




# Factors impacting chronic disease medication adherence in the UAE: a prospective cohort study, 2021–2022

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**Aim:** To assess the evolution of chronic disease medication adherence factors and identify factors predictive of long-term adherence in the UAE. **Materials & methods:** Patients  $\geq 18$  years old; newly diagnosed with one of the following diseases: ankylosing spondylitis, heart failure, multiple sclerosis, psoriasis, or asthma and prescribed long-term medication were followed  $\geq 12$  months (M12), then categorized as followed (continued treatment by prescribing physician) or lost to follow-up. Adherence was assessed using the Patient Needs Assessment Tool (PNAT), which is based on the WHO's five dimensional framework. **Results:** A total of 111 patients were included, 17 (15.3%) were lost of follow-up at M12. Time spent in consultation by medical doctor (MD) (adjusted odds ratio = 6.89, 95% CI = 2.07–12.76) and anxiety and stress level (adjusted odds ratio = 0.18, 95% CI = 0.11–0.67) were significant predictive factors associated with remaining on treatment at M12. Self organizing map methodology identified predictive factors associated with remaining on treatment at M12 as: patient satisfaction with time spent with prescribing MD, patient involvement in treatment decision, disease management ability, satisfaction with support from family/friends, low dependence on others for daily life activities, difficulties joining community activities, and acknowledgement of an influential role of cultural habits/spiritual beliefs. The highest means score differences from M0 to M12 were for difficulties joining community activities (difference [diff] M12-M0 = 1.32,  $p < 10^{-4}$ ), role of cultural habits (diff = 1.05,  $p < 10^{-4}$ ), role of spiritual beliefs (diff = 1.02,  $p < 10^{-4}$ ), patient involved in treatment decision (diff = 0.67,  $p = 0.007$ ), and memory difficulties (diff = 0.62,  $p < 10^{-4}$ ). **Conclusion:** Socio-economic factors changed most significantly over 12 months. The identified factors may be used to develop strategies to improve patient satisfaction with the time they spend with the prescribing MD as well as reduce stress, each of which may improve medication adherence. Understanding patient behavior and accurately quantifying adherence are essential for improving outcomes for patients prescribed chronic disease medication in Gulf Arabic countries.

**Plain language summary: Factors that determine if patients in the UAE prescribed medication for chronic diseases continue to see the prescribing physician one year after starting treatment**

**What is this article about?** This article identifies factors that influence whether or not patients prescribed medication for a chronic disease continue to see the prescribing physician for the year following initiation of treatment.

**What were the results?** The study showed that patients who were satisfied with the amount of time they spent with their doctor, were involved in treatment decisions, able to manage their disease, satisfied with the support they received from family/friends, and had low dependence on others for daily life activities were more likely to keep taking their medicine for a year. Patients who had difficulties joining community activities, had high levels of anxiety and stress, and acknowledged an influential role of cultural habits/spiritual beliefs were more likely to have been lost to follow-up at 1 year. In this study patients lost to follow-up were assumed to have stopped taking their medication, although it is possible that they continued to do so.

**What do the results mean?** The findings of this study might be used to help identify patients who are less likely to continue taking their medication as prescribed. Finding ways to address their concerns and challenges might be important for helping these patients to continue taking their medicine as prescribed.

**Shareable abstract:** New insights into factors driving patients' adherence to chronic disease medication may enable more effective interventions. Improved patient satisfaction with time spent with physicians and reducing stress/anxiety may improve chronic disease medication adherence in the UAE.

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In 2003, the WHO issued a landmark report on medication adherence highlighting the global challenges of poor medication adherence, establishing the expectation that these challenges would increase as chronic diseases became more prevalent, and underscoring the health and economic costs associated with poor adherence to chronic disease medication [1]. The average rate of medication adherence in developed countries was 50%, with lower rates found in low- and middle-income countries (LMICs) [1]. A more recent WHO report found that noncommunicable diseases, which comprise many chronic conditions, continue to be the major cause of disease burden globally, rising from the cause of 60% of deaths in 2000 to 74% in 2019 [2]. Cardiovascular disease, cancer, chronic respiratory disease and diabetes collectively were responsible for the deaths of 33.3 million people in 2019, an increase of 28% compared with 2000 [2]. In this context, increasing the rate of adherence to chronic disease therapy is essential for improving outcomes for the growing number of people living with chronic illnesses.

Despite this knowledge and the urgent need associated with achieving this goal, adherence rates remain suboptimal across diverse geographic areas and chronic diseases. A systematic review and meta-analyses of data from 2010 to 2020 found a global prevalence of nonadherence to antihypertensive medication of 27–40%, with higher rates of nonadherence more prevalent in LMICs [3]. Consistent with this finding regarding economic status and adherence, studies in Ethiopia and India found adherence rates to chronic cardiovascular disease medication of 9 and 20%, respectively [4,5]. Several studies conducted in Gulf Arabic countries found adherence rates for antidiabetic or cardiovascular drugs ranging from 25 to 66%. One study conducted in patients with Type 2 diabetes in Saudi Arabia found that 75% of the patients had poor, low and partial adherence to antidiabetic medication [6] while another found an overall adherence rate of 66% [7]. Similarly, a study conducted in patients with Type 2 diabetes in the UAE during the COVID-19 pandemic reported that 62% of patients were categorized as having low adherence to antidiabetic medication and 29% were categorized as having medium adherence [8], and a cross-sectional study in older adults in Jordan with Type 2 diabetes and cardiovascular comorbidities found that only 59% of patients had a high level of adherence to treatment [9]. While poor adherence may be more prevalent in LMICs, additional studies underscore the global nature of the challenge. For example studies in the USA, Spain and Germany found rates of adherence to chronic disease medication ranging from 52 to 59% [10–12], while a study conducted in The Netherlands found that 68% of patients with resistant hypertension were nonadherent to their medication [13].

Considering these studies based on indication rather than geography also highlights the challenge that non-adherence poses to people living with a variety of chronic diseases. Studies in patients with Type 2 diabetes find adherence rates ranging from 9% in India [5] to 66% in Gulf Arabic countries. [6–9], while rates in patients with cardiovascular conditions were 9% in India [5], 20% in Ethiopia [4] and 38% in The Netherlands [13]. Studies evaluating medication adherence in a variety of chronic disease conditions in Europe and the US found adherence rates of 52–59% [10–12].

