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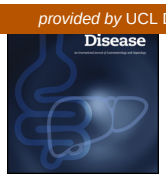

Translation and initial validation of the Medication Adherence Report Scale (MARS) in Italian patients with Crohn's Disease

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ABSTRACT

The MARS-5 (Medication Adherence Report Scale) was developed in English. The aim of this project was to analyse the MARS-5I (© Prof Rob Horne) psychometric properties and to identify whether its Italian translation is suitable for assessing medication adherence in Crohn Disease (CD) Italian patients. The MARS was translated and linguistically validated in Italian. The MARS-5I was used for evaluating medication adherence in the SOLE study, conducted in Italy on 552 subjects with CD. In order to unbias the questionnaire results from the effects of treatment change and/or effectiveness, the analyses were performed on the 277 patients whose disease activity remained stable, selected among the 371 patients who maintained the same treatment between two consecutive visits. Internal consistency was high (Cronbach's alpha of 0.86). Pearson's correlation coefficient was 0.50 ($p < 0.001$) and 0.86 ($p < 0.001$-outliers removed), indicating satisfactory test-retest. MARS 5I scores were not correlated with Treatment Satisfaction Questionnaire for Medication but a small and statistically significant correlation was shown with physician-evaluated medication adherence, indicating convergent validity. MARS-5I, the Italian translation of the English MARS, showed satisfactory internal consistency and test-retest, and a low but statistically significant convergent validity. We confirmed the utility of this tool in patients with CD.

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1. Introduction

Crohn's disease (CD) is a chronic inflammatory condition affecting the gastrointestinal tract, characterized by periods of remission and flare-ups [1]. Although reliable epidemiological studies regarding this clinical condition are not available in Italy, CD has been considered to have a nationwide incidence ranging from 2.3 to 5.8 per 100,000 inhabitants [2,3]. More recently a study carried out on the entire population of the Italian region Lazio reported an incidence of 7.0 per 100.000 inhabitants [4]. These data suggest that the incidence of CD in Italy may be higher than previously anticipated. Patients suffering from CD are often young, therefore will bear the burden of the disease for many years, with a major impact on their daily activities, productivity and quality of life.

The management of CD has been profoundly modified by the introduction of biologic treatments, in particular by the availability of Tumour-Necrosis-Factor-α (TNF-α) inhibitors. TNF-α inhibitors have proven highly effective in CD, reducing rates of hospitalization and surgery [1,5]. However, despite the availability of such effective agents, CD treatment remains often suboptimal and flares remain partly uncontrolled [6].

It has been recently demonstrated that non-adherence to prescribed long-term treatment is a major determinant of treatment efficacy in inflammatory bowel disease (IBD) patients and represents a common problem in IBD management in clinical practice. The frequency of non-adherence ranges from 18 to 30% as reported in several recent international trials [7–10]. In a recent study of potential triggers for IBD flares, which included non-steroidal anti-inflammatory drug use, antibiotic use, stressful life events, cigarette smoking, infections, travel in the preceding 3 months, and medication adherence, only the last one resulted to be significantly associated with flares [11]. These findings are incentives to improve medication adherence, and to set up tools for measuring this parameter easily in real life IBD settings.

Since only a single trial regarding treatment adherence in Italian CD population has been published so far [12], we included this evaluation in the SOLE study (Survey on quality Of Life in Crohn's patiEnts) protocol.

Among the methods for assessing adherence behaviour, self-report measures are the most commonly used in research and clinical care [13]. They represent the most practical tool for measuring adherence, with their easy and flexible administration, low-cost, and minimal patient burden. Self-reported measures of adherence can provide valuable estimates of medication dose-taking behaviour and information regarding psychosocial factors related with adherence (such as reasons for non-adherence and attitudes/beliefs toward medicines) [13].

Nevertheless, self-reported measure of adherence can be frequently inaccurate, because patients often fail to recollect whether they took the drug or not, and tend to over-report their adherence, due to the social desirability of high adherence levels. For these reasons, self-report scales results can suffer from a ceiling effect, with the majority of respondent reporting an unrealistic perfect adherence [13].

