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Investigating the Clinical Utility of the Combined Use of Objective and Subjective Measures of ADHD During Treatment Optimization

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Abstract:

Background: This study investigated the clinical utility of the combined use of objective and subjective measures of attention-deficit/hyperactivity disorder (ADHD) prepharmacological and postpharmacological treatment.

Methods: Adults with ADHD (N = 77) completed the Quantified Behavioral Test, self-ratings of ADHD-related symptoms, and quality of life measures pretreatment and posttreatment.

Results: The use of objective and subjective measures of ADHD-related symptoms during initiation and follow-up of pharmacological treatment resulted in significant improvements in quality of life after 6 months. Both objective and subjective measures captured changes in ADHD-related symptoms, with more patients showing clinically relevant treatment effects on objective measures. Convergence rates between objective and subjective measures were low to moderate, and improvements on these measures correlated with increased quality of life.

Conclusions: Objective and subjective measures of ADHD capture important components of the condition. The findings from this study have important implications for clinical practice.

Key Words: attention-deficit/hyperactivity disorder, QbTest, quality of life, pharmacology, treatment effects

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Attention-deficit/hyperactivity disorder (ADHD) is a debilitating neurodevelopmental condition defined by symptoms of hyperactivity, impulsivity, and inattention criteria (American Psychiatric Association, 2013). Originally conceptualized as a childhood disorder, it is now known that symptoms typically persist through adolescence and into adulthood, affecting approximately 4.4% of the US adult population.^{1–4} Attention-deficit/hyperactivity disorder in adults has been associated with a range of short- and long-term negative outcomes, including lower academic and occupational performance, a higher propensity for injuries, such as motor vehicle accidents, increased rates of sexually transmitted diseases, financial and relationship problems, and high rates of psychiatric comorbidities, among others.^{5–11} Beyond

these negative outcomes, adults with ADHD report reduced quality of life relative to adults without the disorder,^{12,13} with quality of life being negatively associated with ADHD-related symptom severity.¹³

Despite its prevalence and negative prognosis, however, ADHD is a treatable disorder, with pharmacological treatment being the first-line option in the United States. Medications for ADHD can be categorized into psychostimulant (eg, methylphenidate and amphetamine derivatives) and nonpsychostimulant drugs (eg, atomoxetine, clonidine, and guanfacine, among others). There exists a large body of evidence from double-blind randomized trials (RCTs) demonstrating the efficacy of both psychostimulant and nonpsychostimulant medication in producing clinically robust improvements in symptoms relative to placebo, as summarized in various meta-analyses,^{14–16} with a $\geq 30\%$ reduction in symptoms typically considered as a clinically significant treatment effect.^{17,18} In addition, pharmacological treatments have been seen to improve daily functioning and quality of life in patients with ADHD, and these improvements typically correlate with symptom relief.^{19,20}

Importantly, although standard clinical procedures typically involve self-rated evaluations of symptoms as a means for measuring medication effects in adults with ADHD, it has been shown that individuals with the condition are poor in areas of self-reflection and evaluation,²¹ and clinical experience suggests that the majority of patients with ADHD find it difficult to assess improvements in symptoms after pharmacological treatment.²² Further, despite symptom relief being the primary goal in treatment, a symptom-focused approach relies on a narrow conception of health, where the effects of the disorder on daily functioning and quality of life are largely ignored. There is, therefore, a need to modernize and improve standard clinical procedures to better understand treatment optimization in adult patients with ADHD.

Objective measures, such as continuous performance tests (CPTs), have the potential to enhance and streamline standard clinical procedures and optimize treatment efficacy. Continuous performance tests are computer-based vigilance tasks aimed at assessing individuals' ability to sustain attention and inhibit responses, thereby measuring 2 of the core features of ADHD.²³ Although most of the commercially available tests do not measure patients' activity levels, one of the hallmarks of ADHD, the Quantified Behavioral Test (QbTest²⁴) is one of the few tests that provide a measure of hyperactivity by combining a CPT with an infrared camera that follows a reflective marker attached to the patient's head. The adult version of the QbTest has been deemed useful in providing objective measures of ADHD-related symptoms, with a sensitivity of 86% and a specificity of 83% when distinguishing between patients with ADHD and healthy controls.²⁵ Further, a recent study revealed that combining QbTest scores with self-reported ADHD symptoms resulted in a correct classification rate of 91% when differentiating between ADHD and controls in adults older than of 55 years.²⁶ However, findings from studies aiming to differentiate adult ADHD from other clinical

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diagnoses have yielded varying results,^{27–30} suggesting that the QbTest should not be used as a stand-alone tool in the assessment of ADHD, but rather in combination with a standardized clinical interview.

