shown in Figure 2, type *U* patients were more often obese.

Overall, the characteristics of patients belonging to the two typologies, *U* and *S*, were identical in insulin- and noninsulin-treated patients (Figure 2), with the exception of smoking status and physical activity. To explain these discrepancies, it is speculated that type *U* is associated with smoking and absence of physical activity in people not

Table 6 Determinants of the Answer > 6 to the Question “Do You Think You Will Have Changed Not at All or Very Much?” Scale of 0–10, Extremely Changed; Median 6; Univariate Analysis, Entire Population, n = 600

Question	Answer	Test Value	Probability
Do you consider on this scale from 1 to 10 that your diabetes impairs your quality of life? (10 intolerable): Median of answers: 6	Intolerable (>6)	5.878	0.000
Do you ever feel depressed?	Yes	5.325	0.000
Have you ever experienced any adverse effects from your medication? Yes/ No	Yes	4,223	0.000
Do you consider on this scale from 1 to 10 that your diabetes is a burden (10 intolerable): Median of answers: 6	Intolerable	3.846	0.000
Are you a natural Optimist/Pessimist	Pessimist	3.745	0.000
Are you rather Cheerful/Sad?	Sad	3.267	0.001
Is preparing for your future important to you? Scale of 0 to 10; Median of answers: 7	Important (>7)	3,167	0.001
In addition to diabetes, do you have any of the following health problems? Overweight or obese, hypertension, Cholesterol, Gout	At least one	3.133	0.001
We can offer you a diabetes support program. Do you think this would be helpful to you? Scale of 1 to 10, extremely helpful. Median: 6	Helpful (>6)	3.106	0.001
Do you have any complications from diabetes?	At least one	2.768	0.003
Are you particularly bothered by your hypoglycaemia? Scale from 0 to 10, extremely bothered; Median: 2	Yes (> 2)	2.449	0.007
Generally speaking, when you are in the habit of doing something, do you stick to it? Yes/ No	No	2.041	0.021

Note: Answer > 6: n=298, 49.67%.

treated with insulin, which would be fully consistent with the syndromic conception of nonadherence,²¹ as discussed previously. In patients treated with insulin, type *U* is associated with nonsmoking and physical activity, which may mean that individuals in this stage of the disease try to avoid these modifiable risk factors that may aggravate their condition.

The *U/S* Typology and Personality Traits

Among the characteristics of type *U* patients, there were some personality traits such as pessimism, sadness, tendency to depression, and disobedience. Other typologies have already linked personality traits to the occurrence of various morbidities,^{33–35} the perception of health-related quality of life (HRQOL),³⁶ adherence to therapy, and consumption of health services,³⁷ yielding a network consistent with associations reported herein. For instance, optimism predicts lower rates of rehospitalization after coronary artery bypass graft.³⁸ Type *D* (for depressed) and pessimism personality, respectively, possess higher risk of consistently impaired HRQOL.^{39,40} More specific examination of personality characteristics of the Big Five Inventory personality traits (Agreeableness, Conscientiousness, Extraversion, Neuroticism, and Openness) suggested that neuroticism was the characteristic to most likely correlate with the psychosocial aspects of HRQOL.³⁶ There is also evidence that this personality trait is negatively associated with medication adherence in elderly people⁴¹ and in people with type 2 diabetes,⁴² whereas both agreeableness and conscientiousness are positively related to medication adherence.⁴³ Neuroticism was also found to be negatively associated with lifestyle (exercise and diet) in people with type 2 diabetes,⁴⁴ conscientiousness being found to be associated with the practice of self-monitoring of blood glucose and medication adherence in people with type 2 diabetes.⁴⁵ Similar associations between these personality traits and adherence were observed in people with asthma.⁴⁶ In a 2006 meta-analysis of 33 studies, extraversion ($r = 0.23$), neuroticism ($r = -0.11$), and conscientiousness ($r = 0.20$) were identified as correlates of physical activity.⁴⁷

The existence of personality traits reflecting an invariance of the person is not incompatible with the possibility of distinct behaviours when people are faced with different situations.⁴⁸ This concept is illustrated by the differences observed in this study between patients treated and not treated with insulin – for instance the difference discussed above between attitudes concerning smoking and physical activity. For type *U* patients, the analysis of their demands also clearly showed a difference in their priority, with insulin-treated patients asking for more information about the disease and its treatment, whereas noninsulin-treated patients complained primarily about the burden of treatment and the alteration of their quality of life. This demonstrates the importance of the event of starting insulin treatment in people with diabetes.

