

A literature review to explore the link between treatment satisfaction and adherence, compliance, and persistence

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Purpose: To explore the published evidence on the link between treatment satisfaction and patients' compliance, adherence, and/or persistence.

Methods: Articles published from January 2005 to November 2010 assessing compliance, adherence, or persistence and treatment satisfaction were identified through literature searches in Medline, Embase, and PsycInfo. Abstracts were reviewed by two independent researchers who selected articles for inclusion. The main attributes of each study examining the link between satisfaction and adherence, compliance, or persistence were summarized.

Results: The database searches yielded 1278 references. Of the 281 abstracts that met the inclusion criteria, 20 articles were retained. In the articles, adherence and compliance were often used interchangeably and various methods were used to measure these concepts. All showed a positive association between treatment satisfaction and adherence, compliance, or persistence. Sixteen studies demonstrated a statistically significant link between satisfaction and compliance or persistence. Of these, ten demonstrated a significant link between satisfaction and compliance, two showed a significant link between satisfaction and persistence, and eight demonstrated a link between either a related aspect or a component of satisfaction (eg, treatment convenience) or adherence (eg, intention to persist). An equal number of studies aimed at explaining compliance or persistence according to treatment satisfaction ($n = 8$) and treatment satisfaction explained by compliance or persistence ($n = 8$). Four studies only reported correlation coefficients, with no hypothesis about the direction of the link. The methods used to evaluate the link were varied: two studies reported the link using descriptive statistics, such as percentages, and 18 used statistical tests, such as Spearman's correlation or logistic regressions.

Conclusion: This review identified few studies that evaluate the statistical association between satisfaction and adherence, compliance, or persistence. The available data suggested that greater treatment satisfaction was associated with better compliance and improved persistence, and with lower regimen complexity or treatment burden.

Keywords: treatment satisfaction, adherence, compliance, persistence

Introduction

Adherence to medication has been recognized as a key issue in health outcomes and efforts to improve patients' adherence are being made by the pharmaceutical industry, experts, and government bodies alike. The "Ascertaining Barriers for Compliance" European research project is one such initiative, whose aim is to identify and disseminate methods for promoting adherence. Inadequate adherence reduces the effectiveness of treatment, and this can lead to complications, deterioration in health, and ultimately death. This represents a significant burden not just for patients but also for the healthcare team, healthcare system, and society. These costs are both personal

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and societal, such as those caused by complications, hospitalization, or absenteeism.^{1,2}

There are a number of elements that determine a patient's adherence to their treatment, including dosing complexity and frequency, convenience, and satisfaction. Indeed, the association between treatment satisfaction and adherence is clinically intuitive. If a patient is dissatisfied with treatment, this may negatively affect their behaviors in terms of quality of treatment regimen execution but also in terms of their involvement in treatment, their perception and attitude toward treatment, and intention to persist. Satisfaction with treatment is increasingly recognized as an important and sensitive measure for treatment differentiation and its multidimensionality is well documented.³⁻⁸ Indeed, this link is one that is often suggested in articles and research, and yet the evidence available for this link and how it is measured has not been recently reviewed.

The objective of this literature review was to identify the link between treatment satisfaction and adherence. A clear understanding of the nature of this link could be of use for clinical practice and future investigations.

Material and methods

Search strategy and selection criteria

Published data assessing compliance, adherence, or persistence and treatment satisfaction from the past 5 years (from January 2005 to November 2010) was searched for in Medline, Embase, and PsycInfo databases. The search performed used the following commands: ("compliance" OR "persistence" OR "adherence") AND ("satisfaction") AND ("medicines" OR "drug" OR "medication"). These searches were limited to abstracts on human subjects and in English. As there is currently no consensus regarding the definitions of adherence, compliance, or persistence, all three terms were retained in the search. Abstracts were retained for the following step if they included the terms, (a) satisfaction or dissatisfaction, (b) adherence, compliance, or persistence, and (c) reference to a drug or medication or if reference was made to mode of administration associated with adherence, compliance, or persistence. Abstracts meeting these criteria were ranked one, two, or three according to the pertinence of their content and results. Figure 1 illustrates the series of steps followed and ranking criteria used during this abstract

