Psychometric validation of the Weiss Functional Impairment Rating Scale-Parent Report Form in children and adolescents with attention-deficit/hyperactivity disorder

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Abstract

Background: Measurement properties of the Weiss Functional Impairment Rating Scale-Parent Report Form (WFIRS-P), which assesses attention-deficit/hyperactivity disorder (ADHD)-related functional impairment in children/adolescents (6–17 years), were examined.

Methods: Data from seven randomized, controlled trials were pooled. Analyses were conducted in two random half-samples. WFIRS-P conceptual framework was evaluated using confirmatory factor analyses (CFA). Reliability was estimated using internal consistency (Cronbach’s alpha) and test–retest reliability methods. Convergent validity was assessed using correlations between WFIRS-P domain scores and the ADHD-RS-IV and Clinical Global Impression–Severity (CGI–S) scales. Responsiveness was tested by comparing mean changes in WFIRS-P domain scores between responders and non-responders based on clinical criteria.

Results: CFA adequately confirmed the item-to-scale relationships defined in the WFIRS-P conceptual framework. Cronbach’s alpha coefficient exceeded 0.7 for all domains and test–retest reliability exceeded 0.7 for all but Risky Activities. With few exceptions, WFIRS-P domains correlated significantly (p < 0.05) with ADHD-RS-IV Total, Inattention and Hyperactivity-Impulsivity scores and CGI–S at baseline and follow-up in both random half-samples. Mean changes in WFIRS-P domain scores differed significantly between responder and non-responder groups in the expected direction (p < 0.001).

Conclusions: Study results support the reliability, validity and responsiveness of the WFIRS-P. Findings were replicated between two random samples, further demonstrating the robustness of results.

Keywords: Weiss Functional Impairment Rating Scale-Parent Report Form, Attention-deficit/hyperactivity disorder, Reliability, Validity, Responsiveness
burden that ADHD may place on children and adolescents, an improvement in functioning in these areas is of great value both to patients and their caregivers [17].

This recognition has resulted in a need to demonstrate that treatments for ADHD not only improve symptoms but also improve associated functional impairment. The inclusion of a functional outcome has been made an explicit requirement by the European Medicines Agency in their guidance document on investigational medicines for ADHD [18]. This requirement is also consistent with the broader trend of incorporating measures of functioning and well-being as outcomes in clinical trials [19]. Lastly, evidence of functional impairment is an important criteria in diagnosing ADHD [20–23].

For the purpose of evaluating functional impairment in clinical trials, it is necessary to have a reliable, valid and responsive measure of ADHD-specific functional impairment. The Weiss Functional Impairment Rating Scale-Parent Report Form (WFIRS-P) [24, 25] was developed to measure ADHD-related functional impairment and has previously been used in clinical trials of ADHD treatment for children and adolescents [5]. While the instrument has been used in previous clinical trials, there are limited published data [26] on the instrument’s measurement properties, particularly with use in clinical trials. The objective of this study was to evaluate the measurement properties of the WFIRS-P, including a confirmation of the WFIRS-P conceptual framework, and its reliability, validity and responsiveness to change.

Methods
The data for this study came from clinical trials that were conducted in accordance with the Declaration of Helsinki, and local ethics approval in countries where trials were conducted was sought. As these analyses were retrospective secondary clinical trial data analyses, no additional approvals were sought.

Study data
Data from a pooled sample of children and adolescent patients (n = 2357), aged 6–17 years, with a confirmed Statistical Manual of Mental Disorders version IV text revision (DSM-IV-TR) primary diagnosis of ADHD, who participated in one of seven Phase III randomized, double-blind, placebo-controlled trials of guanfacine hydrochloride extended-release (GXR; Intuniv, Shire US, Inc., Wayne, Pennsylvania, USA) or lisdexamfetamine dimesylate (Vyvanse, Shire US, Inc.) [27–33]. In all seven trials, the WFIRS-P was used as a measure of ADHD-related functional impairment. Analyses were conducted using data from the baseline visit and one follow-up visit, conducted approximately at the same number of days from baseline for each study (Table 1).

Data were pooled across the seven trials to increase the sample size available for each tested measurement property of the WFIRS-P. Pooling of WFIRS-P data from all seven trials provided the largest sample size for validation to date and a large enough sample to allow for a random half sample split to replicate results. As the measurement properties of an assessment instrument should hold independent of treatment, data pooling was also done across blinded treatment arms. To evaluate reproducibility of results, patients in the pooled sample were randomly split into two groups of roughly equal size (referred to as sample 1 and sample 2). Therefore, unless stated otherwise, all data analyses include four sets of results: baseline sample 1, baseline sample 2, follow-up sample 1 and follow-up sample 2.

Study measures
WFIRS-P
The WFIRS-P consists of 50 questions where respondents are asked to rate their child’s functional impairment over the past month. The specific version of the WFIRS-P used across trials was Version 2 [25]. The items of the WFIRS-P are scored on a four-point Likert-type rating scale: 0 (never or not at all), 1 (sometimes or somewhat), 2 (often or much) or 3 (very often or very much) and aggregated to produce six domain scores (Family, Learning and School, Life Skills, Child’s Self-Concept, Social Activities and Risky Activities). Each of the six domains is scored omitting items with a missing or ’not applicable’ response. Response options are assigned values from 0 to 3. According to the instructions, scores can be calculated as the number of items scored as a 2 (often or much) or 3 (very often or very much), a sum score or the mean of the non-missing items [24]. The mean of non-missing items was the scoring method used in each of the trials in this study. An overall score (summary index) is also computed from all of the WFIRS-P items. A higher score on each WFIRS-P domain and summary index indicates greater functional impairment.