These different studies demonstrate the ongoing global challenge of medication nonadherence across a variety of highly prevalent chronic diseases 15–20 years after the WHO's landmark report. Collectively, they underscore the need for continued research, investment and innovation in interventions that can significantly improve adherence to chronic disease treatment.

For more than 20 years, adherence to therapy has been viewed through the lens of the WHO's 'five dimensions of adherence', which comprise social- and economic-related factors; health system- and healthcare team-related factors; therapy-related factors; condition-related factors and patient-related factors [1]. Despite the decades-long existence of this multidimensional model, the role(s) of individual factors within these categories remains difficult

to evaluate. Some individual factors, including cultural issues, belief systems, education level, mental health and substance abuse issues, cost of medication, adverse medication effects, complexity of care and the quality of patient–provider relationships have been suggested [14], but a more granular understanding of the role that specific factors play in adherence has not yet been attained. This results in part from the continued evolution of how individuals, communities and countries approach, support and invest in health.

Another challenge in improving adherence rates for chronic disease medication is understanding and identifying ways to modify human behaviors related to change. This challenge is exemplified by a study of medication adherence in patients with chronic diseases in Saudi Arabia that found that the most common reason that patients gave for nonadherence was ‘no specific reason’ [15]. The inability for patients to identify or articulate a reason for not adhering to chronic disease medication makes it difficult to gain insight into what drives this behavior and to develop interventions that can modulate behavior to improve adherence. Behavior related to treatment adherence is often referred to as ‘self-management’ [16]. More recently, a new definition – based on ten attributes organized into three groups – has been proposed for self-management [17]. This new definition states that “*Self-management is the intrinsically controlled ability of an active, responsible, informed and autonomous individual to live with the medical, role and emotional consequences of his chronic condition(s) in partnership with his social network and the healthcare provider(s)*” [17].

The evolving definition of self-management in chronic disease reflects the ongoing need to evaluate and delineate how patients perceive their disease and their role in managing it, and their ability to initiate and sustain activities and behaviors that enable effective management. Toward this end, we previously evaluated factors impacting self-management ability in patients with chronic diseases in the UAE using the WHO five-dimension framework. We identified patient’s understanding of disease, involvement in treatment decision, age more than 40 years, time spent with physician and fear of how patients were perceived by others were the most predictive factors associated with a high ability to self-manage chronic disease [18].

In this second study, the objective was to assess the evolution of adherence factors over time and to identify factors predictive of long-term (12 months) adherence to chronic disease therapy.

## Materials & methods

### Setting & study design

As previously described [18], Axios International implemented an adherence program for chronic diseases in 2019 in the UAE, which had the objectives of designing personalized action plans addressing each patient’s adherence needs, providing educational, emotional and psychological support to enhance patients’ understanding of how to manage their disease, and providing educational support regarding patients’ chronic disease medication [18]. Briefly, the program utilized the Patient Needs Assessment Tool (PNAT), which is based on the WHO’s five dimensional framework [1]. The PNAT, which uses 28 variables to evaluate patients’ self-management needs, was validated prior to its use in the study and implemented in both Arabic and English. The PNAT was deployed in the context of the adherence program in 50 hospitals in the UAE (47.6% of UAE hospitals), including 10 public and 40 private hospitals.

In the current longitudinal study conducted in 2021 and 2022, patients included in the initial cross-sectional study [18] were prospectively followed for 12 months, at which time their status was categorized as the two followed end points: continued treatment (by physician initially prescribing for the chronic disease therapy) or lost to follow-up (LTFU).

### Study population

The study population included 111 patients who were at least 18 years old and newly diagnosed with one of the following chronic health conditions: ankylosing spondylitis, heart failure, multiple sclerosis, psoriasis or asthma. These five chronic diseases, which were included in the PNAT Access Program, persist over time and require continuous medical management to prevent disease progression, complications and deterioration in quality of life. All participants had been prescribed long-term ( $\geq 12$  months) medication. Participants received medication and care at public and private health facilities in the UAE [18].

### Data collection

At inclusion, data were collected using a structured questionnaire, conducted by a bilingual investigator (English–Arabic). Baseline characteristics collected were: gender, age, the highest level of education (secondary school or

lower, undergraduate and graduate studies), employment (yes, no), living status (married, living with parents, family or alone), diagnosis (ankylosing spondylitis, heart failure, multiple sclerosis, psoriasis, asthma), treatment administration (oral, injection) and hospital status where the patient was followed (public, private).

A 5-point Likert scale (strongly disagree = 1, disagree = 2, neither agree nor disagree = 3, agree = 4, strongly agree = 5) was used to evaluate multiple factors that were organized within the WHO's five-dimension framework [1]. As previously used and described in our previous article [18], the collected variables were:

Healthcare system-related factors: quality of information provided, confidence in medical, doctor (MD) explanations, confidence in MD prescription, confidence in hospital care, support of healthcare professionals (HCP), other patients (i.e., in associations of patients), satisfaction with HCP responses, availability of MD, satisfaction with time spent in consultation with the MD and patient involvement in treatment decision.

Treatment-related factors: fear of treatment inefficiency, long-time treatment and adverse events.

Patient-related factors: disease understanding, disease management ability, impact of age on disease management, treatment adherence and fear of how others perceived the patient.

Socio-economic factors: difficulties joining communities activities, interference between living conditions and treatment, and the roles of cultural habits, spiritual beliefs, family and friends.

Condition-related factors: memory difficulties, impaired work performance due to the disease and/or treatment, risk of forgetting to take medication, anxiety and stress level, burden of treatment cost and being dependent on others for daily life activities.

## Outcomes

The objective of the study was to evaluate predictive factors associated with patients continuing treatment at month 12, with patients categorized based on two potential outcomes: followed (continuing to be seen by the prescribing physician) or LTFU. Likert scale-responses to the PNAT were categorized into a high group (Likert scale = 5) and a low and moderate group (Likert scale = 1–4) [19,20].