Strengths and Limitations of the Study

Overall, this typology is consistent with everyday medical practice and clinicians' ability to assess which patients will do well and identify those that they are concerned with. The PHS described here can represent a novel tool helping them to confirm this impression.

However, there are some limitations in our study. Apart from the adherence questionnaire, our overall questionnaire has not been formally validated. Nonetheless, the fact that it allowed us to discover almost by serendipity a new typology suggests a posteriori that it had been grounded on a cogent theoretical foundation (Figure 1) supported by previous empirical studies.^{13,16,18–21,49}

The major weakness is, as for all studies of this type, its self-reporting nature. Moreover, the response rate of the NORSTAT panel (40%), similar to that reported for online surveys (46%)⁵⁰ may represent another source of bias. However, the fact that the respondents were part of a consumer panel rather than a patient panel and that they responded online may restrict the social desirability bias. Nevertheless, we are aware that this type of bias persists, and that it may contribute to the fact that type *S* patients represented the majority of participants in this study. Another factor to consider is that individuals participating in panels may have a high literacy level, which is a major determinant to good clinical outcomes in people with chronic diseases.⁵¹ Nevertheless, it can also be noted that only 39% of the patients were considered as nonadherent in this study, a proportion that is close to that reported for type 2 diabetes in a study based on drug purchase (35%).⁷

Interestingly, 62%, 27%, 7%, and 4% of patients answered “Yes,” “No,” “Don’t know,” or “Don’t understand,” respectively, to the question “Is your current HbA1c (glycosylated haemoglobin) in the target range?” However, 23% of patients answered “No” to the question “Do you know what HbA1c, glycated haemoglobin or glycosylated haemoglobin (%) is?” This discrepancy suggests that some patients may be able to interpret HbA1c data in terms of diabetes control without knowing “what it is,” which illustrates the semantic difficulty of constructing a questionnaire, even though particular attention was paid to the comprehensibility of the questions in a pilot test with 10 people with diabetes, which resulted in changes in the wording of the questions. Nevertheless, it is recognized that caution should be applied when interpreting the relationship between the PHS and HbA1c control.

Our study was conducted in a single country, which restricts the generalizability of the results by ignoring cultural influences. Finally, the practical value of this approach remains to be evaluated, for instance by showing that intervention programs are more effective when they include a high PHS among the inclusion criteria.

Implications for Clinicians

An important question raised by these results is whether in current practice one can transform the PHS described in this study into an eligibility score for a support program. In fact, it is easy to create a calculator that based on the answers to the nine helpfulness questions described here and on the presence of insulin in the treatment, gives a score and alerts if it is above the helpfulness threshold. This calculator could subsequently propose a typology that would lead to the personalization of the proposed interventions; there would essentially be two types, focusing either on reinforcing information about the disease and treatment or on psychological support for achieving quality of life.

However, it must be emphasized that all these data are merely statistical. On the one hand, the sensitivity and specificity of the helpfulness score to detect type *U* patients are far from excellent (AUC of ROC curve, 0.695). On the other hand, a score below the threshold in a patient does not automatically indicate that he or she does not individually present one or more criteria that would require long-term support. The only way to use ethically this quantitative approach is to consider that the calculation of the score should only lead to representing a criterion for inclusion in such a program, and not a criterion for exclusion. In this case, this approach would have the merit of constituting a new method for alerting health professionals to patients at risk (type *U* for Unsafe), for whom they should be particularly worried. This could be a method to combat clinical inertia for those patients for whom it is most harmful.⁵² It could be different in the context of clinical research to evaluate an intervention program. In this context, the method proposed here could represent a criterion for excluding patients who are at baseline in a safe situation, which could improve the chances of demonstrating the effectiveness of an intervention.⁵³