In terms of treatment outcomes, the QbTest has been seen to capture improvements across all 3 features of the disorder in adult patients with ADHD after a single dose of methylphenidate.³¹ Similarly, a study on prisoners with ADHD found significant short- and long-term improvements in ADHD-related symptoms as measured via the QbTest posttreatment initiation.³² Importantly, a study by Bijlenga and colleagues³³ demonstrated a weak correlation between objective and subjective assessments of ADHD in adults, with a high baseline QbTest score (but not a high baseline self-rating symptom score) being able to predict treatment effects. The authors concluded that the QbTest may be more sensitive to medication effects than subjective ratings of symptoms. Importantly, issues with small sample sizes and limited statistical power must be borne in mind when interpreting these findings, with one of the key limitations of the study being the high dropout rate between the first ($n = 82$) and second medication follow-up ($n = 17$). Further, given the focus on symptom reduction, it is unclear whether the objectively measured ADHD symptoms pretreatment and posttreatment are associated with self-rated quality of life. Furthermore, the extent to which clinically relevant treatment effects on the QbTest are related to improvements in quality of life is unknown.

The purpose of the current research was to conduct an exploratory naturalistic study within our current clinical pathway to investigate the clinical utility of the combined use of objective (ie, QbTest) and subjective (ie, self-ratings) measures of ADHD-related symptoms for use in treatment initiation and follow-up. First, we investigated the extent to which objective and subjective measures of symptoms, as well as self-rated quality of life, improved posttreatment initiation. Second, we examined convergence rates between objective and subjective measures of symptoms pretreatment and posttreatment initiation, and whether these were related to self-rated quality of life. Finally, we evaluated the extent to which objectively and subjectively measured symptoms of ADHD were sensitive to clinically relevant treatment effects (ie, a significant reduction in symptoms) and investigated whether these treatment effects were associated with improvements in quality of life.

MATERIALS AND METHODS

Participants

Patients were recruited from our Carolina Attention Specialists clinics at Charlotte and Greensboro in North Carolina (US) between January 2018 and June 2019. One hundred three patients with ADHD agreed to take part in the current study, of which 26 dropped out. Reasons for dropping out included pregnancy, medication issues related to costs/insurance, and appointment non-compliance. This resulted in a final sample size of 71 patients (44 female patients; mean age, 36.00 [9.68] years). All participants provided written informed consent to participate in the study, which was approved by the independent ethics committee Advarra IRB Services (Pro00027291) and was carried out in accordance with the Declaration of Helsinki.

Inclusion criteria for the study were as follows: (a) fluency in English; (b) a diagnosis of ADHD (assessed using a semistructured interview based on the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [DSM-5]* criteria [American Psychiatric Association, 2013]); (c) intention to start pharmacological treatment for ADHD; (d) being free of comorbidities that could significantly affect test performance (pervasive developmental disorder or

psychosis); and (e) not currently taking medication that could significantly affect test performance (atypical antipsychotic, sedative, or antiepileptic drugs, as well as use of ADHD medication at time of recruitment).

Materials

The Quantified Behavioral Test

The QbTest is a computerized test that objectively measures the 3 core symptoms of ADHD: hyperactivity, impulsivity, and inattention. It combines a CPT with a high-resolution motion-tracking system that consists of an infrared camera following a reflective marker attached to a headband. The adult version of the test involves the rapid presentation of 4 types of stimuli: a red circle, a blue circle, a red square, and a blue square. Patients are required to press the responder button if the stimulus is identical in shape and color to the stimulus immediately preceding it, and refrain from pressing the button if this is not the case. A total of 600 stimuli are presented on a computer screen at a rate of 1 stimulus every 2 seconds (0.5 Hz), with a 25% target ratio, resulting in a test duration of 20 minutes. The order of the targets and nontargets is randomized to prevent practice effects over multiple trials.

Outcome measures on the QbTest are calculated and presented as Q-scores, representing the difference between an individual's raw score and the mean raw score for the age- and sex-adjusted normative group expressed as a standard deviation, such that one Q-score equates to one standard deviation. For the purpose of the present study, we used the QbTest's 3 cardinal variables: QbActivity, QbImpulsivity, and QbInattention, measuring hyperactivity, impulsivity, and inattention, respectively. QbActivity is composed of the following measures based on data from the second half of the test only: time active (percentage of time the individual moved more than 1 cm/s), distance (distance traveled in meters by the reflective marker), area (surface covered in square centimeters by the reflective marker), and microevents (change in position of the reflective marker of more than 1 mm). Both QbImpulsivity and QbInattention consist of the following measures: omission errors (no response is registered to a target stimulus), reaction time (RT; average time in milliseconds to [correctly] press the response button after stimulus presentation), reaction time variability (RT variability; standard deviation of the RT), commission errors (response to a nontarget stimulus), and normalized commission errors (ratio of commission errors to correct responses to the targets). QbImpulsivity is based on data from quartiles 2 to 4; parameters with the highest weight are commission errors and normalized commission errors. QbInattention comprises data from the second half of the test only; parameters with the highest weight are omission errors, RT, and RT variation for both versions of the test.