We also assessed the evolution of multidimensional adherence factor scores between inclusion (M0) and follow-up at 12 months (M12) by comparing patient scores on the same questionnaire administered at M0 and M12.

## Statistical analyses

Descriptive statistics were calculated as percentages for qualitative variables and means and their standard deviations (SD) and median (M) values for quantitative variables. Chi-square test and Fisher exact test were used for qualitative data comparisons. Student's *t*-test was used for quantitative comparisons. No sample size was calculated.

In univariate analysis, variables with  $p < 0.20$  were fitted into the multivariate logistic regression in order to identify independent factors associated with patients continuing to be seen by the prescribing physician at M12. Adjusted odds ratios (AOR) and 95% CI were calculated.

To illustrate relationships between answers from the PNAT questionnaire, patient demographics and loss to follow-up, an exploratory, unsupervised analysis was further performed using the self organizing map (SOM) methodology [21]. Briefly, this method makes it possible to reduce a multidimensional dataset into 2D maps that can be more easily interpreted. Each map is divided into small cells (or districts) in which patients are located by the algorithm based on their differences or similarities: patients with similar features are closely located on the maps, whereas patients with differentiated profiles are farther from each other. The SOMs were built with the R Numero package [22] after principal component analysis adapted for qualitative and quantitative variables was applied using the PCAMix method [23].

A two-tailed level of statistical significance was set at  $p\text{-value} \leq 0.05$  (denoted below by \*). Statistical analyses were calculated using Excel Stat (Addinsoft) for descriptive analyses between-group comparisons and regression models, and R 4.4.1 (R Foundation, Vienna, Austria; PCAMix and Numero packages) for unsupervised analyses.

## Ethics statement

The Ethical Committee of Rouen University Hospital (CERDE-HLJ) approved the research (# E2021-74). Patients provided written informed consent to enroll in the Access Program; research written consent was not required for collection of patient data because information from patient files was collected anonymously from medical reports, without collection of personal, patient-identifying information.

**Table 1. Sociodemographic characteristics of patients with chronic disease followed (under treatment) and patients lost to follow-up, UAE, 2019–2022.**

	Followed (n = 94)	Lost to follow-up (n = 17)	p-value
Sex ratio M:W	0.84	1.83	0.16
Mean age (SD)	40.6 (13.2)	45.2 (15.3)	0.21
Education level (%)			
None, primary and secondary school	14.1	31.3	0.26
Undergraduate studies	57.8	43.7	
Graduate studies	28.1	25.0	
Working employment (%)			
Employed	59.1	43.7	0.41
Unemployed	40.9	56.3	
Living status (%)			
Married	66.7	94.1	0.02 <sup>†</sup>
Living with parents or family or alone	33.3	5.9	
Diagnosis (%)			
Ankylosing spondylitis	6.9	5.9	0.03 <sup>†</sup>
Heart failure	11.1	29.4	
Multiple sclerosis	47.3	23.5	
Psoriasis	31.9	23.5	
Asthma	2.8	17.6	
Treatment administration (%)			
Oral	56.9	52.9	0.97
Injection	43.1	47.1	
Hospital status			
Public	25.4	29.4	0.97
Private	74.6	70.6	

<sup>†</sup>p < 0.05.

M: Men; SD: Standard deviation; W: Women.

## Results

A total of 111 patients were included in the current study, all of whom were alive at M12. Results at inclusion were previously reported [18]. Main baseline characteristics at inclusion were a mean age of 41.1 years (SD = 13.0, M = 39.4); sex ratio M:W = 0.80; 56.0% of patients were working. With respect to living status, 71.4% were married, 22.9% were living alone and 5.7% were living with parents or family. With respect to disease indication, patients had psoriasis (37.8%), multiple sclerosis (35.8%), heart failure (12.3%), ankylosing spondylitis (9.4%) or asthma (4.7%). Of the 111 patients included in the initial study (M0), 17 (15.3%) were LTFU at M12.

Table 1 compares baseline characteristics of patients followed and patients LTFU at M12. The groups were quite similar, except for living status (94.1% of patients in group LTFU were married, compared with 66.7% in the followed group) and disease indications (significantly more patients with a diagnosis of heart failure or asthma were in the LTFU group).

Table 2 presents the scores of multidimensional adherence factors in the two groups. Scores for patients satisfaction with time spent with prescribing MD, patient involved in treatment decision and disease management ability were significantly higher in the followed group, while scores for difficulties joining community activities, anxiety and stress level and being dependent of others for daily life activities were significantly higher in the LTFU group.

Logistic regression analysis identified patient satisfaction with time spent in consultation with the prescribing MD (AOR = 6.89, 95% CI = 2.07–12.76) as a significantly positive predictive factor associated with being followed at M12 and anxiety and stress level (AOR = 0.18, 95% CI = 0.11–0.67) as a negative factor associated with being followed at M12 (Table 3).

Table 4 presents the mean scores and differences in the multidimensional adherence factors in the 94 patients followed until M12. For the 28 variables assessed within the WHO five-dimension scale, the highest mean differences between scores at M0 versus M12 were found for difficulties in joining community activities (difference [diff] M12-M0 = 1.32, p < 10<sup>-4</sup>), role of cultural habits (diff = 1.05, p < 10<sup>-4</sup>), role of spiritual beliefs (diff = 1.02, p < 10<sup>-4</sup>), patient involvement in treatment decision (diff = 0.67, p = 0.007) and memory difficulties (diff = 0.62, p < 10<sup>-4</sup>).