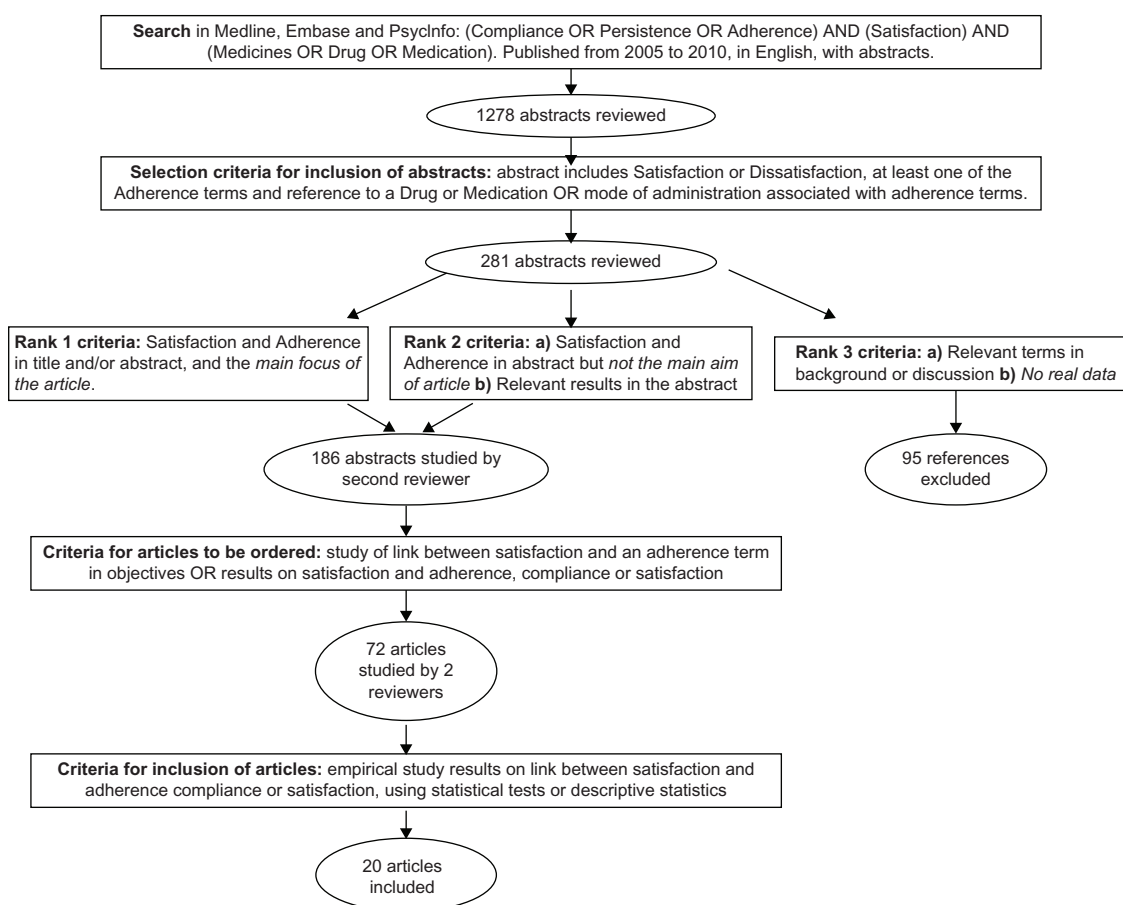


Figure 1 Steps and criteria for abstract and article selection.

and article selection. Articles with no relevant results were ranked three and excluded. Rank one and two abstracts were reviewed in detail by another researcher and a subset of articles that studied the link between satisfaction and adherence, compliance, or persistence, or that had results on both satisfaction and adherence, compliance, or persistence, were ordered. The articles were analyzed in depth and those that reported empirical results on the link between satisfaction and adherence using statistical tests or descriptive statistics were retained. The study design, patient population, study objectives, measurement methods, treatment(s) studied, and results on the link between satisfaction and adherence, compliance, or persistence were reported in a table.