The Adult ADHD Self-Report Scale–V1.1 Symptoms Checklist

The Adult ADHD Self-Report Scale (ASRS) is an 18-item self-report questionnaire based on the *DSM-IV* (American Psychiatric Association, 2000) symptom criteria designed to evaluate current manifestation of ADHD symptoms in individuals aged 18 years or older. Items (eg, “How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?”) are measured on a scale from 0 (“never”) to 4 (“very often”). Patients are required to place an “X” in the box that best describes how they have felt and conducted themselves over the past 6 months, with possible scores ranging from 0 to 36 for both symptoms of inattention and hyperactivity/impulsivity, and a total score ranging from 0 to 72. Patients scoring between 0 and 16 are unlikely to have ADHD, whereas those

scoring between 17 and 23 and ≥ 24 being likely and highly likely to have ADHD, respectively.

The Adult ADHD Quality of Life Questionnaire

The Adult ADHD Quality of Life (AAQoL) is a 29-item self-report questionnaire designed to measure quality of life in adults with ADHD. The questionnaire consists of 4 subscales: life productivity (eg, “getting things done on time”), psychological health (eg, “feeling anxious”), life outlook (eg, “you are as productive as you would like to be”), and relationships (eg, “frustration in relationships”), with items measured on a 5-point Likert scale ranging from 1 (“not at all/never”) to 5 (“extremely/very often”). To derive overall and subscale scores, raw scores are transformed to a 0 to 100 scale, with higher scores indicating better quality of life.

PROCEDURE

Baseline

As part of the routine clinical procedure at our clinics, patients were first required to fill in the ASRS and AAQoL questionnaires. After this, a 1-hour semistructured clinical interview based on the *DSM-5* criteria (American Psychiatric Association, 2013) was conducted with the patient. Patients were then taken to a quiet room where they were shown an instruction video of the QbTest and were provided with additional oral instructions by the test administrator. At this point, patients were asked to put on the headband and sit comfortably while holding the response button in their dominant hand. A practice QbTest trial was then completed to ensure that the patient had fully understood the task. If the patient had not understood the task, the instructions were repeated, and the patient was required to complete another practice trial. Once it was clear that the patient had fully understood the task, they were required to complete the full 20-minute QbTest.

After this, the patient was required to return to the clinician's room, where information based on all sources (ie, self-ratings, QbTest) was used to make a diagnosis. At this point, the clinician would walk the patient through the QbTest results, as well as the information gathered from the self-ratings, to explain the diagnosis to the patient. Patients who met the criteria for ADHD and who had agreed to starting pharmacological treatment were provided with an information sheet about the study. Those who agreed to take part were asked to sign a consent form.

Follow-up 1

Patients were required to return to the clinic 2 to 5 weeks after treatment initiation. At this visit, patients completed the ASRS, as well as the QbTest (under medication). Any adverse effects of medication were documented at this stage. The clinician would then discuss how well the treatment was working with the patient and, together with the QbTest and ASRS results, would decide whether to titrate up/down, switch to a different medication, or make no changes to the treatment plan.

Follow-up 2

Patients were required to return to the clinic 6 months after treatment initiation. At this visit, patients completed the ASRS and the AAQoL questionnaires, as well as the QbTest (under medication). Any adverse effects of medication were documented at this stage. Here, treatment plans were altered if necessary (additional visits were outside the scope of this study).

Data Analytic Strategy

Changes in Objective and Subjective Symptoms and Quality of Life Posttreatment Initiation

First, for the purpose of the current study, a fourth QbTest variable (QbTotal) was created by computing the mean of the 3 cardinal variables (QbActivity, QbImpulsivity, and QbInattention). This allowed us to compare the total ADHD symptoms on the QbTest with total ADHD symptoms on the ASRS. Next, paired *t*-test analyses were conducted to examine changes in ADHD-related symptoms as measured via the QbTest and the ASRS between baseline and follow-up 2. Incremental changes in ADHD-related symptoms as measured via the QbTest and the ASRS were also evaluated between baseline and follow-up 1, as well as between follow-up 1 and follow-up 2 (see Supplemental Table 2, <http://links.lww.com/JCP/A725>). We also examined changes in quality of life measures between baseline and follow-up 2. Effect sizes are reported as Cohen *d* (small, ≥ 0.20 ; medium, ≥ 0.50 ; large, ≥ 0.80 ³⁴).

Convergence Rates Between Objective and Subjective Symptoms and Quality of Life Pretreatment and Posttreatment Initiation

We then examined convergence rates between objective and subjective measures of ADHD-related symptoms pretreatment and posttreatment. To do this, Pearson correlations were calculated between QbActivity, QbImpulsivity, QbInattention, and QbTotal and hyperactive/impulsive, inattentive, and total scores on the ASRS at baseline, follow-up 1, and follow-up 2. We also conducted correlations between total AAQoL, as well as the 4 subscales (ie, life productivity, psychological health, life outlook, and relationships) and total scores on the QbTest and ASRS pretreatment and posttreatment.

Clinical Outcome Posttreatment Initiation

Here, we investigated the number of patients who showed clinically relevant treatment effects according to the QbTest and the ASRS. To ensure compliance with QbTest's labelling information²⁴ and comparability with previous research,³³ a clinically relevant treatment effect on the QbTest was defined as a reduction in QbTotal of ≥ 0.5 Q-scores, whereby 0.5 represents half a standard deviation of the mean. In line with treatment effect studies in ADHD,^{17,18,33} a reduction of $\geq 30\%$ in ASRS total was considered a clinically relevant treatment effect. Finally, we examined the extent to which improvements on the QbTest and the ASRS were associated with improvements in quality of life.

