



Individualized HbA_{1c} Goals, and Patient Awareness and Attainment of Goals in Type 2 Diabetes Mellitus: A Real-World Multinational Survey

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ABSTRACT

Aims: While glycemic control is key in effective type 2 diabetes mellitus management, many patients fail to reach their individualized glycemic goal. This analysis aimed to describe a real-world picture of diabetes management: individualized hemoglobin A_{1c} (HbA_{1c}) goals, rate of goal attainment, HbA_{1c} at each line of therapy, and patient awareness of their glycemic goal. Secondly, we aimed to understand physician satisfaction with HbA_{1c} amongst patients aware vs. those unaware of HbA_{1c} goal. **Methods:** Analysis of physicians and the next ten consulting patients with type 2 diabetes mellitus conducted in Europe and the USA including medical record data abstraction/assessment by physicians, a patient-reported survey and a physician survey. Patients were

diagnosed for 3 months or more with a known current and target HbA_{1c}. For the sub-analysis assessment of patient awareness of HbA_{1c} goal, in addition to the above, these patients had to have completed a patient-reported questionnaire and answer the question on awareness of HbA_{1c} goal.

Results: A total of 730 physicians provided data on 8794 patients with type 2 diabetes mellitus; 5331 patients were eligible for this analysis. Overall, mean (standard deviation, SD) individualized HbA_{1c} goal was 6.8% (0.68%). Of eligible patients, 39.1% met their HbA_{1c} goal; of 60.9% of patients not reaching their HbA_{1c} goal, the mean distance from individualized HbA_{1c} goal was 0.9% (SD 1.0%). Physicians progressed patients' antihyperglycemic therapy when HbA_{1c} was 8% or higher. Among 2560 patients who were included in the sub-analysis assessing the effect of patient awareness of their HbA_{1c} goal on multiple parameters, 70.5% were aware of their HbA_{1c} goal; mean HbA_{1c} goal was 6.8% (0.7%) and current mean HbA_{1c} value 7.1% (1.2%). A total of 949 patients in the sub-analysis (39.2%) achieved their goal; achieving HbA_{1c} goal was not related to knowledge of goal. Patients aware of their HbA_{1c} goal were slightly more adherent to their antihyperglycemic medication. They also were prescribed more antihyperglycemic agents, more often on a later therapy line receiving a GLP-1 receptor agonist, SGLT2i, or insulin, and more often tested their blood glucose levels than patients

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who were unaware. Physicians were not satisfied with the current blood glucose level of one third of their patients, believing that more of those who were aware of their HbA_{1c} goal could achieve better glucose control (32.4% of aware vs. 28.2% of unaware patients; $p = 0.003$).

Conclusions: Our results showed that the proportion of patients with type 2 diabetes mellitus achieving their goals for glycemic control was suboptimal when compared to current guideline criteria, with only about 40% of patients achieving their individualized HbA_{1c} goal. Treatment intensification was often delayed until HbA_{1c} was 8% and higher. Patients aware of their HbA_{1c} goal were slightly more adherent to their antihyperglycemic medication; however, awareness of HbA_{1c} goal did not enhance goal attainment. This highlights the need for a holistic approach to diabetes management, involving patient education, and patient–physician communication and partnership.

Keywords: Glycemic control; Glycemic goal attainment; Individualized HbA_{1c} goal; Individualized HbA_{1c}; Individualized HbA_{1c} target; Patient goal awareness; Patient target awareness; Real world; Type 2 diabetes mellitus

Abbreviations

AHA	Antihyperglycemic agent
ARMS-D	Adherence to Refills and Medicines Scale for Diabetes
BMI	Body mass index
CKD	Chronic kidney disease
COVID-19	Coronavirus disease
CS	Chi-squared test
DSP	Disease Specific Programme™
FE	Fisher's exact test
GLP-1	Glucagon-like peptide 1
HbA _{1c}	Hemoglobin A _{1c}
PCP	Primary care physician
SD	Standard deviation
SGLT2i	Sodium glucose cotransporter 2 inhibitor
SU	Sulfonylurea
TT	<i>t</i> test
UK	United Kingdom
USA	United States of America

Key Summary Points

What is already known about this subject?

Whilst guidelines recommend HbA_{1c} targets of < 7% for a majority of patients to reduce rates of development and progression of micro/macrovacular complications, individualized HbA_{1c} goals can vary in real-world clinical practice, with many patients failing to achieve their goal.

Evidence suggests that the proportion of patients maintaining target glycemic levels decreases over time, regardless of antihyperglycemic therapy.

Patient knowledge of glycemic goal is associated with better glycemic control.

What is the key question?

What is the real-world HbA_{1c} goal for patients with type 2 diabetes mellitus and how does patient awareness impact attainment?

What are the new findings?

Around 60% of patients were not at the HbA_{1c} goal set by their physicians, which was 6.8% on average; mean distance from HbA_{1c} goal was 0.9%.

With each successive therapy line, physicians tended to wait until HbA_{1c} was progressively higher before changing/adding pharmacologic agents.

Patients aware of their HbA_{1c} goal were slightly more adherent to their antihyperglycemic medication; however, awareness of HbA_{1c} goal did not enhance goal attainment.

How might this impact on clinical practice in the foreseeable future?

Results of this analysis highlighted the need for a holistic approach to diabetes management, involving patient education, and patient–physician communication and partnership.