Criterion measures
Two clinician-reported measures that were evaluated during the same visits in which the WFIRS-P was administered were used as criterion measures to evaluate the validity of the WFIRS-P. The first, the ADHD Rating Scale Version IV (ADHD-RS-IV), is an instrument used to measure the severity of ADHD symptoms based on DSM-IV criteria for the diagnosis of ADHD [34]. The instrument comprises 18 items, each rated on a four-point Likert scale. The items are scored on two subscales, each comprising nine items: inattention (odd-numbered items 1 to 17) and hyperactivity–impulsivity (even-numbered items 2 to 18) [34]. A total score is also computed from the sum of all item ratings. Higher scores indicate
Table 1 Data sources and time points used to evaluate the measurement properties of the WFIRS-P

| Study description | Lisdexamfetamine dimesylate studies | Guanfacine hydrochloride extended-release studies |
|-------------------|-------------------------------------|-----------------------------------------------|
|                    | SPD489-317                          | SPD503-314                                    |
|                    | SPD489-325                          | SPD503-312                                    |
|                    | SPD489-326                          | SPD503-316                                    |
| (Total N = 2357)   |                                     |                                               |
| Study Location     | Europe, North America, Australia    | Europe and U.S.                              |
|                    |                                     | Europe                                       |
|                    |                                     | North America                                |
|                    |                                     | U.S.                                         |
|                    |                                     | Europe, North America                        |
|                    |                                     | North America                                |
| Inclusion Criteria | Historical or current inadequate response to MPH therapy; Informed consent; Willing to comply with all testing; Age 6–17; Meet DSM-IV-TR criteria for diagnosis of ADHD; Baseline ADHD-RS-IV total score ≥ 28; Blood pressure within 95th percentile for age, gender and height; functioning at age appropriate level intellectually; able to swallow capsule | Informed consent; Willing to comply with all testing; Age 6–17; Meet DSM-IV-TR criteria for diagnosis of ADHD; combined sub-type or hyperactive/impulsive sub-type; Minimum ADHD-RS-IV total score of ≥ 32; CGI-S score of ≥ 4 at baseline; Blood pressure within 95th percentile for age, gender and height; functioning at age appropriate level intellectually; able to swallow capsule |
|                    | Informed consent; Willing to comply with all testing; Age 6–17; Completed minimum of 4 weeks of double-blind treatment without experiencing AEs; Satisfactory medical assessment; Blood pressure within 95th percentile for age, gender and height; functioning at age appropriate level intellectually; able to swallow capsule | Informed consent; Willing to comply with all testing; Age 13–17; Meet DSM-IV-TR criteria for diagnosis of ADHD, combined sub-type or hyperactive/impulsive sub-type; Minimum ADHD-RS-IV total score of ≥ 32; CGI-S score of ≥ 4 at baseline; Blood pressure within 95th percentile for age, gender and height; functioning at age appropriate level intellectually; able to swallow capsule |
| Age range, years   | 6–17                                | 6–17                                         |
| Baseline           | Baseline (Day 0)                    | Baseline (Day 0)                             |
| Follow-up          | Visit 9/ET (Day 63)                 | Visit 7/ET (Day 49)                          |
|                    | Visit 6 (Day 56)                    | Visit 10 (Day 56)                            |
|                    |                                    | Visit 9 (Week 7)                             |
|                    |                                      | All ages: Visit 2 (Day 0)                    |
|                    |                                      | Ages 6–12: Visit 12 (Week 7)                 |
|                    |                                      | Ages 13–17: Visit 9 (Week 7)                 |

ADHD-RS-IV ADHD Rating Scale Version IV, CGI-S Clinical Global Impression–Severity, DSM-IV-TR Statistical Manual of Mental Disorders version IV text revision, ETend of treatment, WFIRS-P Weiss Functional Impairment Rating Scale-Parent Report Form
greater severity. The ADHD-RS-IV is widely used as a primary efficacy outcome measure in ADHD clinical trials [27, 31, 35–42]. The second criterion measure, the Clinical Global Impression (CGI) scale, is a clinician-rated global assessment of the patient’s global functioning, symptom severity and treatment response (improvement), and was developed for use in clinical trials of patients with mental disorders [43]. It comprises two single-item measures evaluating disease severity and change in patient condition since study admission. The CGI–Severity (CGI–S) scale rates how mentally ill the patient is at the time of the visit, based on the clinician’s total clinical experience with the specific population. Ratings range from 1 (normal, not at all ill) to 7 (among the most extremely ill patients). The CGI–Improvement (CGI–I) scale rates patient improvement relative to their baseline assessment symptoms. Response options range from 1 (very much improved) to 7 (very much worse), with a value of 4 corresponding to ‘no change’.