RESULTS

Demographic characteristics and comorbidities are presented in Table 1. The mean number of days between baseline and follow-up 1 was 33.71 (9.29) and between follow-up 1 and follow-up 2 was 160.24 (20.68). Table 2 shows medication type and mean dosage at follow-ups 1 and 2, whereas Supplemental Table 1 (<http://links.lww.com/JCP/A725>) shows medication type at each visit and treatment decision per individual participant. Thirty participants (42.25%) had their dose increased, whereas 5 (7.04%) had their dose reduced. Twenty-three participants (32.39%) had no change to their medication. Thirteen participants (18.31%) switched from one medication type to another—importantly, this was mostly due to costs/insurance issues rather than adverse effects of medication.

TABLE 1. Demographic Characteristics and Comorbidities at Baseline

	Mean (SD)
Age	36.00 (9.68)
	n (%)
Females	44 (61.97)
Generalized anxiety disorder	19 (26.76)
Social anxiety disorder	18 (25.35)
Sleep disorder	3 (4.23)
Obsessive compulsive disorder	7 (9.86)
Major depressive disorder	12 (16.90)
Non-verbal learning disability	2 (2.82)
Antisocial personality disorder	5 (7.04)
Sensory processing disorder	2 (2.82)
Posttraumatic stress disorder	1 (1.41)

Changes in Objective and Subjective Symptoms and Quality of Life Posttreatment Initiation

First, we evaluated the extent to which objective (QbTest) and subjective (ASRS) measures of ADHD-related symptoms, as well as self-rated quality of life, were sensitive to medication effects. Table 3 shows mean QbTest, ASRS, and AAQoL scores at baseline and follow-up 2, with within-group comparisons. See Supplemental Table 2 (<http://links.lww.com/JCP/A725>) for incremental changes in ADHD-related symptoms between baseline and follow-up 1 and between follow-up 1 and follow-up 2, with within-group comparisons.

The findings indicate that there were significant improvements in ADHD-related symptoms across all measures between baseline and follow-up 2, with large effect sizes. In terms of quality of life, we found significant improvements across all 4 subscales, as well as total quality of life, between baseline and follow-up 2, with large effect sizes.

Convergence Rates Between Objective and Subjective Symptoms and Quality of Life Pretreatment and Posttreatment Initiation

Next, we examined convergence rates between objective and subjective measures of ADHD-related symptoms pretreatment and posttreatment initiation. Table 4 shows correlations between QbTest and ASRS at baseline, follow-up 1, and follow-up 2. We found small to moderate correlations between QbTest and ASRS at baseline, follow-up 1, and follow-up 2, with associations

TABLE 3. Changes in Objective and Subjective Symptoms and Quality of Life Posttreatment Initiation

	Baseline		Follow-up 2		
	Mean (SD)		Mean (SD)		
				<i>P</i>	<i>d</i>
A					
QbActivity	3.05 (0.79)	1.32 (1.15)	<0.001	1.75	
QbImpulsivity	1.22 (1.21)	0.28 (1.15)	<0.001	0.80	
QbInattention	2.20 (1.03)	0.50 (1.28)	<0.001	1.46	
QbTotal	2.16 (0.74)	0.70 (0.85)	<0.001	1.83	
ASRS Hyp/Imp	20.39 (6.64)	12.17 (6.66)	<0.001	1.24	
ASRS Inattention	27.68 (4.70)	16.61 (7.20)	<0.001	1.82	
ASRS Total	48.07 (9.90)	28.77 (12.92)	<0.001	1.68	
B					
Life productivity	38.25 (18.30)	69.13 (21.24)	<0.001	1.25	
Psychological health	44.70 (21.24)	62.69 (19.05)	<0.001	1.16	
Life outlook	48.70 (13.01)	72.45 (22.46)	<0.001	0.75	
Relationships	52.07 (20.92)	72.45 (22.46)	<0.001	0.85	
Total quality of life	44.95 (13.75)	68.40 (18.38)	<0.001	1.36	

Note: 9 patients were missing quality of life data.

between objective and subjective measures tending to increase in magnitude over time.

We also conducted correlations between total AAQoL, as well as the 4 subscales (ie, life productivity, psychological health, life outlook, and relationships) and total scores on the QbTest and ASRS pretreatment and posttreatment (see Supplemental Table 3, <http://links.lww.com/JCP/A725>). The findings revealed a significant negative correlation between QbTotal and life productivity at baseline ($r = -0.31$, $P < 0.05$), as well as significant negative correlations between QbTotal and all quality of life measures at follow-up 2 (r 's ≥ -0.28 , P 's < 0.05). We also found significant negative correlations between ASRS Total and all quality of life measures at both baseline (r 's ≥ -0.29 , P 's < 0.05) and follow-up 2 (r 's ≥ -0.54 , P 's < 0.05).