INTRODUCTION

Glycemic control is the primary goal of diabetes treatment to prevent target organ damage and other disease-related complications. Guidelines recommend a target glycated hemoglobin (HbA_{1c}) value of less than 7.0% (< 53 mmol/mol) for most non-pregnant adults, although these targets are individualized per patient [1–3]. Target values need to be determined individually per patient by the treating physician, with factors influencing this decision including age, comorbidities and complications, or disease duration [3]. Lower HbA_{1c} levels have been observed to reduce rates of development and progression of microvascular complications [4, 5], to maintain reduction in microvascular risk [6], and reduce macrovascular complications [7, 8]. Guidelines also recommend that HbA_{1c} goals are individualized on the basis of patient characteristics, patient preferences and goals, and risk of treatment-related adverse effects such as hypoglycemia and weight gain [1, 2]. Previous real-world studies have focused on the prevalence of adults with type 2 diabetes mellitus achieving an HbA_{1c} goal of < 7.0% despite the recommended individualization of glycemic goals [9–14].

Although knowledge of glycemic goals was associated with better glycemic control [15–17], patient knowledge of their individualized glycemic goals is not well understood on a systematic level [18, 19]. It was estimated that only about one quarter of patients with diabetes understand the meaning of HbA_{1c} or can recall their most recent value [16, 20], while some thought that their HbA_{1c} values above 8% indicated good glycemic control [21]. Understanding patient experiences is essential [22].

The achievement of and distance to the individualized HbA_{1c} goal, and the HbA_{1c} level at which providers intensify patients' treatment regimens by adding or changing to a second or third antihyperglycemic agent (AHA), have not been well characterized. The objectives of this analysis were to (1) describe individualized HbA_{1c} goal and rate of goal attainment; (2) note HbA_{1c} levels as patients progressed through

lines of therapy; (3) understand patient awareness of goal, and association between awareness and goal attainment; and (4) understand differences in number of AHAs, lines of therapy, glucose testing, and physician satisfaction with HbA_{1c} amongst patients aware vs. those unaware of their HbA_{1c} goal.

METHODS

Survey Design

Data were drawn from the Adelphi Diabetes Disease Specific Programme™ (DSP), a large, real-world survey of physicians and their patients conducted in Europe and the USA. The DSP comprised physician surveys and medical record data abstraction by physicians, matched with patient-reported surveys. Data were collected in Germany, Italy, Spain, the UK, and the USA between October 2018 and March 2019. Full DSP methodology has been published and validated [23–25].

Upon providing consent to participate, primary care physicians (PCPs) or diabetologists/endocrinologists involved with the management and treatment of patients with type 2 diabetes mellitus (monthly workload ≥ 25 and ≥ 50 patients with type 2 diabetes mellitus, respectively) enrolled the next ten consecutive patients who presented in their offices and met the patient eligibility criteria, at least 18 years old, not in a clinical trial at time of data capture, and currently receiving at least one AHA. Physicians were also asked to include two additional patients treated with either a sodium glucose cotransporter 2 inhibitor (SGLT2i) or a glucagon-like peptide 1 (GLP-1) receptor agonist, or both of these agents (either alone or in combination with other AHAs), to ensure newer AHAs were represented. The research methodology is designed to maximize the number of physicians sampled while minimizing the burden on each physician by limiting the number of patients on whom they report. This also increases the power of the sample size overall. For each patient who met the eligibility criteria, physicians completed a form containing detailed questions, capturing patient

demographics, tests performed (including current HbA_{1c} value, i.e., “at time of data collection”), HbA_{1c} goal, comorbid conditions, and current and previous treatment including HbA_{1c} at time of initiation.

Physicians then invited the same patients to complete, on a voluntary basis, a patient-reported form, containing questions about demographics and current condition. Patients also answered the question “Do you have an agreed blood sugar target with your doctor?”. In addition, information on medication adherence was reported using the Adherence to Refills and Medicines Scale for Diabetes (ARMS-D) [26, 27]. The ARMS-D is an 11-item self-report measure of adherence that assesses patients’ ability to take and refill diabetes medications, generating total, refill, and medication-taking subscale scores. Each of the items is structured for a response on a 4-point Likert scale and scored as 1 = “none,” 2 = “some,” 3 = “most,” or 4 = “all” of the time, with higher values indicating poorer adherence (total score ranges from 11 to 44) [26, 27].

Physicians also completed a workload form to record a 5-day period of overall patient case-load, including consultation of patients with T2DM, irrespective of patients recruited into the survey.

To be included in this retrospective analysis of the Diabetes DSPTM, patients had to have a physician-reported current and target HbA_{1c}, and have been diagnosed with type 2 diabetes mellitus for at least 3 months. For assessment of patient awareness of HbA_{1c} goal (the sub-analysis), in addition to the above, patients had to have completed a patient-reported questionnaire and answer the question on awareness of HbA_{1c} goal.

The survey obtained ethics approval from the Western Institutional Review Board, study protocol number 1247198, and was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Physicians did not see patient responses, thereby ensuring that future interactions between physicians and their patients were not compromised by patient responses. Patients provided written informed consent for use of their anonymized and aggregated data.

Statistical Analysis

Patient characteristics were summarized using descriptive analyses. Means and standard deviations (SDs) were calculated for continuous variables, and frequency and percentages were calculated for categorical variables. Glycemic control rates were calculated as the proportion of patients with a current HbA_{1c} level lower than the individualized HbA_{1c} goal set by physicians.