Measurement properties

The initial step in the validation of an instrument entails the evaluation of the measurement properties involved and confirmation of the conceptual framework of the WFIRS-P as suggested by the instrument’s developer and implied in the scoring instructions for each of the WFIRS-P domains [24]. The conceptual framework explicitly defines the concepts measured by an instrument and describes the relationships between items, domains and concepts measured, and the scores produced by the instrument [44]. To confirm the conceptual framework of the WFIRS-P, confirmatory factor analysis (CFA) appropriate for categorical-level data [45] was conducted, using polychoric correlations and the weighted least square estimator with robust standard errors and mean-and variance-adjusted chi-square test statistics (WLSMV). The confirmation of the conceptual framework of the WFIRS-P is important for the purpose of supporting the recommended scoring and interpretation of scales. The goodness-of-fit of each CFA model was evaluated using the comparative fit index (CFI) [46], where the suggested cut-off for acceptable fit is CFI >0.90 [47], and the root mean square error of approximation (RMSEA), where the suggested cut-off for acceptable fit is RMSEA <0.10 [48]. Additionally, item-to-factor loadings were examined where it was expected that items would have strong loadings (>0.40) on their respective factor [49]. In confirming the conceptual framework of the WFIRS-P, two sets of CFA models were tested. First, as a base-case model, a one-factor model was tested with the data to support the scoring and interpretation of the summary index. Second, a six-factor model consistent with the conceptual framework of the WFIRS-P was tested and compared against the one-factor model. The a priori pre-specified hypothesis was that the six-factor model representing the conceptual framework of the WFIRS-P would show a much better fit than a one-factor model. Moreover, showing a better fit of the six-factor model over a uni-dimensional model supports the interpretation of each domain as potentially representing distinct and independent concepts of ADHD-related functional impairment.

The reliability of the WFIRS-P domain scores was tested using internal consistency and test–retest reliability methods. Internal consistency reliability evaluates the extent to which the items of a scale measure the same concept. Cronbach’s alpha [50] was computed at baseline and follow-up assessments were performed to estimate the internal consistency reliability of each WFIRS-P domain. Test–retest reliability is the degree to which repeated administration of an assessment produces similar results in a sample where no change has occurred. This was assessed by computing the intra-class correlation coefficient (ICC) between WFIRS-P domain scores at two time points based on an analysis of variance (ANOVA) model [51]. As test–retest reliability assumes that there has been no change in the concept of interest, data from clinical trials are not ideal for this purpose due to an external factor such as a pharmacological or other intervention. To minimize the effects of this potential limitation, evaluation of test–retest reliability was limited to three of the clinical studies that had a short period of time (2–3 weeks) between consecutive visits in which the WFIRS-P was administered. The sample was further limited to patients who were rated as ‘no change’ on the CGI–I scale at the second of the consecutive visits.

Spearman’s rank correlations were computed to assess the convergent and divergent validity of the WFIRS-P domains. Convergent validity is a subtype of construct validity. Convergent validity refers to the degree to which two measures of constructs that theoretically should be related, are, in fact, related [41]. Specific criterion measures used to assess the convergent validity of the WFIRS-P domains included the ADHD-RS and the CGI–S. Symptoms of ADHD are known to have an adverse impact on child functioning and well-being [52, 53]. Therefore, it was expected that scores of the WFIRS-P would, at the minimum, correlate moderately (r > 0.30) [54] with the ADHD-RS-IV total score as well as the Inattention and Hyperactivity/Impulsivity subscales. The CGI–S is a severity rating of mental illness. It has been shown that mental health conditions in children can/may have larger negative effects on test scores, school attainment and function in general than physical health conditions [55]. Therefore, it was expected that all domains and the summary index of the WFIRS-P would at the minimum correlate moderately (r > 0.30) with the CGI–S data.
The responsiveness of a PRO instrument is deemed to be an important measurement property in order for the instrument to be considered a valid endpoint in clinical trials (reference PRO Guidance Document for Industry) [44]. The responsiveness of a PRO instrument is best determined by evaluating the instrument’s ability to detect true changes in the underlying condition being studied or treated. The ability of the WFIRS-P to detect clinically important changes over time [56] was assessed using the method of known-groups validity [57]. The criterion measure for this purpose was the treatment responder definition used in each trial wherein patients were classified as a responder if their ADHD-RS-IV total score improved by ≥30% from baseline to the follow-up assessment and the CGI-I ratings were at least 1 (‘very much improved’) or 2 (‘much improved’) at the follow-up assessment. Student’s t-tests were conducted to test the statistical significance of the difference in mean WFIRS-P change scores between responders and non-responders. It was hypothesized that responders would show statistically significantly larger (p < 0.05) improvement on the WFIRS-P domain and summary index scores than non-responders.

An analysis of differential item functioning (DIF) was conducted using logistic regression methods to determine whether the items of each WFIRS-P scale showed any measurement bias between children (6–12 years) and adolescents (13–17 years) [58]. The results and interpretation of the DIF analyses are presented in Additional file 1.

**Results**

Table 1 provides a brief description of each of the seven trials used for this study. Baseline demographic characteristics for the two random half-samples of study participants (sample 1: n = 1185; sample 2: n = 1172), along with scores for WFIRS-P and clinical measures, are shown in Table 2. Mean (standard deviation) ages were 11.0 (2.9) and 11.1 (2.9) years in samples 1 and 2, respectively, and approximately two-thirds of participants were children aged 6–12 years. The majority of participants were male (~75%). Mean baseline scores for each clinical assessment and the six WFIRS-P domains were nearly identical between the two random half-samples.