Results

The database searches yielded 1278 references. Abstracts that met the inclusion criteria were then submitted to the selection process ($n = 281$). Abstracts that were ranked one or two were reviewed by a second reviewer ($n = 186$), and 72 articles of those were selected for in depth analysis. Finally, 20 articles were identified that reported results on the link between satisfaction and adherence, compliance or persistence.^{9–28} Of the 20 studies included, 15 were observational studies, four were randomized controlled trials, and one was a nonrandomized clinical trial. The most frequent diseases in which these studies were carried out were glaucoma, diabetes, osteoporosis and schizophrenia. These studies and their results are presented in Table 1.

Methods used to evaluate satisfaction and adherence, compliance, or persistence

The studies measuring compliance or adherence used validated or study-specific questionnaires, clinician judgment, or refill/prescription data to measure these behaviors. Persistence was measured with number of days in study, unvalidated questionnaires, or clinician judgment. Satisfaction was measured by validated or unvalidated questionnaires or interviews. Satisfaction was generally measured using self-report questionnaires, a standard and well-accepted way of measuring this outcome.

The terms used: adherence, compliance, and persistence

The articles included in this review did not provide a consensus on definitions of adherence, compliance, or persistence. Various definitions were used for these terms, often interchangeably across publications. For example, eleven studies^{10,11,15,16,18,21–23,25,27,28} measured compliance, that

is to say the quality of drug regimen execution, by asking questions about missing doses, forgetting doses, or skipping doses, or using “objective” measures such as electronic system or pill count, but called it adherence. The multidimensional term of adherence was rarely measured using a questionnaire that measures the concept in its entirety, as defined by the World Health Organization.¹

Methods used to evaluate links

The evaluation methods used were varied in terms of the tests used and their complexity. The majority of studies used statistical tests such as Spearman’s correlation or logistic regressions to evaluate the link between satisfaction and adherence, compliance, or persistence.^{10–19,21,22,24–29} Only two studies reported a link using descriptive statistics such as percentages.^{20,23} Even though the causal relationship between satisfaction and adherence, compliance, or persistence was not explicitly investigated in these studies, the direction of the relationship was studied. An equal number of studies aimed at reporting on compliance or persistence explained by treatment satisfaction^{18–22,24,25,27} and treatment satisfaction explained by compliance or persistence.^{9–16} Four studies only reported correlation coefficients, which do not specify any hypothesis about the direction of the link.^{17,23,26,28}

Links identified

Of the 20 studies that examined the link between satisfaction and adherence, compliance, or persistence, only a small number explicitly stated the study of this relationship in their objectives.^{10,19,22,25} The other studies mentioned either satisfaction or adherence, compliance, or persistence in their objectives, mostly when examining the determinants of one of these elements. All studies showed a positive association between treatment satisfaction and adherence, compliance, or persistence; the most satisfied patients were the most compliant or persistent and the least satisfied were the least compliant or persistent. Of the 20 studies, 16 demonstrated a link between satisfaction and compliance or persistence that was statistically significant.^{9–14,16–19,21,22,25–28} For the four studies that did not demonstrate a statistically significant link, one reported that significant results had been found but did not report what the results were,¹⁵ two did not use statistical tests,^{20,23} and one had results that did not reach statistical significance but showed a trend of positive association between satisfaction and compliance.²⁴

Of the 16 studies that demonstrated statistically significant links, ten showed a link between satisfaction and compliance^{9,11–14,16,18,19,22,27} and two studies showed a

Table 1 Studies examining links between satisfaction and adherence, compliance, or persistence