Being aware of self-administered adherence measures advantages and disadvantages, we decided to adopt one of these tools in our protocol, since we considered ease of use and low burden for patients and investigators outweighing their drawbacks. Among the available tools we chose the 5 items Medication Adherence Report Scale (MARS-5 - ©Professor Rob Horne), a widely used simple self-administered questionnaire [14].

The MARS-5 is aimed to collect information regarding patient's level of adherence to the prescribed pharmacological therapy. It is a generic tool, which can be administered regardless of the disease and the prescribed drug. It has been validated so far in different clinical settings, namely statin therapy [15], rheumatoid arthritis [16], asthma [17], psychosis [18], and has been used for assessing adherence in many clinical studies worldwide [19–37].

The MARS-5 consists of 5 items describing non-adherent behaviours ("I forget to take the medicine / I alter the dose of medicine / I stop taking the medicine for a while / I decided to miss out a dose / I take less than instructed"): patients are asked to evaluate how often they adopt each behaviour with a 5 point scale, ranging from "always" to "never" (1–5 points). The scale total score ranges from 5 (lowest adherence) to 25 points (maximal adherence).

The MARS-5 was originally developed in English [14], and has been translated in German, Swedish, and Portuguese [38–40]. Due to the lack of an Italian version of the MARS-5 (MARS-5I © Prof. Rob Horne), the scale was translated before SOLE study start and the Italian translation performed linguistic validation. The aim of this project was to analyse the MARS-5I psychometric properties and to identify whether its Italian translation is a suitable instrument for assessing medication adherence in CD Italian patients, in order to be able to have a fast and simple tool to quantify the patients' compliance.

2. Materials and methods

2.1. The MARS-5I linguistic validation

The MARS was originally translated into Italian by two independent professional translators. The translations were then discussed during a consensus conference, which both the translators attended along with three supervising gastroenterologists. During the conference the two translations were evaluated; the one considered more clear and accurate was selected and consequently amended according to suggestions made by the physicians.

The final Italian translation was then back translated into English by a mother tongue professional translator; the back translation was approved by the MARS originator, Professor Rob Horne, and then tested in a group of 15 patients. The patients were asked to answer the MARS-5I items and to report any difficulty in understanding them. Following this comprehension evaluation, no further amendments to the MARS-5I were required.

2.2. The SOLE Study

The validated MARS-5I was then used for evaluating medication adherence in the SOLE study, a large multicentre survey, conducted in Italy in 38 referral centres, on adult (≥18 years) subjects with a diagnosis of active CD, prospectively recruited over a 12-month observation period between September 2011 and November 2013 (n = 552), with visits scheduled at baseline, 3, 6 and 12 months.

Patient's disease activity in SOLE study was measured with Harvey-Bradshaw Index (HBI), a five questions, simplified version of the Crohn's Disease Activity Index [41]. HBI index total score ranges from 0 to >16, with scores <5 indicating remission, and scores >16 indicating severe disease. In SOLE study HBI score at enrolment had to be ≥8 (moderate-to-severe disease).

Primary objective of the SOLE study was to evaluate the quality of life (QoL) evolution during the study and its relationship with the patients' working capability and productivity. Secondary objectives were to determine the relationship between QoL and disease activity, patient satisfaction and compliance with treatment, to assess the structural and organizational variables of the involved gastroenterology centres, to estimate the cost of illness of CD in a 12 months period, and to assess its relationship with QoL.

2.3. The MARS-5I evaluation

Here we present some additional analyses of SOLE study results conducted to evaluate the MARS-5I.

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Since the SOLE study was an epidemiological study, conducted as per clinical routine, with no obligations to provide the patients with any particular treatment at any time point, the whole population (552 pts) consisted of patients with all combinations of treatments and start dates. In order to eliminate the bias due to the effects of a treatment change and/or the relevant effectiveness on the questionnaire, we conducted these analyses on a subgroup of 277 patients, whose disease activity (measured with HBI index) remained quite stable (HBI score ±4), selected among the 371 patients who maintained the same treatment between two consecutive visits (visit 2 and visit 3, at 3 and 6 months from study start respectively). This is particularly important for the test-retest reliability that is a measure of how much the results obtained with a scale are consistent across time. It is measured by administering a test twice, at two different time points, supposing the measured phenomenon has not changed. MARS-5I was subjected to statistical analysis in order to evaluate internal consistency, test-retest reliability, and convergent validity.