Results from an unsupervised analysis by the SOM methodology are shown in Figure 1, representing 2D maps of patients grouped according to their characteristics, i.e., LTFU, demographics and PNAT answers. Patients with

**Table 2. Scores of multidimensional adherence factors in patients with chronic disease followed (under treatment) and patients lost of follow-up, UAE, 2019–2022 (results expressed in percentages).**

	Followed (n = 94)	Lost of follow-up (n = 17)	p-value
<b>Healthcare system-related factors</b>			
Quality of information provided	50.0	35.3	0.28
Confidence in MD explanations	26.4	17.6	0.45
Confidence in MD prescription	61.1	47.1	0.29
Confidence in hospital care	56.9	52.9	0.76
HCP support in connecting with other patients	23.6	28.4	0.62
MD availability	41.7	29.4	0.35
Satisfaction with HCP responses	33.3	23.5	0.43
Satisfaction with time spent with MD	47.4	8.8	0.003 <sup>‡</sup>
Patient involved in treatment decision	30.2	11.6	0.01 <sup>†</sup>
<b>Treatment-related factors</b>			
Fear of treatment inefficiency	1.3	11.8	0.72
Fear of long-time treatment	1.3	5.9	0.98
Fear of adverse events	6.7	11.7	0.62
<b>Patient-related factors</b>			
Disease understanding	43.1	41.2	0.89
Disease management ability	47.2	17.6	0.01 <sup>†</sup>
Impact of age on disease management	2.8	5.9	0.52
Treatment adherence	56.9	47.1	0.46
Fear of others' perceptions	4.2	5.9	0.76
<b>Socio-economic factors</b>			
Difficulty joining community activities	2.8	17.6	0.01 <sup>†</sup>
Interference between life and treatment	2.8	5.9	0.52
Role of cultural habits	6.2	3.1	0.56
Role of spiritual beliefs	13.9	5.9	0.37
Role of family and friends	56.9	39.2	0.11
<b>Conditions-related factors</b>			
Memory difficulties	47.1	47.2	0.98
Impaired work performance	9.7	11.8	0.80
Risk of forgetting treatment	52.8	47.9	0.67
Anxiety and stress level	6.3	39.3	0.001
Burden of treatment cost	31.9	41.2	0.47
Dependent on others for daily life activities	63.9	35.3	0.03 <sup>†</sup>

† p < 0.05.  
‡ p ≤ 0.01.  
HCP: Healthcare professional; MD: Medical doctor.

the highest loss to follow-up rates are located in the lower left area of the maps, as shown by the red color in this zone of the map titled 'lost to follow-up' in Figure 1. Visual analysis of this specific area in the maps for other factors mostly confirmed our previous results regarding the associations between loss to follow-up and the following factors: decreased (blue colors) patient satisfaction with time spent with the prescribing MD, patient involvement in treatment decision, disease management ability, satisfaction with support from family/friends and dependence on others for daily life activities; increased (red colors) difficulties joining community activities, anxiety and stress level and acknowledgement of an influential role of cultural habits/spiritual beliefs. Interestingly, apparent associations between loss to follow-up and several other factors were revealed by the SOM analysis, despite these factors not achieving statistical significance in the logistic regression analysis. These include an increased fear of society perception of the patient and lower physician availability.

**Table 3. Predictive factors associated with following of patient treated for chronic disease, UAE, 2019–2022 (logistic regression<sup>†</sup>).**

	AOR	95% CI	p-value
Patient satisfaction with time spent with MD	6.89	2.07–12.76	0.003 <sup>§</sup>
Patient involved in treatment decision	0.75	0.18–3.23	0.71
Disease management ability	3.01	0.84–9.76	0.09
Difficulty joining community activities	0.29	0.09–2.46	0.25
Role of family and friends	0.86	0.28–3.78	0.68
Anxiety and stress level	0.18	0.11–0.67	0.009 <sup>§</sup>
Dependent on others for daily life activities	2.26	0.75–7.85	0.20

<sup>†</sup> Adjusted for sex, age and disease.  
<sup>‡</sup>  $p < 0.05$ .  
<sup>§</sup>  $p \leq 0.01$ .  
AOR: Adjusted odds ratio; CI: Confidence interval; MD: Medical doctor.

## Discussion

To our knowledge, this is the first study in a Gulf Arabic country that has prospectively evaluated the association of a large number of factors with disease medication adherence among patients with chronic disease over the course of 12 months. These factors align with the WHO's five-dimension conceptual framework for adherence and comprise social and economic, healthcare team and system-related, condition-related, therapy-related and patient-related factors. The key findings of the study are that patient satisfaction with time spent with the prescribing MD, low levels of stress, patient involvement in treatment decision, disease management ability, satisfaction with support from family/friends and low dependence on others for daily life activities were significant predictive factors associated with being followed by the prescribing MD 12 months after initiating chronic disease medication. Difficulties joining community activities, anxiety and high stress level, and acknowledgement of an influential role of cultural habits/spiritual beliefs were predictive factors for being LTFU at 12 months. Additionally, the SOMs analysis underscores the interplay among these factors and, in some instances, the potential for positive factors to overcome negative factors.

Patient satisfaction with time spent with the prescribing physician was identified as a predictive factor for remaining on treatment in both the regression and SOMs analyses. Time spent with the physician reflects a variety of patients' perceptions, including quality of care; satisfaction with the amount of time spent in consultation with the MD, and feeling that the MD took sufficient time to explain treatment; potential adverse events; and modalities of follow-up. This finding is consistent with prior studies that have shown that the patient–prescriber relationship and increased disease education were main modifiers of therapeutic conduct [24]. Similarly, prior studies have also shown that higher rates of nonadherence in patients with multiple chronic conditions were associated with patients not receiving information about their medication [11]; that patients were significantly more likely to take their chronic disease medication as prescribed when the provider gave clear instruction about medication use [15]; that receiving complete treatment information and having adequate knowledge about medication regimen were independent factors associated with adherence in patients with chronic conditions [10]; and that adherence to inhalation devices in patients with chronic obstructive pulmonary disease (COPD) is better in patients who were trained to use their device by specialist physicians [25]. A review of interventions to improve medication adherence found that patient education interventions were modestly effective in improving adherence rates [26]. A scoping review of qualitative evidence found that patients consider having the right professional guidance essential for understanding the 'big picture' of their chronic disease condition, and that the absence of this guidance disempowered patients from making effective health decisions [27].