| Author | Compliance/ adherence/ persistence measures | Satisfaction measures | Sample size, disease area | Treatments | Study objectives (as reported by authors) | Study design | Statistical tests: results (as reported by authors) |
|-------------------------------------|--|--|--|--|---|--|--|
| Brod et al ¹⁴ | Unvalidated self-reported questionnaire | ITSQ | N = 299, type 1 diabetes | Preprandial inhaled human insulin versus preprandial subcutaneous injections, both in combination with basal insulin | Validate ITSQ; examine relationships between treatment satisfaction and associated variables | Open-label RCT | Multivariate linear regression: greater medication compliance was associated with greater overall satisfaction ($P < 0.01$) |
| Gharabawi et al ²⁰ | Number of days in study | Unvalidated self-report questionnaire | N = 381, schizophrenia | Three arms: risperidone, quetiapine, placebo | Examine predictors and consequences of patient satisfaction | Double-blind RCT | Graphic: patients who were satisfied clearly remained in the study significantly longer than those who were not satisfied (satisfied persons more than 40 days versus dissatisfied patients less than 30 days) |
| Jordan et al ²² | Unvalidated self-report questionnaire | HIV treatment satisfaction questionnaire | Trial 1: n = 211 Trial 2: n = 342 Trial 3: n = 195, HIV | Trial 1: two NRTIs + protease inhibitors versus two NRTIs + abacavir Trial 2: ZDV/3TC combined + abacavir versus ZDV/3TC combined + indinavir Trial 3: ZDV/3TC + abacavir versus ZDV/3TC + nelfinavir | Analysis of the correlation between adherence and patient satisfaction | Three open- label RCTs | Multivariate logistic regression: patient satisfaction highly correlated with high adherence (odds ratio = 1.14 [1.04; 1.25], $P = 0.006$) |
| Testa and Simonson ²⁸ | Barriers to insulin adherence questionnaire | Unvalidated self-report questionnaire | N = 120 adolescents, N = 207 adults, diabetes | Two arms: one randomized to insulin human inhalation powder and twice- daily neutral protamine Hagedorn insulin inhaled and one randomized to subcutaneous regimen | Compare impact of inhaled versus injected insulin on potential mediators of adherence | Noninferiority efficacy RCT | Spearman's correlation: analyses between end point overall treatment satisfaction and insulin adherence barriers demonstrated greater satisfaction with lower barriers ($r = -0.78$, $P < 0.0001$) |
| Bonnick et al ¹³ | Unvalidated self-report questionnaire | Osteoporosis patient satisfaction questionnaire | N = 1678, osteoporosis | 150 g monthly ibandronate versus previous weekly treatment | Assess patient satisfaction levels and patient treatment preference after switching from weekly oral bisphosphonate to monthly oral bisphosphonate | Nonrandomized clinical trial, longitudinal | Multivariate logistic regression: patients who reported missing three or more doses with prestudy weekly treatment were two times more likely to be satisfied with monthly treatment than patients who did not (81.9% versus 69.4%; odds ratio = 1.82 [1.13; 3.04], $P = 0.017$) |
| Bharmal et al ⁹ | Modified Morisky scale | TSQM-9 | N = 396, hypertension | An antihypertensive medication | Psychometrically validate TSQM-9 | Observational longitudinal | Spearman's correlation: adherence positively correlated with convenience (0.46), effectiveness (0.38), and global satisfaction (0.34). Analysis of covariance: higher satisfaction among medium compliers compared to low compliers (adjusted mean scores respectively, 77.1 versus 66.1 for effectiveness, 84.0 versus 71.7 for convenience and 79.3 versus 68.4 for global satisfaction with all $P < 0.0001$) |