2.3.1. Internal consistency

When different items are used to form a scale, such in the MARS-5I, they need to have internal consistency. In other words, they should be correlated with one another, all measuring the same thing (adherence). To measure the MARS-5I internal consistency we used the Cronbach's alpha coefficient, which ranges from 0 (the items are independent) to 1 (the items are perfectly correlated). Values of 0.7-0.8 are generally regarded as satisfactory [42].

2.3.2. Test-retest reliability

Test-retest reliability is measured by the correlation coefficient between the results collected at two different time points.

For evaluating the MARS-5I test-retest reliability, we compared the results of SOLE study visits 2 and 3 (3 months interval between the two visits, always on the subpopulation remaining on the same treatment and with a modest HBI change) and calculated the Pearson's correlation coefficient. Pearson's coefficient values ranges from −1 to 1, with 1 indicating a perfect correspondence between the two tests, and 0 indicating no correspondence. We used a threshold of 0.8 to consider the MARS-5I reliable.

The MARS-5I reproducibility was also evaluated using Bland–Altman plot [43]. This plot is used for comparing two different measures of the same nature; it consists in a dispersion diagram with the difference between the two measures on Y-axis, and the reference value obtained calculating the arithmetic mean of the two values on X-axis. The horizontal lines represent the mean of differences, and the mean of differences ±2xSD. Bland–Altman plot consists of the investigator's opinion: if the mean variation in the confidence interval is not relevant, the two methods can be considered interchangeable. It is not based on critical values, but on expert opinion.

2.3.3. Validity

In order to evaluate the MARS-5I convergent validity we conducted two different analyses.

In the first one we assumed that results obtained with this scale correlate with those obtained with another scale used in SOLE study: the Treatment Satisfaction Questionnaire for Medication (TSQM, providing a global treatment satisfaction score). We relied on the hypothesis that a high level of treatment satisfaction is directly correlated with a high level of treatment adherence. The hypothesis is widely recognised and confirmed by trials in many therapeutic settings [44–47]. For assessing the hypothesis that a correlation exists between MARS and TSQM we calculated Spearman's rho correlation.

In the second analysis we used Spearman's rho for assessing the correlation between MARS-5I results and a physician evaluated medication adherence score. In fact, during SOLE study investigators were required to evaluate their patients' medication adherence with a 5 point scale, ranging from 1 to 5 (never to always adherent). For this analysis MARS-5I scores were categorized in 5 classes ("never adherent: scores 5-9"; "seldom adherent: 10–14"; "sometimes adherent: 15–19"; "often adherent: 20–24"; "always adherent: 25").

Table 1
Characteristics of the study sample.

	MARS validation sample[a] (n = 277)		Total population[b] (n = 552)	
	N	%	N	%
Gender				
Male	130	46.93	271	49.09
Female	147	53.07	281	50.91
Age class				
18–25	47	16.97	72	13.04
26–35	71	25.63	139	25.18
36–45	60	21.66	127	23.01
46–55	64	23.10	130	23.55
>55	35	12.64	84	15.22
Living with partner				
Yes	145	52.35	307	55.62
No	132	47.65	245	44.38
Education				
Primary school	16	5.78	35	6.34
Junior high school	66	23.83	146	26.45
High school	154	55.70	287	51.99
University	41	14.80	84	15.21
Employment				
Employed	158	57.04	300	54.35
Unemployed	119	42.96	252	45.66
Treatment				
Not biologic drugs	95	34.30	263	51.27
Biologic drugs	182	65.70	260	47.10
Comorbidities				
Yes	184	66.43	352	63.77
Concomitant diseases				
Yes	118	42.60	239	43.30

[a] At the first considered visit (visit 2).
[b] At the final analysis.

2.3.4. Influence of patient characteristics on MARS-5I scores

We analysed all the factors potentially related with treatment adherence with a logistic regression model. A binomial variable based on MARS-5I scores was created:

- *MARS score < 25: lower treatment adherence*
- *MARS score = 25: perfect treatment adherence*

We considered as independent variables: gender, age, education, marital status, employment status, treatment, comorbidities and concomitant diseases. Estimates were corrected for the "centre effect", due to the possible correlation between subjects enrolled by the same centre.