A study conducted in pharmacies found that a high perceived importance of the medication by the patient was significantly associated with chronic disease medication adherence [12]. Such perceptions may be enhanced by effective education about the patient's disease and the value of therapy in managing the disease and improving the patient's health. A meta-analysis found that stronger perceptions of treatment necessity and fewer concerns about treatment – both of which could be addressed in satisfying patient–provider interactions found in the current study – were significantly associated with higher adherence [28]. A study conducted in patients in the UAE with Type 2 diabetes found that only 11% of respondents had adequate levels of health literacy [29], and it is likely that the patients in our study, which also was conducted in the UAE, had a similarly low literacy level about their own

**Table 4. Evolution of scores of multidimensional adherence factors in patients with chronic diseases at inclusion (M0) and 12 months later (M12), UAE, 2019–2022 (n = 94).**

	Mean score (SD <sup>†</sup> ) on a total of 5			
	M0	M12	Difference M12-M0	p-value
Healthcare system-related factors	4.02 (0.98)	3.94 (0.85)	-0.08	0.38
Quality of information provided	4.38 (0.60)	4.34 (0.55)	-0.04	0.72
Confidence with MD explanations	3.83 (0.98)	4.06 (0.64)	0.23	0.14
Confidence with MD prescription	4.65 (0.52)	4.19 (0.60)	-0.46	<10 <sup>-4§</sup>
Confidence in hospital care	4.15 (0.94)	4.19 (0.97)	-0.02	0.98
Support of HCP to join other patients	3.48 (1.43)	3.12 (1.26)	-0.36	0.09
MD availability	4.14 (0.84)	4.04 (0.68)	-0.10	0.48
Satisfaction with HCP responses	4.16 (0.90)	4.00 (0.72)	-0.16	0.15
Satisfaction by time spent with MD	4.04 (1.08)	3.85 (0.98)	-0.19	0.38
Patient involved in treatment decision	3.12 (1.62)	3.70 (1.14)	0.67	0.007‡
Treatment-related factors	2.67 (0.39)	3.08 (0.58)	0.41	0.001§
Fear of treatment inefficiency	3.02 (1.13)	3.31 (0.98)	0.29	0.07
Fear of long-time treatment	2.98 (1.13)	3.40 (0.95)	0.42	0.02†
Fear of adverse events	2.09 (1.13)	2.65 (1.40)	0.56	0.03†
Patient-related factors	3.81 (0.56)	3.72 (0.47)	0.09	0.21
Disease understanding	4.25 (0.79)	4.26 (0.74)	0.01	0.86
Disease management ability	4.28 (1.88)	4.28 (0.86)	0	0.97
Impact of age on disease management	2.90 (1.18)	3.00 (1.19)	0.10	0.77
Treatment adherence	4.41 (0.82)	4.34 (0.62)	-0.07	0.47
Fear of others' perceptions	2.47 (1.34)	2.45 (1.41)	-0.02	0.82
Socio-economic factors	2.37 (0.67)	3.56 (1.13)	1.19	<10 <sup>-4§</sup>
Difficulty joining community activities	1.89 (1.18)	3.21 (1.16)	1.32	<10 <sup>-4§</sup>
Interferences between life and treatment	1.73 (0.97)	1.96 (1.06)	0.23	0.30
Role of cultural habits	1.80 (0.88)	1.85 (1.50)	1.05	<10 <sup>-4§</sup>
Role of spiritual beliefs	2.24 (1.60)	3.26 (1.11)	1.02	<10 <sup>-4§</sup>
Role of family and friends	4.12 (0.92)	4.50(0.61)	0.38	0.01†
Conditions-related factors	3.30 (0.64)	3.17 (0.64)	-0.12	0.33
Memory difficulties	3.73 (1.30)	4.35 (1.03)	0.62	<10 <sup>-4§</sup>
Impaired work performance	2.42 (1.31)	2.20 (1.47)	-0.22	0.35
Risk of treatment forget	2.06 (1.17)	4.57 (0.80)	0.51	0.003‡
Anxiety and stress level	2.76 (1.32)	2.69 (1.57)	-0.06	0.78
Burden of treatment cost	3.25 (1.54)	3.66 (1.39)	0.41	0.04†
Dependent of others for day life activities	1.01 (0.59)	1.23 (0.64)	0.22	0.86

†p < 0.05.  
‡p ≤ 0.01.  
§p ≤ 0.001.  
HCP: Health care professional; MD: Medical doctor; SD: Standard deviation.

chronic disease. Our finding highlights the importance of helping patients understand their disease, including their literacy level and the need for their medication, and addressing patients' concerns related to these topics.

A key challenge in improving patient satisfaction with time spent with their physician is that physicians in many countries are in short supply and already overburdened. This challenge could be overcome by having other groups or individuals, such as nonphysician healthcare workers, peers, peer educators, patient communities or specific adherence programs educate patients about their disease and treatment and be available as resources to support patients on their treatment journey. Systematic reviews have shown that nonphysician task sharing can improve control of diabetes and blood pressure in LMICs [30,31]. Moreover, monitoring patients routinely over the course of their treatment could help identify those with low physician satisfaction levels who, based on the current findings, would be at higher risk for loss to follow-up.