Clinical Outcome Posttreatment Initiation

By follow-up 2, clinical outcome data revealed that 61 patients (85.92%) showed clinically relevant treatment effects on the QbTest (ie, a reduction of ≥ 0.5 Q-scores in QbTotal), whereas 26 patients (36.62%) showed clinically relevant treatment effects on the ASRS (ie, a reduction of $\geq 30\%$ in ASRS Total). Of these, 24 patients (33.80%) showed treatment effects on both the QbTest

TABLE 2. Medication Type and Mean Dosage at Follow-ups 1 and 2

	Follow-up 1		Follow-up 2	
	Mean (SD)		Mean (SD)	
	n (%)	Dose	n (%)	Dose
Methylphenidate	4 (5.63)	38.73 (10.33)	5 (7.04)	44.60 (18.60)
Amphetamine	10 (14.08)	12.18 (1.01)	13 (18.31)	15.24 (3.11)
Lisdexamfetamine	42 (59.15)	27.14 (9.44)	38 (53.52)	37.37 (16.71)
Dextroamphetamine-amphetamine	14 (19.72)	21.07 (10.03)	14 (19.72)	30.36 (16.46)
Atomoxetine	1 (1.41)	80	1 (1.41)	100

No standard deviations are provided for atomoxetine as only 1 patient was taking this medication.

TABLE 4. Convergence Rates Between Objective and Subjective Symptoms Pretreatment and Posttreatment Initiation

		ASRS	ASRS	ASRS
		Hyp/Imp	Inattention	Total
		<i>r</i>		
Baseline	QbActivity	0.24*	0.13	0.22
	QbImpulsivity	0.28*	0.11	0.24*
	QbInattention	0.19	0.18	0.21
	QbTotal	0.30*	0.20	0.30*
Follow-up 1	QbActivity	0.23	0.26*	0.26*
	QbImpulsivity	0.24*	0.13	0.20
	QbInattention	0.26*	0.39	0.35 [†]
	QbTotal	0.28*	0.36 [†]	0.35 [†]
Follow-up 2	QbActivity	0.34 [†]	0.35 [†]	0.37 [†]
	QbImpulsivity	0.10	0.22	0.17
	QbInattention	0.16	0.44 [‡]	0.33 [†]
	QbTotal	0.28*	0.47 [‡]	0.42 [‡]

**P* < 0.05. [†]*P* < 0.01. [‡]*P* < 0.001.

and the ASRS. Further, 37 patients (52.11%) showed treatment effects according to the QbTest but not the ASRS, whereas 2 patients (2.82%) showed treatment effects on the ASRS but not on the QbTest. Finally, 8 patients (11.27%) showed no treatment effects on either of these measures. Figure 1 shows the association

between changes in QbTotal and changes in ASRS Total between baseline and follow-up 2, with individual data points highlighted by clinical outcome.

Next, we explored the extent to which treatment effects as captured by the QbTest and the ASRS were related to changes in total quality of life. Treatment effects on both the QbTest and the ASRS were associated with improvements in total quality of life (*r*'s ≥ 0.39, *P*'s < 0.01). Figure 2 shows a visual depiction of these associations, with individual data points highlighted by clinical outcome. Figure 1A shows associations between QbTotal and total quality of life, whereas Figure 1B shows associations between ASRS Total and total quality of life.

Finally, we ran multiple regression analyses to examine whether changes in QbTotal, ASRS Total, and total quality of life between baseline and follow-up 2 could be explained by the presence/absence of comorbid disorders. The analyses revealed that psychiatric comorbidity did not significantly predict changes in QbTotal (standardized β's ≤ 0.17, *P*'s ≥ 0.20), ASRS Total (standardized β's ≤ 0.23, *P*'s ≥ 0.10), or total quality of life (standardized β's ≤ -0.15, *P*'s ≥ 0.38).

DISCUSSION

The primary objective of this naturalistic study was to evaluate the clinical utility of the combined use of objective (QbTest) and subjective (ASRS) symptom measures of ADHD prepharmacological and postpharmacological treatment. In our pathway, treatment is guided by both objective and subjective presentations of symptoms, which are used during treatment initiation and follow-up. The findings from this study showed that both the QbTest and the ASRS were sensitive to medication

