

Reproducibility of the six-minute walk test and Glittre ADL-test in patients hospitalized for acute and exacerbated chronic lung disease

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ABSTRACT | Background: The 6-minute walk test (6MWT) and the Glittre ADL-test (GT) are used to assess functional capacity and exercise tolerance; however, the reproducibility of these tests needs further study in patients with acute lung diseases. **Objectives:** The aim of this study was to investigate the reproducibility of the 6MWT and GT performed in patients hospitalized for acute and exacerbated chronic lung diseases. **Method:** 48 h after hospitalization, 81 patients (50 males, age: 52±18 years, FEV₁: 58±20% of the predicted value) performed two 6MWTs and two GTs in random order on different days. **Results:** There was no difference between the first and second 6MWT (median 349 m [284–419] and 363 m [288–432], respectively) (ICC: 0.97; P<0.0001). A difference between the first and second tests was found in GT (median 286 s [220–378] and 244 s [197–323] respectively; P<0.001) (ICC: 0.91; P<0.0001). **Conclusion:** Although both the 6MWT and GT were reproducible, the best results occurred in the second test, demonstrating a learning effect. These results indicate that at least two tests are necessary to obtain reliable assessments.

Keywords: physical therapy; reproducibility of results; exercise tolerance; exercise test; lung diseases.

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Introduction

Clinical field tests are used to assess the functional capacity (FC) and exercise tolerance of patients with pulmonary diseases. It is important to know the reproducibility of these tests to achieve an accurate assessment of the patient's FC and responsiveness to treatment¹. The variability of a test must also be known so that its results are reliable; this ensures the differences are due to interventions or the evolution of the patient rather than fluctuations inherent to the test.

The 6-minute walk test (6MWT) is a simple and low-cost field test that provides a comprehensive and integrated measure of the patient's physical condition². The reproducibility of the 6MWT has been tested in patients with various lung diseases, particularly patients with chronic obstructive pulmonary disease (COPD)³⁻⁵ mainly in the outpatient setting. The variability found in these studies has been attributed to a learning effect. A recent study found a difference of 27 m (7%) greater in the second test⁶. Sciurba et al.⁷ found a difference of 20 m (7%), Chatterjee et al.⁸ found a 32-m difference (10%), Stevens et al.⁹ found 42 m (13%), and Jenkins and Cecins¹⁰ identified a 37-m difference (11%).

The reproducibility of the 6MWT has also been studied in patients with idiopathic interstitial pneumonia (ICC: 0.98, standard deviation/mean: 4.2%)¹¹, cystic fibrosis (6.5 m or 4.3%)¹², interstitial lung disease (41 m, 10%)¹⁰, bronchiectasis (22 m, 4%)¹⁰, and asthma (19 m, 4%)¹⁰.

The Glittre ADL-test (GT) is another field test developed to evaluate the capacity to perform activities of daily living (ADL). Its reproducibility was tested in patients with COPD, showing a decrease of 22 s in the time to completion in the second test, which was attributed to a learning effect¹³.

Considering the importance of field-testing in clinical practice, its reproducibility should also be solidly studied in hospitalized patients not only with exacerbation of COPD but also with acute lung conditions, such as community-acquired pneumonia (CAP). To our knowledge, there is no study testing the reproducibility of the 6MWT and GT in hospitalized patients. The ability of the GT to detect exercise-induced desaturation, as previously demonstrated with the 6MWT in COPD¹⁴, should be assessed so that it can be used to identify patients with hypoxemia during

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ADL. The aim of this study was to investigate the reproducibility of the 6MWT and GT in patients hospitalized for acute and exacerbated chronic lung diseases and to compare the desaturation induced by both tests.

Method

Participants

The sample from a cross-sectional study previously published by our group¹⁵ was used for this current work. The sample included 103 adult patients hospitalized for less than 48 h for acute or exacerbated chronic lung diseases, with or without oxygen supplementation and without comorbidities that might limit their performances on the tests. For better characterization of the sample, patients were divided into three groups according to the most prevalent diseases of hospitalization in our hospital: CAP, COPD, and Others (other lung diseases). This study was approved by the Research Ethics Committee of Universidade Nove de Julho, São Paulo, Brazil (protocol no. 273811/2009). All patients signed an informed consent form.