**Conceptual model**

Overall fit of the six-domain model representing the conceptual framework of the WFIRS-P as measured by CFI was close to, but did not reach, the minimum threshold (>0.90) for acceptable model fit (Table 3; Additional file 2). CFI was 0.789 (sample 1) and 0.818 (sample 2) at baseline and 0.861 (sample 1) and 0.880 (sample 2) at follow-up assessments. The other indicator of model fit, RMSEA, was within the range of acceptable model fit (<0.10) for the six-domain model, ranging from 0.084 to 0.094 across analyses conducted at baseline and follow-up assessments. With few exceptions, item factor loadings for the six-factor model exceeded the expected magnitude for item convergence (r > 0.40). The exceptions occurred for the Life Skills domain items (excessive use of TV, computer or video games and keeping clean, brushing teeth, brushing hair, bathing, etc.) and the Risky Activities domain items (smoking cigarettes and taking illegal drugs). By comparison, the one-factor models showed poorer model fit as indicated by both CFI and RMSEA fit statistics. The CFI for a one-factor model ranged from 0.545 to 0.710 and RMSEA ranged from 0.133 to 0.141 across analyses. In addition, all item factor loadings were lower in the one-factor model compared with the six-factor model, and many items failed to show acceptable item convergence (r > 0.40) in the one-factor model.

**Reliability**

All of the scales of the WFIRS-P demonstrated good internal consistency reliability (Additional file 3). Cronbach’s
alpha exceeded 0.8 for all scales in the four samples except for Life Skills and Risky Activities, where values still exceeded the generally accepted cut-off of 0.7 [59]. A small subsample (sample 1: n = 35; sample 2: n = 34) met the criteria for a stable sample required to assess test–retest reliability as previously described. The ICCs observed for each scale met or exceeded acceptable test–retest reliability (r > 0.7). In sample 1, ICCs ranged between 0.73 and 0.89 across the six domains and summary index, with the exception of the Risky Activities domain where the ICC was 0.57. Similar results were found in sample 2.

**Convergent validity**

At baseline, correlations between the WFIRS-P domains and summary index and the ADHD-RS-IV total score and Inattention and Hyperactivity/Impulsivity subscale scores and the CGI-S score ranged from near zero to moderate (maximum correlation = 0.39) (Table 4A). The Family domain and summary index showed the strongest correlations with the ADHD-RS-IV total score and Inattention subscale score in both samples 1 and 2, and the Learning and School and Life Skills domains and summary index showed the highest correlations with the ADHD-RS-IV Hyperactivity/Impulsivity subscale. The Family and Social Activities domains and the summary index showed the highest correlation with CGI-I in both samples 1 and 2. At follow-up, correlations between the WFIRS-P domains and summary index and the ADHD-RS-IV scales and CGI–S score were considerably stronger than those observed at baseline, and in most instances the correlations were moderate in strength as hypothesized (Table 4B). In samples 1 and 2, the Family and Learning and School domains and summary index showed the strongest correlations with the ADHD-RS-IV total score and both Inattention and Hyperactivity/Impulsivity subscales. Similarly, these WFIRS-P domains and summary index showed the strongest correlation with CGI–I in both samples 1 and 2.

**Responsiveness**

Approximately 70 % of patients were categorized as responders in both samples 1 and 2 (Table 5). As hypothesized, greater improvement (i.e. larger negative change scores) was found in the responder than the non-responder group across all WFIRS-P domains and the summary index, and these differences were statistically significant (p < 0.001). In the responder group, the largest improvement was observed for the Learning and School domain (−0.63 and −0.60 in samples 1 and 2, respectively), followed by the Family domain (−0.48 and −0.51 in samples 1 and 2, respectively). The Risky Activities domain had the smallest improvement among responders (−0.22 in both samples), but baseline scores were also the lowest for this domain, indicating less impairment to start with. Overall, change scores in the non-responder group were small, ranging from −0.09 for the Risky Activities domain in sample 2, to −0.21 for the Learning and School domain in sample 1.
Discussion

The purpose of this study was to examine the reliability, validity and responsiveness of the WFIRS-P and to evaluate its appropriateness for assessing functional impairment in children and adolescents with ADHD in the context of clinical trials. To meet this objective, this study was conducted using pooled data from seven randomized controlled clinical trials designed to evaluate the safety/tolerability and efficacy of ADHD treatment. Overall, the results of this study support the reliability, validity and responsiveness of the WFIRS-P. The six-domain conceptual framework of the WFIRS-P as defined by the scoring algorithms showed adequate fit with CFA. Domain scores satisfied accepted minimum standards for internal consistency and test–retest reliability ($r \geq 0.7$) [59]. Many of the WFIRS-P domains correlated significantly with the ADHD-RS-IV scales and CGI–S score, although to varying degrees. The WFIRS-P domain scores were also responsive to change. Mean changes in WFIRS-P domain scores differed significantly between responder and non-responder groups, with responders showing greater improvement in scores than non-responders. All results were replicated between two random samples, indicating that the WFIRS-P has robust psychometric measurement properties.

In evaluating these measurement properties, there were a few notable findings worthy of further discussion. First, while the CFI statistics did not reach pre-specified levels for model fit using CFA, model fit as determined by RMSEA was satisfactory and the tests of the six-domain conceptual framework of the WFIRS-P showed a much better model fit compared with a one-factor model. Fit statistics (CFI and RMSEA) for the six-factor model were much better than those observed in Table 4 Relationship between WFIRS-P domain scores and summary index and ADHD criterion measures (ADHD-RS and CGI–S)