3. Results

Among the 277 patients evaluated the majority were women (53%), and about 26% was between 26 and 35 years old. 52% of patients lived with a partner, 56% had a high school diploma, 57% was employed, 66% was treated with biologic drugs, 66% had comorbidities, and 43% concomitant diseases (Table 1).

The mean disease activity score (HBI) at the first considered visit (visit 2) was 4.9 (SD 2.6; median 5.0; range 0–12; interquartile

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Table 2
Disease activity and MARS-5I score of the study sample at visit 2.

	N	Mean	SD	Minimum	Maximum	25th Pctl	Median	75th Pctl
HBI index	277	4.90	2.61	0.00[a]	12.00	3.00	5.00	7.00
MARS-5I	277	23.73	2.41	5.00	25.00	23.00	25.00	25.0

Pctl: percentile. SD: Standard Deviation. HBI: Harvey–Bradshaw Index. MARS: Medication Adherence Report Scale. MARS-5I: Italian version of the MARS.
[a] 11 patients with disease activity = 0 at the first considered visit (visit 2).

Table 3
Chronbach's alpha results for internal consistency evaluation.

	Cronbach's alpha value (N = 277)
Complete MARS-5I	0.86
Excluding single items of MARS-5I	
Item 1	0.85
Item 2	0.83
Item 3	0.84
Item 4	0.82
Item 5	0.82

MARS: Medication Adherence Report Scale. MARS-5I: Italian version of the MARS.

range: 3.0–7.0); the mean MARS-5I score was 23.7 (SD 2.4; median 25.0; range 5–25; interquartile range 23–25) (Table 2).

3.1. Internal consistency

Internal consistency was satisfactory, with a Cronbach's alpha of 0.86. This value is very good, and falls within the German validation study interval (0.67-0.90) [38] (Table 3). We also reported alpha values calculated after excluding single MARS-5I items. Items 4 ("I decide to miss out a dose") and 5 ("I take less than instructed") seemed to have a little higher weight, i.e. when excluded, alpha value was smaller.

3.2. Test-retest reliability

Retest evaluation included 275 patients and the calculated Pearson's correlation coefficient was 0.50 ($p < 0.001$), quite a suboptimal result. Fig. 1A shows a graphical representation of MARS results pairs obtained at visits 2 and 3 for each patient in the sample group. The majority of values was equal to 25, but there were also outlier values, with a really high difference between visit 2 and 3, that could be due to a real change in adherence.

Bland Altman Plot (Fig. 1B) shows that about 95% of differences fell within −5 and 5; despite the mean value was close to zero (which indicate a good reproducibility), variation remained high (±5). Excluding values which fell outside the ±2 SD interval, the obtained correlation coefficient was 0.86 ($p < 0.001$).

3.3. Validity

The first analysis for validity evaluation, in which TSQM questionnaire was used as comparator (total score and subscores), is reported in Table 4. The correlation values showed the absence of relation between the two questionnaires. The second analysis, in which we assessed the correlation between the physician evaluated medication adherence score and MARS-5I score, showed a weak level of correlation (rho = 0.15, $p = 0.014$), although statistically significant (Table 4).

3.4. Incidence of patients characteristics on reported adherence

Table 5 shows results of the logistic model we used to evaluate the patients characteristics related with perfect adherence ("perfect adherence predictors"). Patient characteristics which showed significant correlation with adherence were increasing age (OR