Inferential analyses were used to explore differences in patients’ characteristics between those achieving and those not achieving individualized HbA_{1c} goals. Fisher’s exact test was used for binary categorical variables, chi-squared test was used for unordered categorical variables (more than two groups), and a *t* test was used for continuous variables.

Multivariate regression was performed to determine the relationship between patient knowledge of their HbA_{1c} goal and goal achievement, controlling for age, gender, time since diagnosis, body mass index (BMI), previous HbA_{1c} value, Charlson Comorbidity Index (performed excluding diabetes as a comorbidity) [28], and number of AHAs currently used. A *p* value of less than 0.05 was taken as statistically significant.

RESULTS

Participant Characteristics

Physician Demographics

A total of 730 physicians, 306 (58%) PCPs and 424 (42%) diabetologists/endocrinologists, provided data on 8794 patients with type 2 diabetes mellitus (Fig. 1). Country-level differences are reported in Supplementary Table 1.

Patient Demographics

Of 5331 patients eligible for the analysis, 1126 (54.0%) patients were male with no differences across countries or previous waves of the survey. The median (IQR) duration of diabetes was 4.7 (2.0–9.6) years (Table 1). Physicians reported that after diabetes, the most common

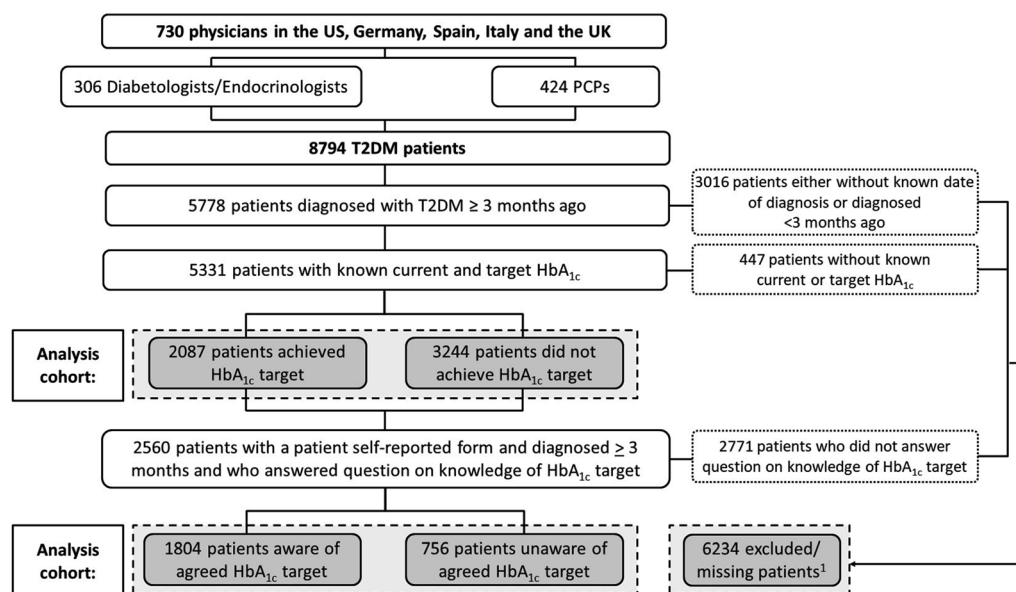


Fig. 1 Participant flow diagram. HbA_{1c} glycated hemoglobin, PCPs primary care physicians, T2DM type 2 diabetes mellitus. ¹These patients did not have a known physician-reported current or target HbA_{1c}, were diagnosed with type 2 diabetes mellitus less than 3 months ago, chose not to complete a self-reported record form, or chose

not to answer the question on awareness of their HbA_{1c} goal. Patients may or may not have been aware of their HbA_{1c} goal

cardiovascular-metabolic comorbid condition across the patient cohort was hypertension (67.1%), followed by CKD (6.8%) and coronary artery disease (6.6%).

Non-eligible patients are described in the Supplementary File.

Individualized HbA_{1c} Goals, Patient Attainment of Their HbA_{1c} Goal and HbA_{1c} at Pharmacologic Change/Addition

Individualized HbA_{1c} Assessment

Overall, patients had a mean (SD) individualized HbA_{1c} goal of 6.8% (0.68%). Of those patients with a known current and target HbA_{1c} ($n = 5331$), 39.1% met their individualized HbA_{1c} goal ($n = 2087$). Among those patients not reaching their individualized HbA_{1c} goal ($n = 3244$; 60.9%), the mean (SD, median) distance from individualized HbA_{1c} goal was 0.9% (1.0%; 0.6%). Individual country data also showed that patients in the UK had the longest disease duration and highest current HbA_{1c},

HbA_{1c} goal, and HbA_{1c} at pharmacologic change/addition compared with all other countries; Germany had the shortest disease duration and lowest HbA_{1c} at change/addition second lowest current HbA_{1c}, HbA_{1c} goal, indicating good correlation between disease duration and the HbA_{1c} difference. Overall, characteristics of patients not achieving their HbA_{1c} goal were similar to those achieving their goal (Table 1).

HbA_{1c} at Change/Addition of Pharmacologic Agents by Line of Therapy

Physicians' decision to change/add patients' pharmacologic agents at lines of therapy typically occurred above an HbA_{1c} of 8%. Pharmacologic change/addition from first-line of therapy to second-, third-, and fourth-line of therapy was made when HbA_{1c} levels were 8.3% ($n = 1998$), 8.3% ($n = 535$), 8.5% ($n = 116$), and 9.1% ($n = 16$), respectively (Fig. 2).