Relationship between change in QbTotal and change in ASRS Total

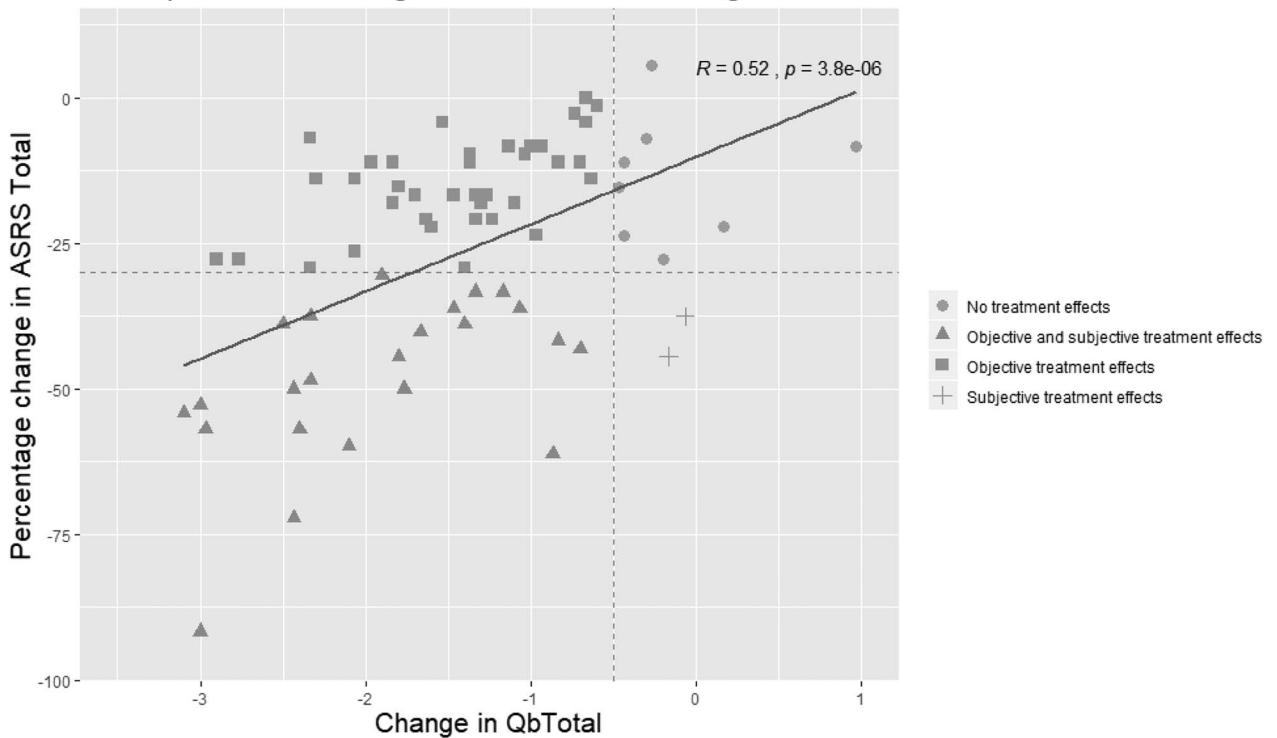
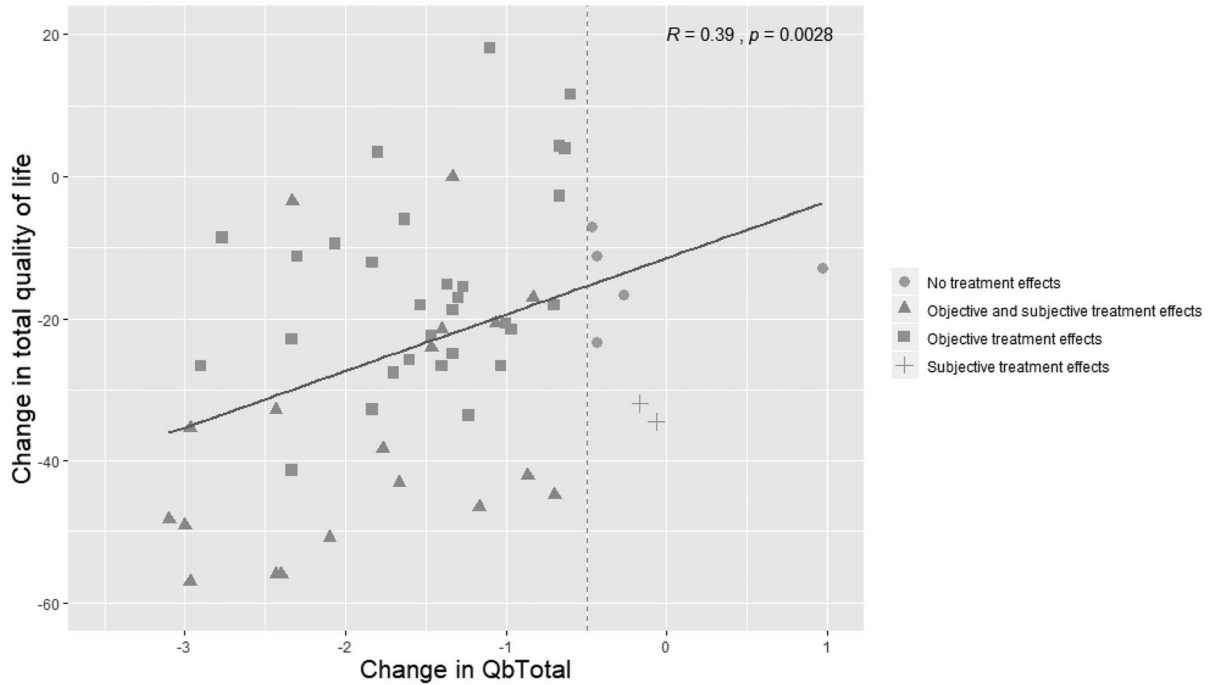


FIGURE 1. The association between changes in QbTotal and changes in ASRS Total between baseline and follow-up 2, with individual data points highlighted by clinical outcome (no treatment effects, objective and subjective treatment effects, objective treatment effects, and subjective treatment effects).