### Table 4 Relationship between WFIRS-P domain scores and summary index and ADHD criterion measures (ADHD-RS and CGI–S)

|                      | Sample 1 |             | Sample 2 |             |
|----------------------|----------|-------------|----------|-------------|
|                      | ADHD-RS-IV | CGI–S   | ADHD-RS-IV | CGI–S |
|                      | Total | Inattention | Hyperactivity | Impulsivity | Total | Inattention | Hyperactivity | Impulsivity |
| Scale                | rho   | rho         | rho       | rho         | rho   | rho         | rho         | rho         |
| Family domain        | 0.37  | 0.35        | 0.17      | 0.29        | 0.34  | 0.32        | 0.10        | 0.25        |
| Learning and School domain | 0.26  | 0.21        | 0.21      | 0.17        | 0.31  | 0.21        | 0.22        | 0.16        |
| Life Skills domain   | 0.25  | 0.22        | 0.21      | 0.15        | 0.21  | 0.12        | 0.20        | 0.10        |
| Child’s Self-Concept domain | 0.11  | 0.07        | 0.11      | 0.15        | 0.02$^*$ | 0.01$^*$ | 0.07$^*$ | 0.07$^*$ |
| Social Activities domain | 0.28  | 0.29        | 0.09      | 0.23        | 0.26  | 0.25        | 0.11        | 0.23        |
| Risky Activities domain | 0.25  | 0.28        | 0.10      | 0.19        | 0.28  | 0.26        | 0.10        | 0.18        |
| WFIRS-P summary index | 0.38  | 0.35        | 0.20      | 0.26        | 0.35  | 0.31        | 0.20        | 0.24        |

All correlations are statistically significant with $p < 0.001$ unless noted otherwise; $^*$ $p < 0.05$; $^*$ not significant

ADHD attention-deficit/hyperactivity disorder, ADHD-RS-IV ADHD Rating Scale Version IV, CGI–S Clinical Global Impression–Severity, $r$ Pearson correlation coefficient, rho Spearman rank correlation, WFIRS-P Weiss Functional Impairment Rating Scale-Parent Report Form
the one-factor model. Furthermore, in the one-factor model, many items showed item-factor loadings of <0.4, which is a minimum standard for item-convergent validity [49] calling into question the interpretation of a single global score using item-level data. In an effort to improve model fit, CFA analyses were conducted with an alternative specification of the conceptual framework of the WFIRS-P. Model fit was shown to improve considerably (CFI > 0.9 and RMSEA < 0.1) when the items of the School Learning-Behavior scale were modelled as two concepts, School Learning and School Behavior. Future studies should focus on testing these two concepts separately using other sources of WFIRS-P data, such as observational study data.

In this study, the availability of criterion measures to evaluate the validity of the WFIRS-P domains was limited to ADHD symptoms, as measured by the ADHD-RS-IV scale, and ADHD severity, as measured by the CGI–S scale. In order to demonstrate convergent validity, it is generally recommended that the correlation between the measure in question (WFIRS-P) and the criterion measure meet or exceed 0.30 [60]. However, given the lack of studies conducted that have investigated the measurement properties of the WFIRS-P, there was little basis to formulate hypotheses about the magnitude of correlation that should be observed between the WFIRS-P domains and the ADHD-RS-IV and CGI–S scales in this study. Hypotheses were generated under the general framework that more symptoms (frequency or severity) or greater severity should be associated with greater functional impairment [61]. In this study, it was found that some concepts of the WFIRS-P showed higher correlations with symptoms (ADHD-RS-IV) and severity (CGI–S) of ADHD than others. For example, the Family, Learning and School, and Life Skills domains generally showed stronger correlations with ADHD-RS-IV and CGI–S than other WFIRS-P domains such as Child Self-Concept or Risky Activities. These findings do not necessarily invalidate those WFIRS-P domains with lower correlations, but rather help us to understand what concepts are more proximal to, and what concepts appear to be more distal to, the symptoms and severity of ADHD. This finding is consistent with results of qualitative studies conducted to define a measurement model for assessing functional impairment in ADHD [62]. One implication of this finding concerns selecting specific WFIRS-P domains for evaluating treatment efficacy. If treatment is aimed at reducing the symptoms and severity of ADHD, then it is more likely the case that domains showing stronger correlations with ADHD symptoms and severity will respond to treatment than domains showing weaker correlations with ADHD symptoms and severity. More importantly, these results reinforce the need for further exploration of the validity of the WFIRS-P using criterion measures other than those related to the symptoms and severity of ADHD, in particular criterion measures that are patient-based or parent-based as opposed to clinician-based, as they may have differing perspectives on patient functional impairment.

Another observation in this study highlights that the results of analyses conducted with follow-up data yielded better measurement properties than those conducted with baseline data. For example, model fit statistics from CFA were much better with follow-up data, and correlations between WFIRS-P domain scores and the criterion measures were considerably stronger with follow-up data. This may have been due in part to the impact of the inclusion and exclusion criteria of each study on baseline data. The inclusion and exclusion criteria of each study were in part designed to identify patients with more severe symptoms of ADHD, which resulted in a fairly homogenous sample with respect to symptoms, severity and functional impairment. In fact, the inclusion and exclusion criteria in all seven studies included a minimum ADHD-RS-IV total score, and the four GXR trials also included a minimum CGI–S score, both of which were criterion measures used to evaluate the
convergent validity of the WFIIRS-P. As a consequence, there was less variability in the criterion measures at baseline, resulting in attenuated correlations between the WFIIRS-P and the criterion measures. At follow-up, however, study inclusion and exclusion criteria were likely to be less impactful as half of the patients of each trial were treated and thus were expected to improve in symptoms and severity versus those in the placebo group. As a consequence, the sample at follow-up was more heterogeneous with respect to underlying symptoms, severity and functional impairment, all of which contributed to the better psychometric results observed with follow-up data.

Several limitations of this study should be considered when interpreting the study results. First, the study population was enrolled into randomized controlled clinical trials using stringent inclusion and exclusion criteria. This population may not be representative of all children and adolescents with ADHD seen in general practice settings, and hence it is not known how well the WFIIRS-P would perform in a more general patient population from these study results. However, in determining the adequacy of an instrument for measuring functional impairment in clinical trials of ADHD treatment, the results of this study suggest that the WFIIRS-P has acceptable measurement properties that support the reliability and validity of the instrument as a measure of functional impairment in clinical trials.