Finally, in a very general manner, the question raised here is in fact that of the relationship between statistical data and individual characteristics. The results presented in this study have above all an epistemic value. They demonstrate that it is possible to define uniform behaviours with regard to a situation such as the presence of a chronic disease, which can be referred to as typology, class, etc. The fact that this is possible probably reflects the universality of human behaviours.⁴⁹ Nevertheless, the statistical nature of these epistemic data represents a limitation to their applicability to practice. This need to consider individuals had been observed by Aristotle as “For it is not man that the physician cures, except incidentally, but Callias or Socrates or some other person similarly named, who is incidentally a man as well. So if a man has theory without experience, and knows the universal, but does not know the particular contained in it, he will often fail in his treatment; for it is the particular that must be treated.”⁵⁴ Thus, the medical decision must consider not only the statistical data of the clinical trials but also individual patients’ preferences and the expertise of the physician.⁵⁵

Further Research

The existence of a personality typology opens the pathway for research into whether it has a genetic^{56,57} and/or neurobiological⁵⁸ basis and how it can be influenced by social context and interventions. This may apply to the *U/S* typology described in this study.

Conclusion

MCA of the answers to a 64-item questionnaire enabled the discovery of the existence of a typology that clearly separates patients who appear to have and do not have aspects of concern, a typology called safe (*S*) and unsafe (*U*). Type *S* and *U* patients differ in their adherence to medication and their clinical outcomes (control of diabetes and presence of complications). They also differ in personality traits, and this typology bridges these personality traits with clinical outcomes of people with type 2 diabetes. Finally, type *U* patients manifest a desire to participate in a support program, which is not the case for type *S* patients. Furthermore, a simple method was designed based on the nine questions (see [Box 2](#)) that proved to be the determinants of the answer to this question when it was directly asked to patients.

This typology could serve two purposes. Firstly, it could draw physicians' attention to these unsafe patients (type *U*), and, secondly, in clinical trials designed to evaluate an intervention, it could help exclude patients who do not need this intervention (type *S*). Finally, this approach is in harmony with person-centred therapy that incorporates the needs and preferences of patients, which is important in an age of advancing technology.^{59,60} We believe that this *S/U* typology, described here in people with type 2 diabetes treated or not treated with insulin, can be adapted for other chronic conditions.

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Author Contributions

GR, the president of the Timkl Study Group, designed the study and analyzed the results with LB, statistician. He wrote the first draft of the article. The analysis of the data and the article were discussed in depth during several meetings of the Timkl Study Group. Thus, all the authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

GR reports receipt of personal fees as speaker at symposia organized by Novo-Nordisk, Lilly, Novartis, Sanofi-Aventis, Merck-Serono, GSK, Ipsen, Abbott-Pharma, BMS, Pfizer, Roche-Pharma, Roche-Diagnostics, Abbott-Diagnostics, Lifescan, Bayer-Diagnostics, Dexcom, BioGen, AbbVie, Servier, Novartis, Takeda, and Mylan-Viatis: lectures on patients' adherence, doctors' clinical inertia, patient education, and hospitality in hospital; personal fees as participants in scientific boards for Lifescan, Bayer Diagnostics, Lilly, Sanofi-Aventis, Novo-Nordisk, Abbott, Takeda, and Timkl outside the submitted work. PYB has received speaker honoraria from Abbott, Roche, Eli Lilly, Novo Nordisk, and Sanofi; has served on advisory board panels for Abbott, Dexcom, Diabeloop, Insulet, LifeScan, Eli Lilly, Medtronic, Novo Nordisk, Roche, Sanofi, and Timkl; and owns shares in Diabeloop SA outside the submitted work. BD declares having received honoraria for participation in symposia organized by Sanofi, Novo-Nordisk, Lilly, Astra-Zeneca, Abbott, Insulet, Pfizer, Recordati, Ipsen, and Novartis outside the submitted work. SD declares having received honoraria for participation in symposia organized by Sanofi, Novo-Nordisk, Lilly, Astra-Zeneca, Abbott, and Medtronic outside the submitted work. DG declares having received honoraria for participation in symposia organized by Novo-Nordisk, Lilly, Sanofi-Diabète, Astra Zeneca, and Abbott and in boards for Lilly, Sanofi-Aventis, Novo-Nordisk, Abbott, and Timkl outside the submitted work. BG reports grants, personal fees, and non-financial support from Sanofi; personal fees from Orkyn (provider), grants, personal fees, and non-financial support from Vitalaire/Air Liquide (provider); personal fees and non-financial support from Abbott; personal fees and non-financial support from Novo Nordisk; grants, personal fees, and non-financial support from Eli Lilly; personal fees and non-financial support from Boehringer Ingelheim; personal fees and non-financial support from

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