Table 1 Patient demographic and clinical characteristics by achievement of HbA_{1c} goal

	Overall (<i>N</i> = 5331)	Patients achieving HbA _{1c} goal (<i>N</i> = 2087)	Patients not achieving HbA _{1c} goal (<i>N</i> = 3244)	<i>p</i> value
Characteristic				
Age, years, mean (SD)	59.9 (12.1)	60.7 (12.1)	58.0 (12.0)	< 0.0001 (TT)
Male, <i>n</i> (%)	2934 (55.0)	1126 (54.0)	1808 (55.7)	0.2045 (FE)
Body mass index, kg/m ² , mean (SD)	30.1 (5.5)	29.7 (5.3)	30.4 (5.6)	< 0.0001 (TT)
Duration of diabetes, years, median (IQR)	4.7 (2.0, 9.6)	4.3 (2.0, 8.9)	4.9 (2.0, 10.0)	0.005 (MW)
HbA _{1c} assessment, mean (SD)				
Individualized HbA _{1c} goal	6.8 (0.7)	6.8 (0.6)	6.8 (0.8)	0.1039 (TT)
Most recent HbA _{1c}	7.3 (1.2)	6.5 (0.6)	7.7 (1.3)	< 0.0001 (TT)
Distance from individualized HbA _{1c} goal ^a	0.5 (1.0)	− 0.3 (0.3)	0.9 (1.0)	< 0.0001 (TT)
Comorbidities (physician-reported), <i>n</i> (%)				
Missing, <i>n</i>	1	0	1	–
Atrial fibrillation	275 (5.2)	104 (5.0)	171 (5.3)	0.6575 (FE)
Chronic kidney disease	362 (6.8)	147 (7.0)	215 (6.6)	0.0811 (FE)
Coronary heart/arterial disease	351 (6.6)	129 (6.2)	222 (6.8)	0.3654 (FE)
Heart failure	134 (2.5)	53 (2.5)	81 (2.5)	0.9288 (FE)
Hypertension	3286 (61.7)	1348 (64.6)	1938 (59.8)	0.0004 (FE)
Post-myocardial infarction	177 (3.3)	61 (2.9)	116 (3.6)	0.2104 (FE)
Peripheral vascular disease	154 (2.9)	55 (2.6)	99 (3.1)	0.4028 (FE)

Table 1 continued

	Overall (<i>N</i> = 5331)	Patients achieving HbA _{1c} goal (<i>N</i> = 2087)	Patients not achieving HbA _{1c} goal (<i>N</i> = 3244)	<i>p</i> value
Post-stroke	46 (0.9)	25 (1.2)	21 (0.6)	0.0473 (FE)

Total sample included where there are no missing data reported

FE Fisher's exact test, HbA_{1c} glycated hemoglobin, IQR interquartile range, MW Mann–Whitney, SD standard deviation, TT *t* test

^aFor those patients who did not attain their HbA_{1c} goal

Patient Awareness of Their Individual Glycemic Goal and Effect on Goal Attainment and Physician-Reported Assessment of Patient HbA_{1c} Testing

Patient Demographics, HbA_{1c} Value and Goal

Of 5331 patients with type 2 diabetes mellitus diagnosed for at least 3 months with a known current and target HbA_{1c}, 2560 (48.0%) patients qualified for the sub-analysis of whether they were aware of their HbA_{1c} goal agreed with their physician.

Of these 2560 patients, 1804 (70.5%) patients were aware of their HbA_{1c} goal. Overall,

patients in this sub-analysis had a mean (SD) age of 58.4 (11.7) years and 1396 (54.5%) were male (Table 2). There were no statistically significant differences in the demographics of patients who were aware and unaware of their HbA_{1c} goal. Overall, patients in the sub-analysis were currently using a mean of two AHAs, including metformin (62.5%) and very long-acting insulin (13.7%).

As 70.9% of the patient sample (6234/8794) did not qualify for this sub-analysis, demographics and outcomes were also compared between those qualifying and not qualifying for the sub-analysis (i.e., patients with an unknown