Another potential limitation of this study concerns the limited number of criterion measures available across all trials for purposes of assessing the convergent-divergent validity and responsiveness of the WFIIRS-P domains. The criterion measures relied upon in this study were symptom-based and severity measures were clinician-reported. While it was expected that more severe symptoms would be associated with greater functional impairment, the results of this study showed that some domains of the WFIIRS-P were weakly correlated with the criterion measures and that correlations tended to be low in general. For example, the Child’s Self-Concept domain was weakly correlated with the ADHD-RS-IV. This finding does not necessarily invalidate the Child’s Self-Concept domain, but calls into question the appropriateness of the ADHD-RS-IV as a criterion measure for validating this domain. It has been reported that some concepts of ADHD-related functional impairment are more distal to the symptoms of ADHD than others, which would help explain the low correlations observed for some WFIIRS-P domains [62].

The fact that the criterion measures were clinician reported may also factor into the interpretation of the convergent validity correlations observed in this study. While for many WFIIRS-P domains correlations with the criterion measures met the minimum threshold \( r > 0.3 \) for convergent validity, the WFIIRS-P Child’s Self-Concept domain showed lower correlations than the minimum threshold. This may be driven in part by the use of clinician-reported measures as criterion measures, which do not always reflect the patients’ or parents’ perspectives. Further study of the validity of the WFIIRS-P domains would benefit from the use of other conceptually related patient-reported outcome measures.

Conclusion
Despite the limitations of this study, the evidence generated from the analyses conducted showed adequate support for the six-domain conceptual framework of the WFIIRS-P and demonstrated that the WFIIRS-P domains are reliable, valid and responsive. The evidence supporting the conceptual framework of the WFIIRS-P items and domains was adequate and replicated between random half-samples. All WFIIRS-P domains met the minimum standards of internal consistency reliability and test–retest reliability, and with few exceptions, correlations between WFIIRS-P domains and each criterion measure met the minimum value to support convergent validity. Lastly, all WFIIRS-P domains were shown to be responsive to changes in ADHD status as defined using criteria implemented to determine treatment response. These findings support the use of the WFIIRS-P as a measure of functional impairment in clinical trials of children and adolescents with ADHD.

Additional files

Additional file 1: Differential item functioning test of WFIIRS-P. (DOCX 33 kb)
Additional file 2: Confirmatory factor analysis of the WFIIRS-P factor loadings for the six-factor and one-factor models. (DOCX 27 kb)
Additional file 3: Internal consistency and test–retest reliability of the WFIIRS-P. (DOCX 19 kb)

Competing interests
Ms Gajria, Dr Sikirica and Dr Haim Erder were employees of Shire at the time this work was completed. Mr Kosinski and Dr Livote are employees of QualityMetric, which has received funding from Shire Development, LLC for conducting the study and manuscript preparation assistance. Ms Reilly was an employee of QualityMetric at the time this work was completed. Professor Huss is an advisory board member/advisor/recipient of honoraria for Eli Lilly, Janssen-Cilag, Medice, Novartis and Shire, and has received consultation fees from Engelhard Arzneimittel and Steiner Arzneimittel. Professor Dittmann has received compensation as a consultant/speaker, xor he/his institution has received research support/royalties from: EU (ETP Programme), US NIMH, German Federal Ministry of Health/Regulatory Agency, German Federal Ministry of Education and Research, German Research Foundation, Volkswagen Foundation, Boehringer Ingelheim, Ferring, Janssen-Cilag, Eli Lilly, Otsuka, Shire, Sunovion and Theravance; and he holds stocks in Eli Lilly.