A. Relationship between change in QbTotal and change in Quality of Life



B. Relationship between change in ASRS and change in Quality of Life

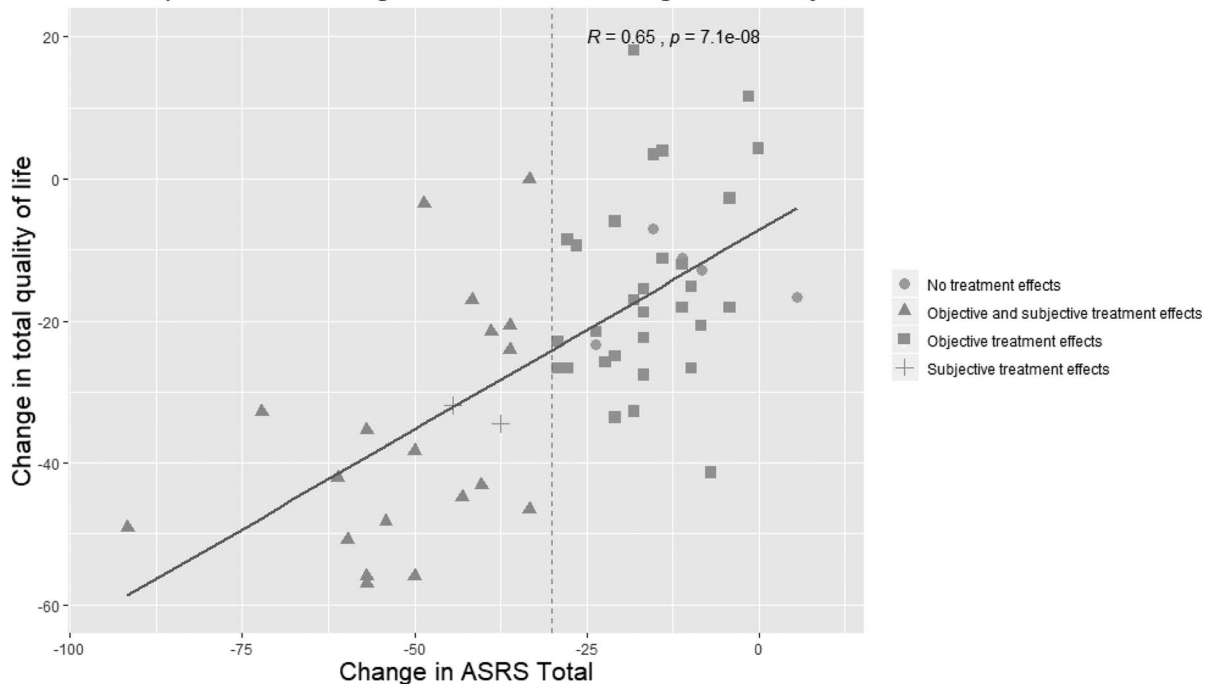


FIGURE 2. Associations between changes in QbTotal and ASRS Total and changes in total quality of life between baseline and follow-up 2, with individual data points highlighted by clinical outcome (no treatment effects, objective and subjective treatment effects, objective treatment effects, and subjective treatment effects). A, Image shows the relationship between changes in QbTotal and changes in total quality of life between baseline and follow-up 2. B, Image shows the relationship between changes in ASRS Total and changes in total quality of life between baseline and follow-up 2. Note: 9 patients were missing quality of life data.

effects. In line with Bijlenga et al,³³ incremental changes in symptoms were observed between baseline and follow-up 1, with analyses revealing significant improvements on both the QbTest and the ASRS. Interestingly, we also found further significant

incremental improvements in ADHD-related symptoms between follow-up 1 and follow-up 2. Overall changes in symptoms were associated with large effect sizes for both QbTotal (1.83) and ASRS Total (1.68) 6 months after treatment initiation. The largest

individual effect sizes were associated with changes in QbActivity and ASRS Inattention. These findings are consistent with studies showing that QbActivity is a sensitive marker for medication effects^{32,35} and that self-rated improvements in symptoms after pharmacological treatment tend to be larger for inattentive relative to hyperactive/impulsive symptoms.³³

To better understand the impact of our treatment pathway on patients' general wellbeing, we used the well-validated AAQoL questionnaire. In a study by Brod et al,¹² it was shown that total AAQoL improved by 15.80 points after pharmacological treatment in a US sample of ADHD patients, with an improvement of 4 to 8 points being deemed clinically relevant. In our study, the mean change in total AAQoL from baseline to follow-up 2 was 23.45 (reflecting a change from 44.95 at baseline to 68.40 at 6 months). Improvements in life productivity and psychological health were associated with the largest effect sizes (1.25 and 1.16, respectively), indicating that patients were better able at getting things done and felt less overwhelmed, anxious, or depressed as a result of our treatment pathway.