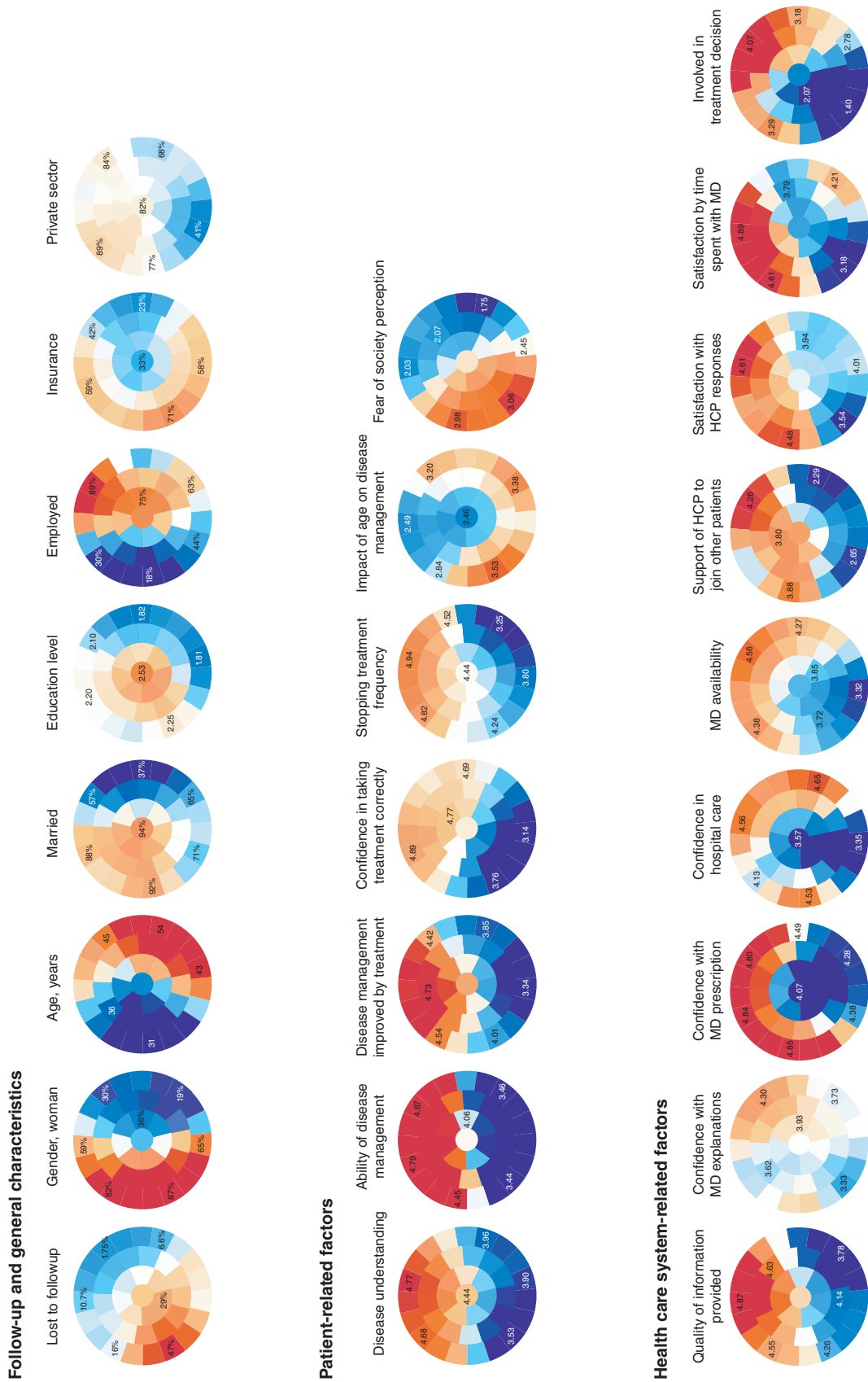
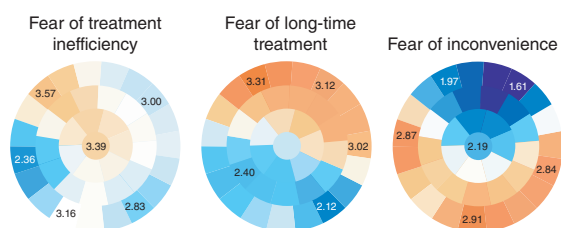
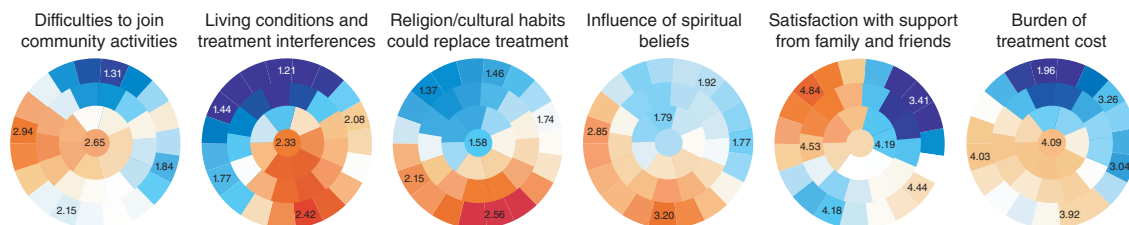


Figure 1. Results from the clustering analysis by self-organized maps.

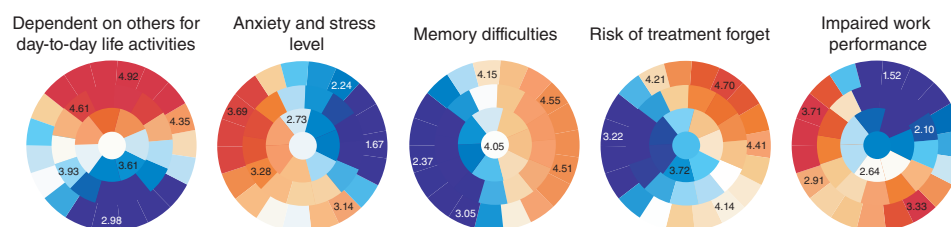
**Treatment-related factors**



**Socio-economic factors**



**Condition-related factors**



**Figure 1. Results from the clustering analysis by self-organized maps (cont.).**

Anxiety and stress level also was identified as a predictive factor for remaining on treatment (low level) in the regression analysis and as a factor for being LTFU (high level) in the SOMs analysis. Recently, psychological disorders were shown to have a significant and negative correlation with medication adherence in patients in Saudi Arabia with Type 2 diabetes [6]. A recent study in older adults with chronic neurological diseases found that scores on the Becker Depression Inventory II were the most influential contributor to nonadherence [32] while another found that no or minimal depression was significantly correlated with adherence [12]. A systematic review found a significant and negative association between depression and adherence and also found that depressed patients who were adherent to antidepressant medication were more likely to adhere to their COPD treatment [33]. Psychosocial interventions may reduce depression in patients with chronic kidney disease [34]. In the context of our finding that low levels of anxiety and stress predict continuing to be followed, these studies emphasize the importance of addressing mental health issues as a mechanism for improving adherence to chronic disease medication. Additionally, continuous and routine mental health screening of patients taking medication for chronic disease could identify those at greatest risk for loss to follow-up, again allowing more targeted and effective interventions to address anxiety, stress and depression.