Authors’ contributions
All authors were involved with the analysis and interpretation of data, critically reviewed the manuscript for important intellectual content and approved the final article for publication. KG and VS were involved with the concept and design of the study, the acquisition of data and drafting of the
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References
1. Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. Am J Psychiatry. 2007;164:942–8.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. DSM-IV. 4th ed. Washington DC: APA; 1994.
3. Gordan M, Antshel K, Farone S, Barkley R, Lewandowski L, Hudziak JJ, et al. Symptoms versus impairment: the case for respecting DSM-IV’s criterion D. J Atten Disord. 2006;9:465–75.
4. Bagwell CL, Molina BS, Pelham Jr WE, Hoza B. Attention-deficit hyperactivity disorder and problems in peer relations: predictions from childhood to adolescence. J Am Acad Child Adolesc Psychiatry. 2001;40:1285–92.
5. Banaschewski T, Soutullo C, Lecendreux M, Soutullo C, Johnson M, Zuddas A, Hodgkins P, et al. Health-related quality of life and functional outcomes from a randomized, controlled study of lisdexamfetamine dimesylate in children and adolescents with attention deficit hyperactivity disorder. CNS Drugs. 2013;27:269–80.
6. Barkley RA, Guevremont DC, Anastopoulos AD, DuPaul GJ, Shelton TL. Driving-related risks and outcomes of attention deficit hyperactivity disorder in adolescents and young adults: a 3- to 5-year follow-up survey. Pediatrics. 1993;92:212–8.
7. Becker A, Roessner V, Breuer D, Döpfner M, Rothenberger A. Relationship between quality of life and psychopathological profile: data from an observational study in children with ADHD. Eur Child Adolesc Psychiatry. 2011;20 Suppl 2:2567–75.
8. Bernardi S, Farone SV, Cortese S, Kendrie BT, Pallanti S, Wang S, et al. The lifetime impact of attention deficit hyperactivity disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Psychol Med. 2012;42:875–87.
9. Brook U, Boaz M. Attention deficit and hyperactivity disorder learning disabilities (ADHD/LD): parental characterization and perception. Patient Educ Couns. 2005;57:96–100.
10. Cussen A, Sciberras E, Ukoumunne OC, Efron D. Relationship between symptoms of attention-deficit/hyperactivity disorder and family functioning: a community-based study. Eur J Pediatr. 2012;171:271–80.
11. Danckaerts M, Sonuga-Barke EJ, Banaschewski T, Buitelaar J, Doghman M, Hollis C, et al. The quality of life of children with attention deficit/ hyperactivity disorder: a systematic review. Eur Child Adolesc Psychiatry. 2010;19:83–105.
12. Escobar R, Schacht A, Wehmeier PM, Wagner T. Quality of life and attention-deficit/hyperactivity disorder core symptoms: a pooled analysis of 5 non-US atomoxetine clinical trials. J Clin Psychopharmacol. 2010;30:145–51.
13. Gouardères JB, Marques JC, Casella EB. Quality of life and psychomotor profile of children with attention deficit hyperactivity disorder (ADHD). Arq Neuropsiquiatr. 2011;69:630–5.
14. Harpin VA. The effect of ADHD on the life of an individual, their family, and community from preschool to adult life. Arch Dis Child. 2005;90 Suppl 1:72–7.
15. Taanila AM, Hurtig TM, Miettunen J, Ebeling HE, Mollenen IK. Association between ADHD symptoms and adolescents’ psychosocial well-being: a study of the Northern Finland Birth Cohort 1986. Int J Circumpolar Health. 2009;68:133–44.
16. Wehmeier PM, Schacht A, Barkley RA. Social and emotional impairment in children and adolescents with ADHD and the impact on quality of life. J Adolesc Health. 2010;46:209–17.
17. Dulcan M. Practice parameters for the assessment and treatment of children, adolescents, and adults with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 1997;36 Suppl 1085S–121.
18. European Medicines Agency. Guideline on the clinical investigation of medicinal products for the treatment of attention deficit hyperactivity disorder (ADHD). http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003474.pdf. Accessed 1 Jul 2014.
19. Scoggins JF, Patrick DL. The use of patient-reported outcomes instruments in registered clinical trials: evidence from ClinicalTrials.gov. Contemp Clin Trials. 2009;30:289–92.
20. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth edition, Text Revision. Washington, DC: APA; 2000.
21. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Arlington: American Psychiatric Publishing; 2013.
22. Parente N, Johnston J. Facts, values, and attention-deficit hyperactivity disorder (ADHD): an update on the controversies. Child Adolesc Psychiatry Ment Health. 2009;3:1.
23. World Health Organization. International Statistical Classification of Diseases and Related Health Problems 10th Revision. http://apps.who.int/classifications/icd10/browse/2010/en. Accessed 9 Mar 2015.
24. CADDRA. Canadian ADHD practice guidelines. http://caddra.ca/pdfs/caddraGuidelines2011.pdf. Accessed 1 Jul 2014.
25. Weiss MD, Dickson R, Wasdell M, et al. Weiss Functional Impairment Rating Scale-Parent Report (WFRS-P). Presented at: American Psychiatric Association 158th Annual Meeting, Atlanta, GA, May 21–26 2005.
26. Weiss MD, Brooks BL, Iverson GL, Lee B, Dickson R, Wasdell M. Reliability and validity of the Weiss functional impairment rating scale. Presented at: AACAP 54th Annual Meeting, Boston, MA., 23–28 October 2007.
27. Coghill D, Banaschewski T, Lecendreux M, Soutullo C, Johnson M, Zuddas A, et al. European, randomized, phase 3 study of lisdexamfetamine dimesylate in children and adolescents with attention-deficit/hyperactivity disorder. Eur Neuropsychopharmacol. 2013;23:1208–18.
28. Coghill DR, Banaschewski T, Lecendreux M, Johnson M, Zuddas A, Anderson CS, et al. Maintenance of efficacy of lisdexamfetamine dimesylate in children and adolescents with attention-deficit/hyperactivity disorder: randomized-withdrawal study design. J Am Acad Child Psychiatry. 2014;53:647–57. e1.
29. Dittmann RW, Caruso E, Nagy P, Anderson CS, Bloomfield R, Caballero B, et al. Efficacy and safety of lisdexamfetamine dimesylate and atomoxetine in the treatment of attention-deficit/hyperactivity disorder: a head-to-head, randomized, double-blind, phase IIIb study. CNS Drugs. 2013;27:1081–92.
30. Hervas A, Huss M, Johnson M, McNicholas F, van Stralen J, Sreckovic S, et al. EPA-0666 - Long-term maintenance of efficacy of extended-release guanfacine hydrochloride (GXR) in children and adolescents with ADHD: an update on the controversies. Child Adolesc Psychiatry Ment Health. 2009;3:1.
31. European Medicines Agency. Guideline on the clinical investigation of medicinal products for the treatment of attention deficit hyperactivity disorder (ADHD). http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003474.pdf. Accessed 1 Jul 2014.
32. Newcorn JH, Harpin V, Huss M, Johnson M, Ramos-Quiroga JA, van Stralen J, et al. EPA-0666 - Long-term maintenance of efficacy of extended-release guanfacine hydrochloride (GXR) in children and adolescents with attention-deficit/hyperactivity disorder (ADHD): double-blind, placebo-controlled, multicentre, Phase 3 randomized withdrawal study design. Eur Psychiatry. 2014;29 Suppl 1:1–1407.
33. Wilens TE, Harper L, Young JL, Sikirica V, Bloomfield R, Lyne A, et al. Guanfacine extended release in adolescents with ADHD: a multicenter, randomized, placebo-controlled trial (Abstract 2.33). https://aacap.org/2014/webprogram/Paper22617.html. Accessed 9 Mar 2015.