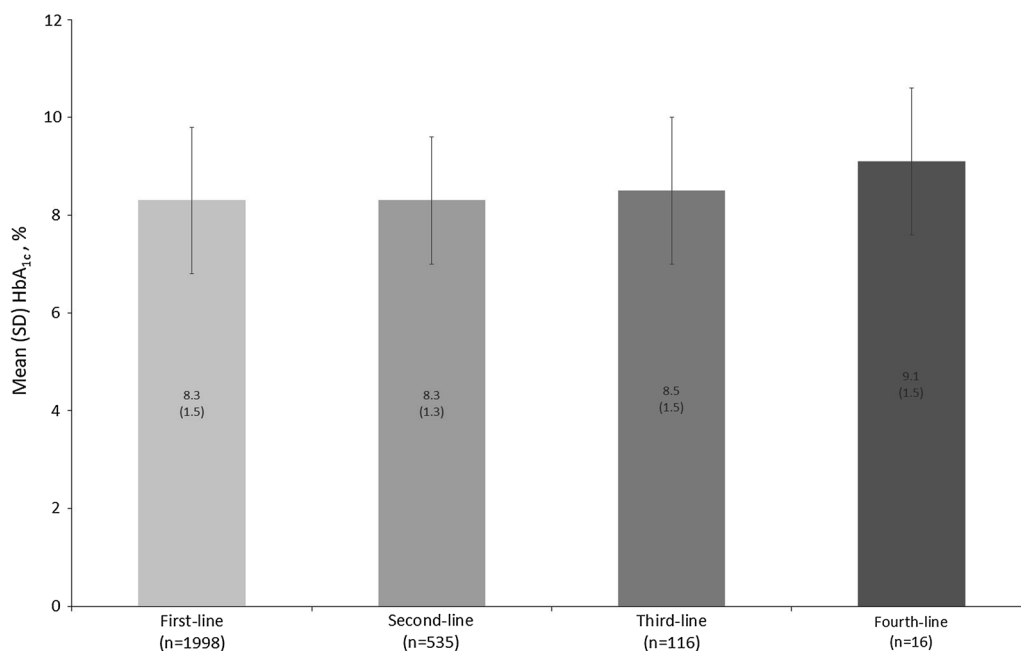


Fig. 2 Mean HbA_{1c} at change/addition of line of therapy. HbA_{1c} glycated hemoglobin, SD standard deviation. HbA_{1c} value is physician-reported

Table 2 Physician and patient characteristics by awareness of agreed HbA_{1c} goal

	Overall (<i>N</i> = 2560)	Patients unaware of agreed HbA _{1c} goal (<i>N</i> = 756)	Patients aware of HbA _{1c} goal (<i>N</i> = 1804)	<i>p</i> value
Physician-level information				
Physician characteristics				
Physician specification				< 0.0001 (FE)
Primary care physician	1556 (60.8)	507 (67.1)	1049 (58.1)	
Specialist (diabetologist/ endocrinologist)	1004 (39.2)	249 (32.9)	755 (41.9)	
Physician qualifying year				< 0.0001 (CH)
Before 1982	147 (5.7)	49 (6.5)	98 (5.4)	
1982–1994	912 (35.6)	287 (38.0)	625 (34.6)	
1995–2004	991 (38.7)	237 (31.3)	754 (41.8)	
2005–2015	464 (18.1)	166 (22.0)	298 (16.5)	
After 2015	46 (1.8)	17 (2.2)	29 (1.6)	
Physician 5-day workload, mean patients with T2DM, <i>n</i> (SD)	44.8 (35.1)	43.2 (35.4)	45.4 (35.0)	0.1341 (TT)
Patient-level information				
Patient demographics				
Age, years, mean (SD)	58.4 (11.7)	59.0 (12.5)	58.2 (11.3)	0.0819 (TT)
Male, <i>n</i> (%)	1396 (54.5)	413 (54.6)	983 (54.5)	0.9653 (FE)
Body mass index, kg/m ² , mean (SD)	29.8 (5.3)	29.9 (5.3)	29.8 (5.3)	0.8081 (TT)
Physician-reported clinical characteristics				
Median time since diagnosis, years (IQR)	4.3 (1.9, 8.7)	4.4 (2.0, 8.9)	4.3 (1.9, 8.6)	0.4012 (MW)
Mean most recent HbA _{1c}				
Missing, <i>n</i>	107	34	73	
Mean % (SD)	7.1 (1.2)	7.1 (1.2)	7.1 (1.1)	0.5659 (TT)
Mean target HbA _{1c}				
Missing, <i>n</i>	31	18	13	

Table 2 continued

	Overall (<i>N</i> = 2560)	Patients unaware of agreed HbA_{1c} goal (<i>N</i> = 756)	Patients aware of HbA_{1c} goal (<i>N</i> = 1804)	<i>p</i> value
Mean % (SD)	6.8 (0.7)	6.8 (0.9)	6.8 (0.7)	0.1705 (TT)
At (or below) current HbA _{1c} % goal				
Missing, <i>n</i>	136	51	85	
<i>n</i> (%)	949 (39.2)	292 (41.4)	657 (38.2)	0.1430 (FE)
Current therapy class, <i>n</i> (%)				
Missing, <i>n</i>	1	1	0	
Metformin	1600 (62.5)	499 (66.1)	1101 (61.0)	0.0176 (FE)
Metformin monotherapy	669 (26.1)	267 (35.4)	402 (22.3)	< 0.0001 (FE)
SU	263 (10.3)	76 (10.1)	187 (10.4)	0.8865 (FE)
DPP4i	259 (10.1)	80 (10.6)	179 (9.9)	0.6152 (FE)
SGLT2i	407 (15.9)	101 (13.4)	306 (17.0)	0.0243 (FE)
GLP-1	510 (19.9)	98 (13.0)	412 (22.8)	< 0.0001 (FE)
Very rapid-acting insulin	134 (5.2)	32 (4.2)	102 (5.7)	0.1727 (FE)
Very long-acting insulin	350 (13.7)	76 (10.1)	274 (15.2)	0.0005 (FE)
Any insulin	532 (20.8)	114 (15.1)	418 (23.2)	< 0.0001 (FE)
Mean number of drugs in current regimen				
Missing, <i>n</i>	1	1	0	
<i>n</i> (SD)	1.93 (0.89)	1.77 (0.88)	1.99 (0.88)	< 0.0001 (TT)
Mean current line of therapy				
Missing, <i>n</i>	467	115	352	
<i>n</i> (SD)	1.68 (0.80)	1.57 (0.72)	1.73 (0.83)	< 0.0001 (TT)