Patients' ability to self-manage their disease was a nearly significant predictive factor for continuing to be followed in the regression analysis and was identified as a factor associated with remaining on treatment in the SOMs analysis. This is consistent with several studies that have shown the potential for self-management programs to increase medication adherence for patients with a variety of chronic conditions. A randomized clinical trial conducted in patients with mechanical heart valves found that patients participating in an intervention comprising two small-group, 1 h self-management education sessions; educational materials; and brief weekly follow-up calls for 8 weeks had significant improvements in medication adherence and quantitative laboratory assessments compared with patients who did not participate in the intervention [35]. A systematic review of clinical trials assessing the effect of Type 2 diabetes self-management education in patients in Middle East countries also found that these programs

significantly improved patient-reported medication adherence, self-management behavior and self-efficacy and objective clinical glycaemic outcomes [36]. A pre- and post-intervention study conducted in patients with Type 2 diabetes in Saudi Arabia similarly found that patient activation (a measure of knowledge, skill and confidence in managing health that has been proposed as an approach for enhancing chronic disease self-management) significantly increased after the intervention (three monthly in-person sessions followed by three monthly follow-up calls), as did objective clinical diabetes outcomes [37].

Our analysis identified additional factors associated with remaining on treatment or being LTFU at 12 months that were not significant in the regression analysis. Patient involvement in treatment decision, satisfaction with support from family/friends and low dependence on others for daily life activities were predictive of remaining on treatment, while difficulties joining community activities and acknowledgement of an influential role of cultural habits/spiritual beliefs were predictive of being LTFU.

With respect to patient involvement in treatment decision, a systematic literature review found that interventions that were acceptable to both the patient and the physician were more likely to be successful [38]. However, a recent cross-sectional study found no association between the level of involvement that patients experienced and medication adherence [39]. The lack of concordance between the regression and SOMs analyses regarding this factor in the current study also suggest that additional evaluation is needed to understand the predictive value of this factor with respect to continuing treatment.

The other factors identified in the SOMs analysis relate to patients' interactions with their families, communities and cultural norms. We and others have previously found that family (having a spouse, sibling or child) and social support had a positive effect on continuing treatment and adhering to medication for chronic diseases [4,9,40–43]. A scoping review found a nuanced effect of family on patients' self-management abilities [27]. While these effects could be supportive, in some cases patients felt compelled to incorporate family members' recommendations in the context of their family's traditions and expectations, or withdrew from activities rather than facing societal pressures [27]. A chronic disease self-management program comprised of six workshop sessions focused on self-perceived health also found that social risk decreased the likelihood that participants would 'remain well', especially for women at social risk [44]. Collectively, these findings suggest that educating patients' families and caregivers about the patients' disease and its management and the importance of adhering to therapy could help align their input with the goals of therapy.

Our results also suggest more subtle associations between factors. Patients located in the area at the bottom right of the SOMs maps (Figure 1) had low values in disease understanding and disease management ability, but demonstrated low loss to follow-up rates, likely in line with these patients' high confidence in hospital care and feeling of involvement in their treatment decision. Patients located in the top left area of the maps had particularly high levels of anxiety and stress, but had low loss to follow-up rates. This may be due to these patients' high satisfaction with family/friends, time spent with physician and physician availability. These findings underscore the complexity of adherence factors and their interactions with one another.

Longitudinal follow-up of the patient cohort evaluated in the current study identified adherence factors in four of the five categories that changed significantly over time between M0 and M12: healthcare system-related factors (confidence with MD prescription and patient involved in treatment decision), treatment-related factors (fear of long-term treatment and fear of adverse events); socio-economic-related factors (difficulty joining community activities, role of cultural habits, role of spiritual beliefs and role of family and friends), and condition-related factors (memory difficulties, risk of forgetting treatment and burden of treatment cost). None of the patient-related factors changed significantly between M0 and M12. The most pronounced increases were seen for the category of socio-economic factors, which became more problematic over time. This underscores the importance of both continued follow-up with patients and the deployment of interventions as patients' needs and perceptions evolve over the course of their chronic disease treatment. These insights should be considered when developing medication adherence interventions.

In this study, scores for patient involvement in treatment decision significantly increased between M0 and M12, consistent with the identification of this factor in both the regression and SOMs analyses. All of the socio-economic factors that changed significantly over time in the current study also were identified as predictive factors (difficulties joining community activities, role of cultural habits/spiritual beliefs and role of family and friends).

The findings of the current study add to our understanding of the factors associated with continuing to be followed or being LTFU for patients taking chronic disease medication, and provide insight into how these factors evolved over time. As such, they should help to inform both future research into factors that impact adherence

as well as interventions designed to improve adherence. With respect to the former, our findings may help to identify some of the causes of nonadherence, which is one of four pillars of adherence research [45]. Additional research also is needed, as a scoping review of factors associated with being LTFU in patients undergoing chronic disease ambulatory care found that factors associated with LTFU were generally inconsistent across studies [46]. This highlights the need for consistent methodological approaches to evaluating factors associated with adherence and LTFU.

As for the latter, the predictive factors identified here and the evolving scores for specific adherence factors over time should be considered in the development of innovative mitigation strategies. For example, our findings suggest that adherence programs should include elements designed to foster productive patient–physician relationships and include interventions to address anxiety, stress and socio-economic factors throughout the follow-up. Moreover, given the global shortage of physicians, health systems, policy makers and payers should also identify, implement and invest in processes and clinical workflows that enable other personnel (such as nurse educators, social workers, psychologists, trained peer-educators) to educate and collaborate with patients on understanding their disease, selecting a treatment, helping them navigate their treatment journey.

Additional research focused on better understanding the role of stress and anxiety in patients with chronic disease also is needed in order to develop effective mitigation strategies. Survey data from patients in the USA with chronic liver disease found that self-reported poor health, being widowed, fear of developing hepatocellular carcinoma, higher household income and Hispanic ethnicity were associated with moderately severe/severe depression [47]. It is likely that factors associated with stress, anxiety and depression will vary from one disease to another, and disease-specific investigation should help to identify relevant factors in particular indications. Innovative, technology-based approaches to understanding and mitigating factors that drive adherence are being developed and deployed [48], including a mobile health app that has shown promise in helping people with chronic conditions and disabilities better manage their conditions with support from caregivers and clinicians [49]. Such technologies may help to improve chronic medication adherence by identifying and mitigating stress and anxiety.