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|---------------------------------|---------------------------------------|--|-----------------------------------|---|--|-------------------------------|---|
| Biderman et al ¹⁰ | Unvalidated self-report questionnaire | Diabetes treatment satisfaction questionnaire | N = 630, type 2 diabetes | Diet, oral hypoglycemic agent, insulin or both | Determine relationship between treatment satisfaction and sociodemographic, clinical, adherence, treatment, and health perception factors | Observational cross-sectional | Analysis of variance: satisfaction was lower in patients with difficulties in adherence than patients with no difficulties for three questionnaire items of four ($P = 0.054$, 0.027 , <0.001 , <0.001). Multivariate linear regression: difficulties in adherence were independently associated with lower treatment satisfaction ($P < 0.001$ for two items of four) Pearson's correlation: overall satisfaction was positively correlated with adherence ($r = 0.46$, $P < 0.0001$). Multivariate linear regression: adherence issues were independently associated with treatment satisfaction but explain only 2% of the variance of the model |
| Blalock and Patel ¹¹ | Unvalidated self-report questionnaire | Scale to assess patients' perceptions of drug therapy problems | N = 200, no specific disease area | Prescription medication (various) | Development of drug therapy problems questionnaire | Observational cross-sectional | Pearson's correlation: overall satisfaction was positively correlated with adherence ($r = 0.46$, $P < 0.0001$). Multivariate linear regression: adherence issues were independently associated with treatment satisfaction but explain only 2% of the variance of the model |
| Bolge et al ¹² | Morisky medication adherence scale | Unvalidated self-report questionnaire | N = 345, overactive bladder | Patients with extended-release tolterodine or oxybutynin but no other prescription product for overactive bladder | Evaluate the effects of individual and condition characteristics on satisfaction with extended-release tolterodine or oxybutynin in overactive bladder | Observational cross-sectional | Chi-square: satisfied respondents were more likely to use their medication closer to every day and reported more adherent attitudes than those less satisfied ($P < 0.001$ for both). Multivariate linear regression: longer duration of use and more frequent medication use were apparent predictors of medication satisfaction but were not statistically significant ($P = 0.052$ and 0.096 , respectively) Multivariate analysis of variance: patients who sustained use of triptans had a significantly higher level of satisfaction than lapsed users with nontriptan medication (no statistical results shown). Multivariate linear regression: adherence was not identified as a predictor of satisfaction (no statistical results shown) Chi-square: dissatisfaction with treatment was associated with nonadherence and nonpersistence ($P = 0.05$ and $P < 0.001$, respectively). Multivariate logistic regression: adherence was significantly associated with less dissatisfaction with treatment (odds ratio = 1.65 [0.44 ; 0.97], $P = 0.04$). Cox proportional hazard model: nonpersistence was significantly associated with dissatisfaction with treatment (hazard ratio = 1.83 [1.38 ; 2.43], $P = 0.0001$) |
| Cady et al ¹⁵ | Refill or prescription data | Unvalidated self-report questionnaire | N = 785, migraine | Triptans | Identify factors that predict adherence to triptans by migraine patients | Observational cross-sectional | Multivariate analysis of variance: patients who sustained use of triptans had a significantly higher level of satisfaction than lapsed users with nontriptan medication (no statistical results shown). Multivariate linear regression: adherence was not identified as a predictor of satisfaction (no statistical results shown) Chi-square: dissatisfaction with treatment was associated with nonadherence and nonpersistence ($P = 0.05$ and $P < 0.001$, respectively). Multivariate logistic regression: adherence was significantly associated with less dissatisfaction with treatment (odds ratio = 1.65 [0.44 ; 0.97], $P = 0.04$). Cox proportional hazard model: nonpersistence was significantly associated with dissatisfaction with treatment (hazard ratio = 1.83 [1.38 ; 2.43], $P = 0.0001$) |
| Carr et al ¹⁶ | Unvalidated self-report questionnaire | Unvalidated self-report questionnaire | N = 533, osteoporosis | Bisphosphonates | Determine the factors associated with adherence and persistence to bisphosphonate therapy in osteoporosis | Observational cross-sectional | Multivariate analysis of variance: patients who sustained use of triptans had a significantly higher level of satisfaction than lapsed users with nontriptan medication (no statistical results shown). Multivariate linear regression: adherence was not identified as a predictor of satisfaction (no statistical results shown) Chi-square: dissatisfaction with treatment was associated with nonadherence and nonpersistence ($P = 0.05$ and $P < 0.001$, respectively). Multivariate logistic regression: adherence was significantly associated with less dissatisfaction with treatment (odds ratio = 1.65 [0.44 ; 0.97], $P = 0.04$). Cox proportional hazard model: nonpersistence was significantly associated with dissatisfaction with treatment (hazard ratio = 1.83 [1.38 ; 2.43], $P = 0.0001$) |

(Continued)

Table 1 (Continued)