Table 2 continued

	Overall (<i>N</i> = 2560)	Patients unaware of agreed HbA _{1c} goal (<i>N</i> = 756)	Patients aware of HbA _{1c} goal (<i>N</i> = 1804)	<i>p</i> value
Charlson Comorbidity Index score (SD) ^a	0.3 (0.9)	0.4 (0.9)	0.3 (0.8)	0.1758 (TT)
Patient-reported adherence and therapy satisfaction				
Mean total ARMS-D score (range 11–44) ^b				
Missing, <i>n</i>	73	19	54	
Mean (SD)	15.0 (3.7)	15.5 (3.9)	14.8 (3.6)	< 0.0001 (TT)
Mean ARMS-D refill subscale score (range 4–16)				
Missing, <i>n</i>	47	13	34	
Mean (SD)	6.2 (1.7)	6.5 (1.7)	6.1 (1.7)	< 0.0001 (TT)
Mean ARMS-D medication-taking subscale score (range 7–28)				
Missing, <i>n</i>	58	15	43	
Mean (SD)	8.8 (2.6)	9.0 (2.7)	8.7 (2.5)	0.0108 (TT)
Physician-reported glucose testing				
Proportion of patients self-testing glucose levels				
Missing, <i>n</i>	7	2	5	
<i>n</i> (%)	1745 (68.4)	412 (54.6)	1333 (74.1)	< 0.0001 (FE)
Are physicians satisfied with the patient's current blood glucose level? <i>n</i> (%)				
				0.0012 (CH)
Yes	1494 (58.4)	455 (60.2)	1039 (57.6)	
No, but this is the best that can be realistically achieved	236 (9.2)	88 (11.6)	148 (8.2)	
No, and I believe that better control can be achieved	830 (32.4)	213 (28.2)	617 (34.2)	

Table 2 continued

	Overall (<i>N</i> = 2560)	Patients unaware of agreed HbA _{1c} goal (<i>N</i> = 756)	Patients aware of HbA _{1c} goal (<i>N</i> = 1804)	<i>p</i> value
Consulting physician specialty	Overall (<i>N</i> = 2560)	Primary care physician (<i>N</i> = 1556)	Specialist (<i>N</i> = 1004)	
Patient-reported awareness of agreed HbA _{1c} goal, <i>n</i> (%)				
Aware	1804 (70.5)	1049 (67.4)	755 (75.2)	< 0.0001 (FE)

ARMS-D Adherence to Refills and Medications Scale for Diabetes, *CS* chi-squared test, *DPP4i* dipeptidyl peptidase 4 inhibitor, *FE* Fisher's exact test, *GLP-1* glucagon-like peptide 1 receptor agonist, *HbA_{1c}* glycated hemoglobin, *IQR* interquartile range, *MW* Mann–Whitney, *SD* standard deviation, *SGLT2i* sodium glucose cotransporter 2 inhibitors, *SU* sulfonylurea, *TT* *t* test

Total sample included where there are no missing data reported

^aScale of 0, 1–2, 3–4, and ≥ 5; each increasing level represents an increase in the cumulative mortality attributable to comorbid disease

^bScale of 1, none of the time to 4, and all of the time; higher ARMS total and subscale scores indicate poorer adherence

^cScale of 1, very dissatisfied; 2, dissatisfied; 3, neither dissatisfied nor satisfied; 4, satisfied; and 5, very satisfied

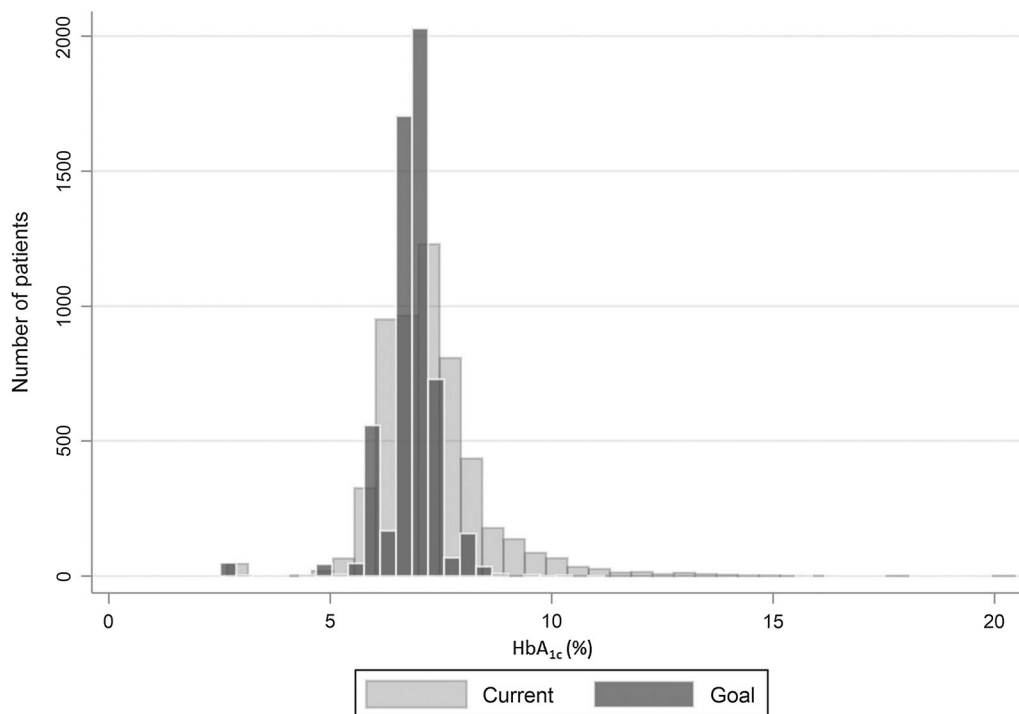


Fig. 3 Distribution of current and target HbA_{1c} among patients. HbA_{1c} glycated hemoglobin