This study has strengths, including its longitudinal design, lack of missing data and robust outcomes measures (LTFU and treatment continued). There are a number of limitations in this study. We did not calculate sample size, which may affect the generalizability of our findings, potentially generate excessively wide 95% CIs in our results, and reduce the precision of our findings. Additionally, we defined adherence as continuing to be seen by the prescribing physician over the 12 months of follow-up. However, we cannot exclude the possibility that a patient continuing to be seen by the prescribing physician during the study period might not have taken medication at home as prescribed. This limitation should be considered when interpreting our findings, as adherence observed in a controlled setting, such as a clinic or physician's office, may not fully reflect real-world adherence behaviors. Stress was assessed subjectively rather than with a validated scale. A review of studies evaluating the relationship between anxiety, stress and treatment adherence found that the associations in these studies were previously poorly investigated and had high heterogeneity, which resulted in weak and variable relationships [31]. This underscores the potential limitations related to methodologies for evaluating stress and anxiety, including the subjective approach used here. Despite this potential bias and the potential for the limited sample size to compromise reliability, statistical significances were achieved for multiple variables. The binary categorization of the main outcome (LTFU and remaining on treatment) would be expected to reduce the risk of potential information bias. While the PNAT has been validated in English, a potential limitation in this study is the use of an Arabic version of the PNAT, which has not been validated. While this could potentially introduce an information bias, such bias, if present, remains small.

## Conclusion & recommendations

### Conclusion

More than 20 years since the WHO report on the challenges of medication nonadherence, adherence rates remain unacceptably low, increasing morbidity and mortality for people living with chronic diseases in a Gulf Arabic country.

This is the second study to show the potential benefit of using the PNAT as a tool for developing personalized chronic disease self-management strategies, and the first to evaluate PNAT factors associated with adherence longitudinally. Identifying factors predictive of remaining on treatment or being LTFU is an important step in understanding the basis of the association and developing interventions to improve medication adherence. Our finding that scores for socio-economic factors changed most significantly over 12 months adds to our understanding

of how patients experience chronic disease treatment over time, highlights the importance of continuous monitoring and follow-up of patients to mitigate the risk of stopping medication, and suggests areas for further research and intervention.

### Recommendations

Given our findings, interventions that enhance patient satisfaction with their physician, increase patient involvement in treatment decisions, help to achieve/maintain low levels of stress and anxiety, and address the socio-economic and cultural factors identified in this study warrant evaluation and investment in the UAE. Routine and continuous assessment of these factors should also be considered as a way to identify patients at risk for loss to follow-up. Integrating nonphysician resources, including peer educators, social workers, psychologists, patient communities, family members and caregivers, into the support network for patients taking chronic disease medication may help to mitigate the significant factors identified here that are associated with loss to follow-up without increasing the burden on physicians' time.

Additional research to understand the connection between these factors and medication adherence should also be a focus. We recommend broader use of the PNAT as a tool for identifying patients' self-management needs – both to understand the factors that drive or impede adherence and to enable the design of tailored support programs that leverage this understanding. Additional tools for accurately identifying nonadherence in clinical settings also are needed. A recent review highlighted that there is no gold standard method for assessing medications adherence in clinical practice [48]. Understanding patient behavior and accurately quantifying adherence are both essential components of improving outcomes for patients taking chronic disease medication in low and middle income countries.

### Summary points

- It has been known for more than 20 years that rates of adherence to chronic disease medication is poor, as low as 9% in some cases.
- Low rates of adherence persist despite awareness and effort to improve them.
- Understanding why patients with chronic disease do not adhere to their prescribed medication regimen is essential for developing interventions that can improve adherence rates.
- In a prior cross-sectional study we used a novel tool, the Patient Needs Assessment Tool, to evaluate factors among patients in the UAE with chronic diseases. In that study, we identified several factors that predicted how well patients could self-manage a chronic disease. The most predictive factors were: patient's understanding of disease, patient involvement in treatment decision, age > 40 years, time spent with physician and fear of how patients were perceived by others.
- In the current study, we assessed the evolution of adherence factors over time and identified factors predictive of long-term adherence to chronic disease therapy after of 12 months of follow-up.
- We found that patient satisfaction with time spent with the prescribing physician is a significantly positive predictive factor associated with being followed at month 12 (M12) and that anxiety and stress level is a significantly negative predictive factor associated with being followed at M12.
- Additional factors associated with remaining on treatment (involvement in treatment decision, disease management ability, satisfaction with support from family/friends and low dependence on others for daily life activities) or being lost to follow-up (difficulties joining community activities and acknowledgement of an influential role of cultural habits/spiritual beliefs) were also identified.
- The highest mean differences between scores at the initial screen (M0) versus M12 were found for difficulties joining community activities, the role of cultural habits, role of spiritual beliefs, patient involvement in treatment decision and memory difficulties. These overlap with several of the predictive factors identified in the self organizing maps analysis.
- Understanding the factors that predict which patients stop taking their chronic disease medication can help develop tools for identifying patients at risk for nonadherence and interventions that may improve adherence rates.

### Author contributions

J Saba, A Sawsan, A Nofal, M Ammar, E Audureau and J Ladner were responsible for the study conception and design; M Rana, E Audureau, J Saba and J Ladner were responsible for the acquisition of data and data analysis; all authors critically reviewed and revised manuscript drafts; all authors have approved the final version of the manuscript for publication.

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The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

### Writing disclosure

Under the direction of authors, S Seiler provided writing assistance for the manuscript.

### Ethical conduct of research

The Ethical Committee of Rouen University Hospital (CERDE-HLJ) approved the research (no. E2021-74). Patients provided written informed consent to enroll in the Access Program; research written consent was not required for collection of patient data because information from patient files was collected anonymously from medical reports, without collection of personal, patient-identifying information.

### Data sharing statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable and justified request.

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