| Author | Compliance/ adherence/ persistence measures | Satisfaction measures | Sample size, disease area | Treatments | Study objectives (as reported by authors) | Study design | Statistical tests: results (as reported by authors) |
|--------------------------------|---|---|--|---|--|--|---|
| Day et al ¹⁷ | Clinician judgment | TSS-IOP | N = 250, glaucoma and ocular hypertension | Currently treated with marketed glaucoma ophthalmic drop medication in at least one eye | Psychometrically validate the TSS-IOP | Observational one part cross-sectional and one part longitudinal | Spearman's correlation: patients' reluctance to use medications negatively correlated with perceived effectiveness ($r = -0.29$, $P < 0.001$), convenience of use ($r = -0.24$, $P < 0.001$), and ease of use ($r = -0.15$, $P < 0.05$). Physician ratings of patient compliance were not significantly related to any dimension of patient satisfaction ($P < 0.05$) Polynomial regression: patient's dissatisfaction was correlated with poor adherence (odds ratio = 2.69) |
| Dreno et al ¹⁸ | Elaboration d'un outil d'évaluation de l'observance des traitements médicamenteux (Development of an evaluation tool for treatment compliance) [French] | Unvalidated self-report questionnaire | N = 3339, acne | Topical and/or systemic therapy | Evaluate the risk of poor adherence with acne therapies and identify major factors influencing adherence in patients treated with topical and/or systemic agents | Observational cross-sectional | |
| Gasquet et al ¹⁹ | Unvalidated self-report questionnaire and clinician judgment | Unvalidated self-report questionnaire | N = 933, schizophrenia | Two cohorts: patients who initiated therapy with or changed to olanzapine and patients who initiated therapy with or changed to a nonolanzapine antipsychotic | Analyze relationships between patient satisfaction, clinical status, quality of life, compliance, and the type of antipsychotic treatment. Assess elements of validity of an overall evaluation of patient satisfaction with psychotropics | Observational longitudinal | Chi-square: statistically significant relationship between persistence and change in patient satisfaction ($P = 0.001$): higher treatment continuation among patients with higher satisfaction. Structural equation model: direct significant relationship was observed on compliance (coefficient = 0.16) with higher satisfaction leading to higher compliance |
| Gray et al ²¹ | Clinician judgment | SWAM | N = 44, prisoners taking antipsychotic medication | Antipsychotic medication | Explore relationships between medication adherence and demographic, prison, social, and clinical factors in prisoners taking antipsychotic medication | Observational cross-sectional | Pearson's correlation: adherence positively correlated with SWAM "treatment acceptability" dimension. Multivariate linear regression: SWAM "treatment acceptability" dimension had an impact on adherence (estimate = 0.70, $P < 0.001$) |

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|-------------------------------|---|---------------------------------------|---|---|--|--|---|
| Miasso et al ²³ | Morisky–Green Test | Semi-structured interview | N = 21, bipolar affective disorder | Any treatment for bipolar affective disorder | To verify the adherence of people with bipolar affective disorder to medication and compare, among adherent and nonadherent patients, satisfaction with the health team and treatment | Cross-sectional, observational, qualitative, and quantitative study in Brazil. Semi-structured interviews used for data collection | Descriptive statistics: of six patients who adhered, three (50%) were satisfied, one (16.7%) had doubts about its efficacy and two (33.3%) patients were dissatisfied |
| Regnault et al ²⁴ | EDSQ and electronic system | EDSQ | N = 180, glaucoma | Glaucoma treatment | Ascertain the scoring and assess the psychometric properties of the EDSQ | Observational cross-sectional | Kruskal–Wallis: no association found between the six EDSQ dimension scores and compliance profiles (low, moderate, high): $P > 0.079$ for all |
| Rofail et al ²⁵ | Satisfaction with ICT | Satisfaction with ICT | N = 107, thalassemia sickle cell disease or myelodysplastic syndromes | Lifelong ICT, oral chelator deferasirox | To describe the development scoring and validity of the satisfaction with ICT instrument. To assess satisfaction with ICT. To explore relationship between satisfaction and adherence to ICT | Observational cross-sectional | Multivariate linear regression: satisfaction domains (perceived effectiveness, burden, and side-effects) were predictors of “never thinking about stopping” (coefficient = 0.44, 0.42, and 0.27; $P = 0.003$, 0.002, and 0.01, respectively) |
| Ruiz et al ²⁶ | Morisky–Green Test and clinician judgment | Glaucoma satisfaction questionnaire | N = 98, glaucoma | Glaucoma treatment | Report on development and initial psychometric properties of glaucoma satisfaction questionnaire | Observational cross-sectional | Spearman's correlation: compliance was correlated with patient's self-reported effectiveness ($r = 0.403$, $P = 0.003$) and tolerability ($r = 0.456$, $P = 0.001$) |
| Shigemura et al ²⁷ | Unvalidated self-report questionnaire | Unvalidated self-report questionnaire | N = 1151, depressive disorder | Various antidepressant treatments (patients already taking them): amitriptyline, amoxapine, clomipramine, fluvoxamine, imipramine, maprotiline, milnacipran, nortriptyline, paroxetine, sulpiride, trazodone, others. | Ascertain the relationships between antidepressant adherence, sociodemographic factors, pharmacological characteristics, and subjective perceptions | Observational cross-sectional | Student's t-test: low adherence was associated with low drug satisfaction ($P = 0.001$). Pearson's correlation: satisfaction score negatively correlated with nonadherence ($r = -0.115$, $P < 0.001$) |