34. Dupaul GJ, Power TJ, Anastopoulos A, Reed R. The ADHD rating scale IV checklist, norms and clinical interpretation. New York: Guilford Press; 1998.

35. Brans M, Weisler R, Findling RL, Gasior M, Hamdani M, Ferreira-Connell MC, et al. Maintenance of efficacy of lisdexamfetamine dimesylate in adults with attention-deficit/hyperactivity disorder: randomized withdrawal design. J Clin Psychiatry. 2012;73:977–83.

36. Findling RL, Childress AC, Cutler AJ, Gasior M, Hamdani M, Ferreira-Connell MC, et al. Efficacy and safety of lisdexamfetamine dimesylate in adolescents with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2011;50:395–405.

37. Findling RL, Cutler AJ, Saylor K, Gasior M, Hamdani M, Ferreira-Connell MC, et al. A long-term open-label safety and effectiveness trial of lisdexamfetamine dimesylate in adolescents with attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol. 2013;23:11–21.

38. Stein MA, Waldman ID, Chamney E, Aryal S, Sable C, Gruber R, et al. Dose effects and comparative effectiveness of extended-release dexmethylphenidate and mixed amphetamine salts. J Child Adolesc Psychopharmacol. 2011;21:581–8.

39. Weisler RH, Pandina GJ, Daly EJ, Cooper K, Gassmann-Mayer C. Randomized clinical study of a histamine H3 receptor antagonist for the treatment of adults with attention-deficit hyperactivity disorder. CNS Drugs. 2012;26:421–34.

40. Wilens TE, Bukstein O, Brans M, Cutler AJ, Childress A, Rugo T, et al. A controlled trial of extended-release guanfacine and psychostimulants for attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2012;51:74–85.

41. Kollins SH, Jain R, Brans M, Segal S, Findling RL, Wigal SR, et al. Clonidine extended-release tablets as add-on to psychostimulants in children and adolescents with ADHD. Pediatrics. 2011;127:e1406–13.

42. Jain R, Segal S, Kollins SH, Khayrallah M. Clonidine extended-release tablets for pediatric patients with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2011;50:171–9.

43. Guy W. ECDEU assessment manual for Psychopharmacology. Rockville: Department of Health, Education and Welfare; 1976.

44. FDA. Guidance for industry. Patient-reported outcome measures: use in medical product development to support labeling claims. http://www.fda.gov/downloads/Drugs/Guidances/UCM193282.pdf. Accessed 9 Mar 2015.

45. Muthén B, Muthén L. Mplus User's Guide, Version 1. Los Angeles: Muthén & Muthén; 1998.

46. Bentler PM. Comparative fit indexes in structural models. Psychol Bull. 1990;107:238–46.

47. Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. Struct Equation Model. 1999;6:1–55.

48. Browne MW, Cudeck R. Alternative ways of assessing model fit. Sociol Meth Res. 1992;21:230–58.

49. Comrey AL, Lee H. A first course in factor analysis. 2nd ed. Hillsdale: Lawrence Erlbaum Associates; 1992.

50. Cronbach LJ. Coefficient alpha and the internal structure of tests. Psychometrika. 1951;6:297–334.

51. Shroff PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol Bull. 1979;86:420–8.

52. Conners CK. Conners’ rating scales - revised. Technical manual. New York: Multi-Health Systems Inc; 1997.

53. Lerner JW. Learning disabilities: theories, diagnosis, and teaching strategies. 9th ed. Boston: Houghton Mifflin; 1988.

54. Cohen J. Statistical power analysis for the behavioural sciences. 2nd ed. Hillsdale: Lawrence Erlbaum Associates; 1988.

55. Currie J, Stabile M. Child mental health and human capital accumulation: the case of ADHD. J Health Econ. 2006;25:1094–118.

56. Guyatt GH, Deve SE, Charlson M, Levine MN, Mitchell A. Responsiveness and validity in health status measurement: a clarification. J Clin Epidemiol. 1989;42:403–8.

57. Kerlinger FN. Foundations of behavioral research. New York: Holt, Rinehart and Winston; 1973.

58. Zumbo BD. A handbook on the theory and methods of differential item functioning (DIF). Logistic regression modeling as a unitary framework for binary and Likert-type (ordinal) item scores. Ottawa: Directorate of Human Resources Research and Evaluation, Department of National Defense; 1999.

59. Nunnally JC, Bernstein IH. Psychometric theory. 3rd ed. New York: McGraw-Hill; 1994.

60. Campbell DT, Fiske DW. Convergent and discriminant validation by the multitrait-multimethod matrix. Psychol Bull. 1959;56:81–105.

61. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. JAMA. 1995;273:59–65.

62. Pokrzywinski R, Setyawan J, Khan S, Ender MH, Hodgkins P, Hareendran A. Development of a conceptual disease model to inform strategy to evaluate treatment impact in adolescents with attention-deficit hyperactivity disorder (ADHD). Value Health. 2013;16:644–5.