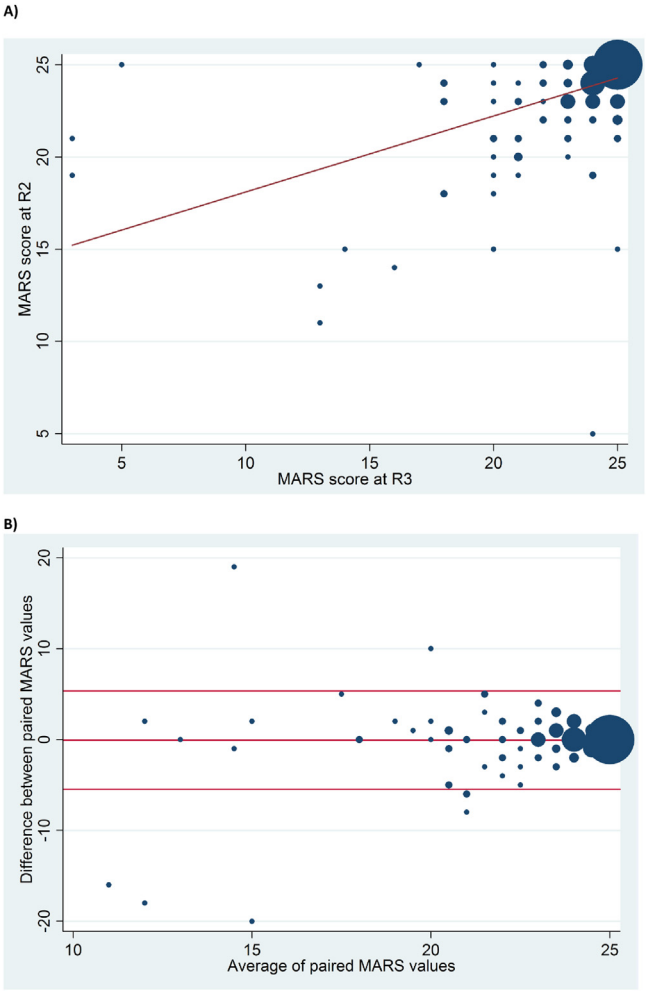

Fig. 1. A) Scatter plot of MARS-5I values at visit 2 and 3. Line represents the fitted regression between MARS values. Circles have diameter dimensions proportional to the frequency of paired values; B) Bland Altman plot of MARS scores differences and means for test-retest reliability evaluation. Circles' diameter is proportional to frequencies of patients presenting the same differences and same means.
MARS: Medication Adherence Report Scale.

Table 4
Correlation between MARS-5I scores and TSQM scores or physician evaluated adherence scores for validity analysis, calculated with Spearman's rho.

	N	Spearman's rho	P value
TSQM			
General satisfaction	276	0.05	0.378
Adverse events	277	0.03	0.650
Efficacy	276	0.03	0.586
Convenience	276	0.04	0.479
Adherence evaluated by physicians	277	0.15	0.014

MARS: Medication Adherence Report Scale. MARS-5I: Italian version of the MARS. TSQM: Treatment Satisfaction Questionnaire for Medication.

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Table 5
Patient characteristics potentially related to perfect treatment adherence (MARS-5I = 25).

	Subgroup analysis (n = 277)				SOLE total population (n = 466)			
	OR	95%IC		p value	OR	95%IC		p value
Gender								
Male	1.00				1.00			
Female	1.11	0.67	1.82	0.681	1.11	0.79	1.55	0.536
Class age								
18–25	1.00				1.00			
26–35	1.47	0.68	3.19	0.322	1.59	0.76	3.34	0.209
36–45	1.54	0.68	3.51	0.291	1.85	0.96	3.56	0.066
46–55	2.25	1.08	4.70	0.032	1.81	0.93	3.52	0.081
>55	3.38	1.59	7.16	0.002	2.65	1.34	5.23	0.006
Living with partner								
Yes	1.74	1.08	2.8	0.024	1.60	1.11	2.30	0.013
No	1.00				1.00			
Education								
Primary school	2.14	0.75	6.16	0.152	2.66	1.24	5.70	0.014
Junior high school	1.16	0.67	2.04	0.572	0.87	0.52	1.45	0.575
High school	1.00				1.00			
University	2.35	0.98	5.65	0.055	1.59	0.92	2.75	0.093
Employment								
Employed	1.00				1.00			
Not employed	1.12	0.66	1.88	0.669	0.35	0.62	1.47	0.815
Treatment								
Not biologic drugs	1.00				1.00			
Biologic drugs	3.73	2.02	6.88	<0.001	3.42	2.23	5.27	<0.001
Specific treatment								
Not biologic drugs	1.00				1.00			
Infliximab	2.24	1.32	7.95	0.012	2.89	1.52	5.49	0.002
Adalimumab	4.17	2.24	7.77	<0.001	3.85	2.34	3.66	<0.001
Comorbidities								
No	1.00				1.00			
Yes	1.77	0.87	3.61	0.114	1.65	0.97	2.83	0.065
Concomitant diseases								
No	1.00				1.00			
Yes	1.30	0.76	2.23	0.325	1.26	0.63	1.73	0.156