HbA_{1c} goal, diagnosed with type 2 diabetes mellitus for less than 3 months, patients who did not chose to complete a self-reported record form, or those who chose not to answer the question on awareness of their HbA_{1c} goal) to investigate potential for bias. Minimal differences were seen between patients qualifying and not qualifying for this sub-analysis (Supplementary Table 2).

The individualized mean HbA_{1c} goal was 6.8% (0.7%) for the combined 2560 patients who were aware and unaware of their HbA_{1c} goal (Table 2). A higher proportion of patients aware of their HbA_{1c} goal were in the 6% to 7.5% patient groupings when compared to other HbA_{1c} goal groupings i.e. <6% and 7.5%+ (Supplementary Table 3). Their current mean HbA_{1c} value was 7.1% (1.2%). Distribution of current and target HbA_{1c} among patients is shown in Fig. 3.

Awareness of Glycemic Goal and Effect on Goal Attainment

Although the majority of patients included in the sub-analysis were aware of their HbA_{1c} goal, physicians reported that only 949 patients (39.2%) of these patients were successful in achieving their goal.

Achieving HbA_{1c} goal was not related to knowledge of goal; 38.2% of patients aware of their HbA_{1c} goal achieved it vs. 41.4% of those unaware of their goal ($p = 0.143$) (Table 2).

Age, gender, BMI, time since diagnosis, most recent previous HbA_{1c} measure, or Charlson Comorbidity Index [28] did not differ among patients aware and unaware of their HbA_{1c} goal (Table 2). Multivariate logistic regression controlling for these factors showed that patients who were aware of their HbA_{1c} goal were not more likely to meet it than those who were unaware (odds ratio 0.925; 95% confidence interval 0.721–1.19; $p = 0.541$).

Patients who were aware of their individual HbA_{1c} goal were using more AHAs in their current treatment regimen than those who were unaware of their HbA_{1c} goal; 68.4% vs. 55% of patients, respectively, received more than one AHA ($p < 0.0001$). Those receiving vs. not receiving a GLP-1 receptor agonist, SGLT2i, or insulin were more aware of their HbA_{1c} goal

($p < 0.05$). Patients aware of their HbA_{1c} goal were also on a later line of therapy than patients who were unaware; 53.3% of patients aware of HbA_{1c} goal were on second-line of therapy or later vs. 44.8% of patients unaware of goal.

While both patient groups who were aware and unaware of their agreed HbA_{1c} goal reported good adherence to their AHAs, those who were aware of their goal reported slightly higher adherence (ARMS-D total score 14.8 vs. 15.5, respectively; $p < 0.0001$).

Physician-Reported Glucose Testing and Patient Awareness

Physicians reported that those patients who were aware of their HbA_{1c} goal were more likely to test their blood glucose levels than patients who were unaware (74.1% vs. 54.6%; $p < 0.0001$) (Table 2). Physicians were not satisfied with the current blood glucose level of approximately one third of these patients. They believed that a higher proportion of patients who were aware of their HbA_{1c} goal could achieve better glucose control as opposed to those who were unaware (32.4% vs. 28.2%, respectively; $p = 0.003$). Physicians were more satisfied with the current blood glucose level of patients aware of their HbA_{1c} goal in the sub-analysis than those excluded patients not aware of their HbA_{1c} goal (58.4% vs. 49.0%; $p < 0.0001$).

Physician Profiles

The physicians' year of medical qualification and 5-day workload of patients with T2DM did not affect whether their patients were aware of an agreed HbA_{1c} goal or not. However, patients of diabetologists/endocrinologists were more aware of their agreed HbA_{1c} goal than patients of PCPs (75.2% vs. 67.4%; $p < 0.0001$) (Table 2).

DISCUSSION

Major international guidelines recommend the determination of glycemic goals on an individual level based on the respective patient's clinical profile. Data on individual glycemic goals

and the proportion of patients achieving them are generally not available from large datasets, such as claims data. Therefore, we aimed to assess this important question in a survey of 8794 patients with type 2 diabetes mellitus in the USA and Europe. We found that two thirds of patients were not at the HbA_{1c} goal set by their physician, which was on average 6.8%, and that physicians were not changing/adding AHAs until HbA_{1c} was above 8%. The HbA_{1c} goal of 6.8% in our analysis is comparable to patient-reported HbA_{1c} goals set by physicians in other countries (6.1–6.9%), where 26–70% of patients reported that they had a specific HbA_{1c} goal [29].