In terms of convergence rates between objective and subjective measures of symptoms, we found significant weak to moderate correlations between the QbTest and ASRS parameters pretreatment and posttreatment initiation, which is in line with findings from previous studies.^{33,36} Interestingly, the magnitude of the correlations between our objective and subjective measures of ADHD-related symptoms tended to increase over time. It could be argued that individuals with ADHD may be better at evaluating their ADHD symptoms after pharmacological treatment. Alternatively, this could be an effect of patients having spent time with a clinician discussing ADHD-related subjective symptoms as well as going through their QbTest results and thereby gaining a better understanding of their own struggles and the condition. Importantly, this was true for inattention but not impulsivity, suggesting that it may have been easier for patients to evaluate symptoms associated with inattention than those linked to impulsivity. On the other hand, it could be argued that impulsivity on the QbTest denotes a slightly different concept than impulsivity in everyday life (eg, interrupting others).

Our findings on clinically relevant treatment responses at the individual level revealed that, although approximately 86% of patients showed a clinically significant treatment effect on the QbTest, only 37% showed treatment effects on the ASRS. Overall, over 50% showed clinically relevant treatment effects according to the QbTest (but not the ASRS), whereas approximately 3% showed treatment effects on the ASRS (but not on the QbTest). Further, although a third of patients showed relevant treatment effects on both the QbTest and the ASRS, approximately 11% showed no treatment effects on either measure. Importantly, clinical outcome was not explained by psychiatric comorbidity. Our findings are in line with previous research where it has been argued that the QbTest may be more sensitive to medication effects than self-rated measures of symptoms³³ and that individuals with ADHD may find it difficult to assess improvements in symptoms after pharmacological treatment.²²

Critically, it is important to note that the QbTest measures ADHD-related performance-based measures in a controlled environment, whereas self-rated symptoms may be more likely to reflect day-to-day functioning. In adults who have lived with the condition for many years, discrepancies between objective and subjective treatment effects may reflect a time lag between the medication optimally treating the condition and the development of new life skills in navigating the day-to-day environment. Therefore, objective symptom measures could be used as early indicators of treatment effects. From a clinical perspective, patients who show a clinically relevant treatment effect on the QbTest

but not on the ASRS should not only be considered for pharmacological treatment but also cognitive behavioral therapy or coaching/counseling to help with life skills. In this regard, objective measures may facilitate the evaluation and management of patients' response to medication while avoiding unnecessarily high doses and associated adverse events.

Finally, although treatment effects on both the QbTest and the ASRS were related to improvements in quality of life, this association was stronger for the ASRS. Given that subjective data were collected via self-report only, this finding may reflect single reporter bias. Future studies should therefore investigate associations between the ASRS and quality of life in multiple respondents, such as close relatives or friends. Notably, the findings are in line with studies showing that pharmacological treatment can improve daily functioning and quality of life in patients with ADHD, with improvements correlating with self-rated symptom relief.^{19,20} This study goes a step further by demonstrating that improvements in objective measures of ADHD-related symptoms are also associated with improvements in quality of life. This novel finding suggests that the QbTest captures a measurable component of the condition and that improvements on the test are related to real-life subjective improvements in daily functioning. To our knowledge, this is the first study to explore the relationship between objective measures of ADHD-related symptoms and self-rated quality of life measures.

Critically, the current research had some limitations. First, as this was a naturalistic study, we could not directly examine the clinical utility of the QbTest within our pathway. Randomized trials are needed to gain a better understanding of the use of objective and subjective measures of ADHD symptoms as a means for treatment decision planning and management. Second, although a reduction in QbTotal of ≥ 0.5 Q-scores was deemed a relevant treatment effect, in line with QbTest's labelling information²⁴ and previous research,³³ further studies in this area are necessary. Third, because only 2 patients showed improvements on the ASRS only (but not on the QbTest), we could not compare groups based on improvement type (eg, subjective vs objective improvements only). Finally, the current research had a cutoff point of 6 months. Additional follow-ups were outside the scope of the study, which could have revealed further insights into our clinical pathway.

CONCLUSIONS

Taken together, this study showed that, by using objective and subjective measures of ADHD-related symptoms during initiation and follow-up of pharmacological treatment, significant improvements in quality of life can be achieved after 6 months. The convergence validity between the 2 measures increased over time, indicating that pharmacological treatment or consultations with an experienced clinician can result in patients' evaluations of their symptoms to be more in line with what can be objectively measured. The finding that more patients showed clinically relevant effects when the symptoms were measured by objective (QbTest) than subjective (ASRS) measures calls for further studies to evaluate if an increased emphasis on objective measures can refine treatment management in ADHD.

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AUTHOR DISCLOSURE INFORMATION

N.M.K. was employed by Qbtech between August 2017 and September 2019. At the time of publication, P.R. and A.S. were paying to use QbTests within their practice.

The authors declare no other conflicts of interest.

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