Results of a logistic regression model based on a binomial variable derived from MARS-5I scores: MARS score <25, lower treatment adherence; MARS score = 25, perfect treatment adherence. Independent variables: gender, age, education, marital status, employment status, treatment, comorbidities and concomitant diseases. Estimates were corrected for the "center effect". MARS: Medication Adherence Report Scale. MARS-5I: Italian version of the MARS.

for patients >55 years old 3.38, 95% CI 1.59–7.16 p = .002), living with a partner (OR: 1.74, 95% CI1.08-2.08, p = 0.024), and treatment with biologic drugs both considering the whole drug category (OR: 3.73, 95% CI 2.02–6.88, p < 0.001), and the two different active ingredients [OR for infliximab and adalimumab 2.24 (95% CI 1.32–7.95,p = 0.012) and 4.17 (95% CI 2.24–7.77, p < 0.001) respectively]. These factors were also found to be significant predictors for perfect adherence in the total population.

4. Discussion

In our analysis the Italian version of the widely used MARS scale showed a satisfactory internal consistency, and the level of test-retest reliability was good when excluding outlier patients (out of ±2SD). As for validity evaluation, a low correlation was shown between MARS-5I and physician evaluated medication adherence scores, probably due to a different perception of the patient's adherence from the physician point of view, while we failed to show any correlation between MARS-5I and TSQM results.

It is important to recognise that our study was not originally designed for evaluating the MARS-5I scale. Consequently our analyses present several important limitations and are not a comprehensive evaluation of validity and test-retest reliability. For instance, the selection of our sample group (n = 277), based only on stability of disease activity, could be biased. In fact, compared with the total population of SOLE study, in our sample there were several discrepancies in medication adherence related characteristics. The sub-group used for the MARS-5I evaluation comprised more males, more patients living without a partner, with a high level of education, employed, on biologic drugs, than the full SOLE participants, although the statistical significance of these differences has not been evaluated. Moreover, in the subgroup analysed, MARS scores did not show a uniform distribution, but were generally above 20, indicating generally high reports of adherence.

The study design did not afford a true test of assessment of test-retest reliability as the duration between assessments was too long. It is reasonable to assume that, for some participants, levels of adherence may have changed significantly during this period. In this case, low correlation between MARS scores at 1 vs 3 months could be a reflection of changing adherence rates rather than low test-retest reliability. The fact that test-reliability figures were significantly higher after removal of outliers supports this explanation. Based on this data we consider the MARS-5I to have adequate test-retest reliability.

In the German and Swedish MARS linguistic validation studies, the intervals between tests for the test-retest evaluation were shorter than in our analysis, namely 3-4 weeks and ≥7 days respectively [38,39]. In the Portuguese study the interval was even shorter, consisting in only 2 days [40]. Our interval was much longer, far from the ideal time span of 2–4 weeks; this could have resulted in objective major changes in patients characteristics influencing adherence, such as general health status and anxiety level.

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Moreover, although the disease activity remained quite stable between the two visits (since this was the main criteria we used to select this subgroup of patients), 3 months is a long enough time span for the typical CD seasonal variations [48] to be observed, with a possible effect on adherence.

The two validity analysis we conducted gave contradictory results. The one based on MARS-5I correlation with TSQM failed to prove MARS-5I convergent validity. On the contrary, the one based on MARS-5I correlation with the physician evaluated medication adherence score showed a low value, nevertheless with statistical significance. The results of our first analysis could be due to the fact that MARS and TSQM scales assess very different constructs: the first one assesses a reported behaviour (reported adherence), while the second one assesses a perception (perception of treatment satisfaction). This discrepancy is likely to be the reason of our results. In fact, using two scales measuring the same construct (medication adherence) such as MARS-5I and the physician evaluated medication adherence score, we obtained a fair better result. Our Spearman's Rho value (0.15, $p < 0.014$) was similar to the one obtained in the German MARS evaluation [38] (0.26, $p < 0.01$), in which a Satisfaction with Information about Medicine Scale (SIMS-D) was used as a comparator for MARS-5I in the convergent validity analysis.