Abbreviations: 3TC, lamivudine; EDSQ, Eye-Drop Satisfaction Questionnaire; HIV, human immunodeficiency virus; ICT, iron chelation therapy; ITSQ, Insulin Treatment Satisfaction Questionnaire; NRTI, nucleoside reverse transcriptase inhibitor; RCT, randomized controlled trial; SWAM, Satisfaction with Antipsychotic Medication; TSQM-9, Treatment Satisfaction Questionnaire for Medication-9; TSS-IOP, Treatment Satisfaction Survey-Intraocular Pressure; ZDV, zidovudine.

significant link between satisfaction and persistence.^{16,19} The multidimensional aspect of satisfaction and adherence was not always fully studied. The four other studies that showed statistically significant results were among several studies that demonstrated a link between either a related aspect or a component of satisfaction and adherence, compliance, or persistence. For instance, treatment convenience, effectiveness, ease of use, acceptability, or tolerability were investigated as elements of treatment satisfaction.^{9,21,26} Concepts close to compliance or adherence, such as “reluctance to use medications,” “never thinking about stopping,” or “barriers to adherence”^{10,17,21,25,28} were also analyzed.

Significant relationships between satisfaction and compliance or persistence were found more frequently in observational studies than in randomized controlled trials; the majority of these observational studies were cross-sectional in design.

Four studies focused on the change in treatment frequency or route of administration and demonstrated that less treatment burden entailed greater satisfaction and greater compliance. Two randomized controlled trials compared subcutaneous to inhaled treatment for diabetes; patients with less previous or current treatment burden had higher treatment satisfaction,¹⁴ and lower adherence barriers were found for patients with inhaled insulin versus subcutaneous insulin injection.²⁸ A nonrandomized clinical trial demonstrated that patients with poor compliance with previous weekly treatment were twice more likely to be satisfied with new monthly treatment for osteoporosis.¹³ In an observational study on subcutaneous versus oral treatment for iron chelation therapy, greater satisfaction in the oral treatment group was found and “never thinking about stopping treatment” was associated with less burden of treatment.²⁵

Discussion

The purpose of this review was to explore the evidence available on the link between treatment satisfaction and adherence, compliance, or persistence. Even though the number of published studies was quite limited, the data available supported a positive link between treatment satisfaction and compliance and/or persistence. The link between satisfaction and compliance is well established; greater satisfaction being associated with greater compliance or on the contrary, greater dissatisfaction being associated with poorer compliance. This link was demonstrated for a large spectrum of diseases (eg, osteoporosis, diabetes, psychosis, glaucoma) and in different settings (clinical trials and observational studies). This link was also studied with different routes and frequencies of administration; greater satisfaction or

compliance being associated with lower regimen complexity or treatment burden. The link between satisfaction and persistence was also demonstrated, albeit less frequently; greater satisfaction was associated with more time in the study or more time on medication. These results were consistent with theoretical models^{6,30} in which satisfaction with treatment leads to positive behaviors. Thus, the evidence from 16 of the 20 studies that demonstrated the statistical link between satisfaction and adherence, compliance, or persistence supported the intuitive and theoretical link between these concepts. Moreover, the direction of the link was also examined and significant results were reported in both directions: satisfaction explaining compliance/persistence and compliance/persistence explaining satisfaction. This is evidence of the interrelated and dynamic nature of these concepts that certainly have some common drivers.