Design

The study was conducted in two visits on consecutive days. On the first visit, spirometry was performed, the body mass index (BMI) was calculated, and dyspnea was assessed according to the Medical Research Council (MRC) scale. The randomization was performed using sealed and opaque envelopes that each contained a card indicating the 6MWT or GT. A person uninvolved in the research selected one of these envelopes, which determined which test would be performed first (6MWT or GT).

An hour of rest was allowed between testing and retesting. On the second visit (24 h apart), the other test was performed. The total period of hospitalization was recorded.

Assessments

Spirometry

Spirometry was performed with the Pony portable spirometer (COSMED, Italy). The acceptability and reproducibility criteria adopted for the technical procedures were those recommended by the Brazilian guidelines for the testing of lung function¹⁶. The values of forced vital capacity (FVC), forced expiratory volume in the first second (FEV₁), and the FEV₁/FVC ratio

were expressed in absolute values and as percentage of the predicted value for the Brazilian population¹⁷.

Body mass index

BMI was calculated by dividing the body weight of the patient in kilograms (kg) by the square of the height in square meters (m²), and the result was expressed in kg/m² ¹⁸. The patient was classified as underweight if BMI<18.5 kg/m², normal weight if 18.5–24.9 kg/m², overweight if 25–29.9 kg/m², and obese if BMI>30 kg/m² ¹⁹.

Medical Research Council's dyspnea scale

The Medical Research Council's (MRC) scale of dyspnea includes five items. The patient chooses which of the items corresponds to the perceived limitations of dyspnea on his/her ADLs. The patient selects a value from 1–5; the higher the score the greater the limitations dyspnea imposes on the patient's ADL²⁰.

Six-minute walk test (6MWT)

The 6MWT was performed on a 20-meter-long flat corridor. Two tests with 1-h rest times were performed on the same day. Other procedures and standardizations were performed according to the American Thoracic Society recommendations². The test with the longest distance walked was selected for analysis, and the distance walked was expressed in m and predicted values²¹. Heart rate (HR) and oxyhemoglobin saturation (SpO₂) were measured at rest, at 3 min, and at the end of the test using a pulse oximeter (Nonin 9500 model, Minnesota, United States). The scores for sensation of dyspnea (Borg D) and lower limb fatigue (Borg LL) were measured at rest and at the end of the test according to the modified Borg scale²².

Evaluation of oxygen desaturation was also obtained from the longest test considering the lowest SpO₂ recorded. Oxygen supplementation, when necessary, was maintained in accordance with the prescription of the medical team. A covered distance <82% of the predicted value was considered below normal²³.

Glittre ADL-test (GT)

The GT comprises a circuit of functional activities the patient must cover 5 times in the shortest time possible. The patient performs activities such as walking, using stairs, sitting on a chair and standing up, and handling 1-kg weights to simulate moving objects from one shelf to another and then to the floor. Throughout the test, the patient wears a weighted backpack¹³.

Two tests were performed on the same day, with a 1-h rest interval between them. HR, SpO₂, and time to completion were measured at rest and at the end of each completed lap. The Borg D and Borg LL²² scores were also evaluated at rest and at the end of the test. The test's total time to completion was recorded at the end.

Evaluation of oxygen desaturation was obtained from the test with the shorter duration considering the lowest SpO₂ recorded. As described for 6MWT, oxygen supplementation, when necessary, was maintained in accordance with the prescription of the medical team.

Statistical analysis

The data analysis was performed using SPSS for Windows version 20.0 (SPSS, Chicago, Illinois, USA). The Shapiro-Wilk test was used to verify the compliance of the data distribution with the normality curve. Parametric data were express ed as mean and SD. Non-parametric data were expressed as median and interquartile intervals. In the sample characterization, comparisons between groups were performed by one-way analysis of variance (ANOVA) with post-hoc Tukey's analysis. Interclass correlation

coefficient and Bland-Altman analysis were used for test–retest reproducibility. Intragroup comparisons for parametric data were performed by paired *t*-tests for dependent samples, and by the Wilcoxon test for the non-parametric data. P<0.05 was considered statistically significant.