Waiting to change/add therapies could suggest therapeutic inertia, whereby physicians delaying intensification of treatment regimen of patients with type 2 diabetes mellitus when appropriate to achieve good glycemic control [30]. Moreover, it may also indicate that guideline recommendations of a target HbA_{1c} of < 7.0% [1–3] are not being fully implemented by physicians in clinical practice. Studies have previously found that a considerable proportion of patients with type 2 diabetes mellitus with suboptimal glycemic control experience a delay in receiving treatment intensification with AHAs [31, 32]. The average time to treatment intensification from one to two AHAs agents in patients with HbA_{1c} \geq 7.0% was 2.9 years, 1.9 years in patients with HbA_{1c} \geq 7.5%, and 1.6 years in patients with HbA_{1c} \geq 8.0% [31]. Evidence suggests that patients with type 2 diabetes mellitus do not receive intensified treatment for over a year after monotherapy failure, with half of patients waiting over 5 years [33].

Similarly to our analysis, other studies confirm that patients do not receive treatment intensification until their HbA_{1c} is $>$ 8 [33, 34]. Of concern, therapy for around half of patients with an HbA_{1c} of 8 to \geq 9% is not intensified [35]. Patients with type 2 diabetes mellitus who intensified treatment earlier have been found to have higher mean HbA_{1c} levels, suggesting that physicians react to disease severity [33, 36]. Early treatment intensification also resulted in patients achieving a greater mean decline in HbA_{1c} level [33, 36]. Moreover, patients

receiving rapid treatment intensification appear to achieve a maintained HbA_{1c} reduction faster than patients with delayed treatment intensification or no second-line therapy, despite a higher HbA_{1c} at baseline [37].

Challenges for healthcare systems such as poor communication between healthcare providers, lack of a coordinated care plan, and time limitations may also play a role in inertia with later therapy lines [38, 39].

Over two thirds of patients in our analysis (68.1%) were utilizing more than one AHA; most were receiving metformin with fewer on insulin, a GLP-1 receptor agonist, and/or a SGLT2i. A study with a cohort of around 21,000 newly treated patients with type 2 diabetes mellitus (76% initiated on metformin) in the Republic of Ireland found that about 20% of those who remained on their initial therapy were non-persistent to their treatment (i.e., treatment gap of more than 12 weeks within 365 days of treatment initiation) [40]. Of those changing treatment regimens, treatment additions were more frequent than changes. After metformin, treatment additions were sulfonylurea followed by a dipeptidyl peptidase 4 inhibitor, and changes were most frequently to a sulfonylurea followed by a metformin combination product [40].

Although the majority of patients ($n = 1804$, 70.5%) included in the sub-analysis were aware of their HbA_{1c} goal, interestingly, awareness of HbA_{1c} goal did not enhance goal attainment. Other studies have reported that two thirds or more of patients with type 2 diabetes mellitus did not know their last HbA_{1c} [20, 41]. In one study, the few patients who knew their last HbA_{1c} value reported a biomedically accurate level of diabetes control and better understanding of diabetes care compared with those who did not know their HbA_{1c} value [20]. However, such knowledge of HbA_{1c} did not translate into improved diabetes self-management [20].

With a decline in beta-cell function and mass, more treatments fail to control glycemic levels and there is an increasing risk of the development of complications [42]. Patients may become more aware of their goal if they have more recalcitrant disease because it makes

goal achievement more difficult. Our analysis indicated that patients who were aware of their HbA_{1c} goal were on more agents and insulin, and to consult with a specialist rather than a PCP. They had also used more lines of therapy and tested their glucose level more frequently. Patients on metformin monotherapy, typically those who are easier to treat, met their goal even though they were less likely to know what that goal was.

Our findings should be considered in light of the survey limitations. The non-random sample of physicians led to over-representation of specialists based on national PCP-to-specialist ratios [43]. Potential differences between PCPs and diabetologists/endocrinologists in knowledge level and diabetes management may have affected patient treatment and clinical outcomes. Furthermore, the patient population was not truly random because of the inclusion of the next ten consecutive consulting patients and two additional patients receiving SGLT2i or GLP-1 therapy. Additionally, analysis of the overall patient population excluded 39.4% of patients for whom current HbA_{1c} or individualized HbA_{1c} goals were unavailable, or who had been diagnosed with type 2 diabetes mellitus for less than 3 months. Although unsurprising, the reduction of patient numbers evaluated at each change/addition in line of therapy was also recognized. Lastly, this analysis included patients from different European countries and the USA; therefore, findings may have been affected by country variations in clinical practice and may differ should data be drawn from one or more other countries. Further research is required at a country level. Of note, data was collected prior to the emergence of coronavirus disease (COVID-19) and does not reflect shifting practice patterns caused by the pandemic.

In conclusion, we demonstrated that the proportion of patients with type 2 diabetes mellitus achieving their goals for glycemic control remained suboptimal when compared to current guideline criteria. Despite the availability of many new antihyperglycemic medications, about 60% of patients with type 2 diabetes mellitus did not achieve their individualized HbA_{1c} goal. Intensification of treatment was often delayed until HbA_{1c} was 8% or higher.

Results of this analysis highlighted the need for a holistic approach to diabetes management, involving patient education, and patient–physician communication and partnership.

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Compliance with Ethics Guidelines. The survey obtained ethics approval from the Western Institutional Review Board, study protocol number 1247198, and was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Physicians did not see patient responses, thereby ensuring that future interactions between physicians and their patients were not compromised by patient responses. Patients provided written informed consent for use of their anonymized and aggregated data.

Data Availability. All data relevant to the analysis are included in the article. All data that support the findings of this survey are the intellectual property of Adelphi Real World. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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