These results should be considered in light of the variability in definitions used for adherence, compliance, and persistence. Indeed, the review confirmed that there is no acknowledged single definition for these terms, and adherence, compliance, and persistence are often used interchangeably across publications. The multidimensional aspects of satisfaction and adherence were not always fully studied. Moreover, there was great diversity in measurement methods used for satisfaction, adherence, compliance, and persistence. Questionnaires used across studies were different even for a same condition, and many of them were partially or not at all validated. It was noted that there is no commonly accepted threshold for “good” or “bad” satisfaction and “acceptable” or “inadequate” compliance or persistence rates, meaning that results are interpreted inconsistently.

Possibilities for the generalization of study results may be limited by the diversity in study designs, definitions, and measurement methods used for satisfaction, adherence, compliance, and persistence, as well as by the variability in methods used to evaluate the link in terms of tests and complexity.

The studies considered were reports from different research designs: randomized controlled trials, nonrandomized clinical trials, and observational studies. Measuring compliance in clinical studies is important since inadequate compliance can reduce the effectiveness of a treatment or intervention. A high compliance rate in randomized controlled trials ensures the quality of the study and is critical for the success of therapeutic outcomes evaluation. However, clinical trials have limitations when measuring compliance as these studies are conducted in specific settings, with a highly selected population and close patient monitoring that

do not reflect real life conditions. Moreover, it is unlikely that patients would refuse a treatment after consenting to participate and they are likely to be more motivated to use it. For these different reasons, rates of compliance in clinical trials are more likely to be overestimated compared to real life and the findings cannot be extrapolated. In addition, measuring persistence for chronic long-term therapies is limited by the length of the trial. If the majority of patients discontinued their treatment in the first year for example, the follow-up of patients within a 6-month study can produce incomplete or biased results. Similarly, cross-sectional study design limits the analysis of the link between treatment satisfaction and adherence, compliance, or persistence over time.

Another possible limitation of this review is the potential publication bias; the association may be only reported when it is present and simply not reported when it was not significant.

There is a clear need for a consensus on definitions and a framework for interpretation, to ensure that results of well-designed studies that appropriately assess this association using a rigorous methodological approach can be fully explored. In the management of patients with chronic diseases, it is important to understand the determinants of patient satisfaction with various therapeutic alternatives as these factors are likely to have a great impact on compliance and persistence with therapy over time. In the context of clinical practice, the routine assessment of satisfaction with treatment and/or adherence using validated patient questionnaires could help physicians to identify patients facing adherence or satisfaction issues and needing specific support. The support may take the form of further information and discussion about medication and disease, change of medication, regimen, or mode of administration.

Conclusion

The review of the empirical evidence on the link between treatment satisfaction and adherence, compliance, and persistence with medication identified few studies that evaluate the statistical association between these concepts. The available data suggested that greater treatment satisfaction was associated with better compliance and improved persistence. These results should be taken with caution since there are some limitations in terms of measurement methods, study designs, and inconsistency in definitions used for these concepts. Well-conducted observational longitudinal studies including a rigorous measurement strategy for satisfaction and adherence, compliance, and persistence, and designed specifically to explore their relationships would be worthwhile to confirm these associations.

A deeper understanding of the nature of the association between satisfaction and adherence, compliance, or persistence, and especially evidence of a causal direction, could have implications in the context of clinical practice and could help to identify strategies to increase patient satisfaction and promote positive behaviors with regards to treatment. One of the most actionable barriers for improving compliance, adherence, and persistence may include improving components of treatment satisfaction, such as treatment convenience or side effects.

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Disclosures

Carla Dias Barbosa and Nicola Germain are employees of Mapi Consultancy, a consulting company commissioned by Novartis for this study. Maria-Magdalena Balp and Karoly Kulich are employees of Novartis. Diana Rofail was employed by Mapi Values UK while this project was conducted. She is now employed by a pharmaceutical company.

CDB participated in the definition of study objective and search strategy, conducted the analysis and interpretation of results, and drafted the manuscript. MMB initiated the study, participated in the definition of the study objective, participated in the interpretation of results, and critically reviewed the manuscript. KK participated in the interpretation of results and critically reviewed the manuscript. NG participated in the conduct of analysis and participated in the results section of the manuscript. DR participated in the definition of the project objective and search strategy, interpretation of the results, and critically reviewed the manuscript. All authors approved the final version of the manuscript.

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