Our exploratory data examining association between dichotomized MARS and other variables do not constitute a formal test of validity. Yet they are interesting, because they highlight individual characteristics significantly associated with better reported adherence, allowing us to provide more targeted interventions with the aim of supporting adherence in our patients.

In previously published studies parameters associated with greater adherence to medical therapy in IBD patients were age, follow-up by a gastroenterologist, and immunosuppressant use [8,9]. Lower rates of treatment adherence were associated with employment status, high scores on the Obstacles to Medication Use Scale, short disease duration, high education level, dissatisfaction with the patient–doctor relationship, mood disorders, and age younger than 40 [7–10,49]. Moreover, patients' personal beliefs about the IBD and its treatment are important, potentially modifiable, determinants of both adherence and nonadherence [50,51]. A large study of UK patients with IBD found that nonadherence was related to implicit evaluations of maintenance treatment, with nonadherence related to doubts about personal need for maintenance treatment and concerns about potential harm associated with regular use over the long-term [50]. These findings suggest that interventions to improve adherence should take account of the perceptions (e.g. medication necessity beliefs and concerns) as well as practicalities (e.g. capability and resources) influencing motivations and ability to adhere to treatment [52]. Interventions to support adherence should therefore ensure that doubts about personal need for the medication are not based on misconceptions about illness and treatment, and that the patients concerns about treatment have been elicited and addressed [53].

Our analysis suggests increasing age may be associated with improved medical adherence, and highlights for the first time that treatment with biologic drugs is significantly associated with higher reported adherence in CD. This is consistent with a previous report in psoriasis, where self-reported adherence to biologics was found to be significantly greater than that of other drug classes [54]; the reasons were supposed to be a higher motivation due to the severity of the disease and/or to the training patients are supplied on the use of biologics. This is true both for the whole drug class and for the two different active ingredients considered in our analysis (infliximab and adalimumab). In CD, adalimumab adherence has been reported to be higher than infliximab in a systematic review [55]. The observed differences in the odds of being fully adherent between infliximab and adalimumab showed in our study could be related more to the type of administration than to the type of drug itself. In fact, physicians might be more prone to administer adalimumab to adherent patients and infliximab, due to its intravenous administration, to less adherent patients [55]. Adalimumab, on the contrary, can be administered subcutaneously by the patient, after an initial training.

Our analysis represents the first attempt to validate an Italian translation of MARS scale using data of a wide, multicentre, observational study. We have confirmed the utility of this tool in medication adherence evaluation in patients with CD, and for simply finding those at higher risk of reduced adherence, requiring an intervention in order to improve their therapeutic outcomes.

In our study MARS-5I, the Italian translation of the original English MARS scale, showed a satisfactory internal consistency and a low but statistically significant convergent validity based on the correlation with a physician evaluated medication adherence score.

The low level of MARS-5I test-retest reliability emerged in this analysis is probably due to the long time passed between the two questionnaire administrations. Further studies, with shorter intervals between tests, will be needed to clarify this point.

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Conflict of interest

None declared.

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Ethical approval

The SOLE study has been approved by local Ethics Committees according to Italian regulations.

Informed consent

Informed consent was obtained from all individual participants included in the study

Research involving human participants

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Disclosure of potential conflicts of interest

Sara Di Fino, Giuliana Gualberti, Rocco Merolla are employees of AbbVie and may own AbbVie stocks/options. Michela di Fonzo was employees of AbbVie and may own AbbVie stocks/options. M.L. Scribano has served as a speaker and/or advisory board member for Abbvie, Biogen Idec, Janssen, Mundipharma, Pfizer, and Takeda. F. Caprioli served as consultant to: Mundipharma, Abbvie, MSD, Takeda, Janssen, Roche, Celgene; he received lecture fees from Abbvie, Ferring, Takeda, Allergy Therapeutics, Janssen and

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