Results

Sample

Of the 103 patients enrolled in the study, 10 were excluded for failure to perform the 6MWT and 12 for failure to perform the GT because of hospital discharge. At the end of the study, 81 subjects (50 men) were surveyed.

Fifty-one patients (63%) had a diagnosis of CAP, 16 patients (20%) were diagnosed with exacerbated COPD, and 14 (17%) were diagnosed with other diseases (lung cancer = 7, asthma = 4, and tuberculosis = 3). According to BMI, 3 patients (4%) were classified as underweight, 39 (48%) as normal weight, 19 (23%) as overweight, and 20 (25%) as obese.

The patients with CAP were younger than those in the COPD group (P<0.0001). Additionally, BMI and dyspnea were higher in the COPD group compared with patients in the CAP group (all P<0.05). The hospitalization period did not differ between groups. Spirometry differed among groups (Table 1).

Table 1. Characteristics of the studied patients.

	Results		
Variables	CAP (n=51)	COPD (n=16)	Others (n=4)
Demographic data and BMI			
Age, years	47±17*	66±9	62 (29 – 71)
BMI, Kg/m ²	25±4#	29±6■	25±5
Pulmonary function			
FVC, L	2.1±0.8	1.8±0.7■	2.6±0.9
FVC, % of the predicted value	55.7±17.4	53±19.4 ■	74.9±17.4
FEV ₁ , L	1.8±0.7 [#]	1.1±0.4	2.0 (1.3 – 2.7)
FEV ₁ , % of the predicted value	58.5±17.9♯■	42.8±16.2	72.1±22.7*
FEV ₁ / FVC, %	88.5 (78.0 − 93.4)* ■	66.6 (57.5 – 69.2)	75.2±15.9
Dyspnea			
MRC scale	2 (2 – 4)#	4.5 (2 – 5)	3.5 (1 – 5)
Hospitalization			
Time of hospitalization, days	13 (8 – 16)	12.5 (7 – 18)	16±10

CAP: community-acquired pneumonia; COPD: chronic obstructive pulmonary disease; BMI: body mass index; Kg/m^2 : kilogram per square meter; L: liters; FVC: forced vital capacity; FEV_1 : forced expiratory volume in the first second; MRC: Medical Research Council score. *P<0.0001 compared to COPD group; *P<0.05 compared to others group.

Reproducibility

No significant difference was found in the distance covered between the two 6MWTs, with a 14-m increase in the second test (4% increase). 49 patients (61%) covered a greater distance in the second test and 50 patients (62%) had a difference of <27 m between the two tests. HR, SpO₂ and dyspnea, and lower limb fatigue scales were equivalent (Table 2).

In the GT, a 42-s difference was found in the second test (17% increase, P<0.001), and 71 patients (88%)

performed the second test in less time than the first. As in the 6MWT, the HR, SpO₂ and dyspnea, and lower limb fatigue scales were equivalent in both tests (Table 3).

The Bland-Altman analysis reveals that the patients improved the distances covered in the second test of the 6MWT (Figure 1) and the GT (Figure 2), showing a narrow mean difference. However, the confidence interval of the means of the differences was wide, showing great variability of results between testing and retesting.

Table 2. Results for the 6MWT.

Variables	6MWT -1	6MWT – 2	ICC (95% CI)*
Rest			
HR, bpm	89±16	91±17 [#]	0.94 (0.90 – 0.96)
SpO ₂ , %	96 (95 – 98)	96 (95 – 98)	0.87 (0.79 - 0.91)
Borg d	0.5(0-1)	$0(0-0.75)^{\sharp}$	0.64 (0.45 – 0.77)
Borg LL	0(0-0.5)	0(0-1)	0.84 (0.76 - 0.90)
3 ^{rd.} Minute			
HR, bpm	111 (98 – 121)	109 (96 – 120)	0.85(0.77 - 0.90)
SpO ₂ , %	93 (90 – 96)	94 (88 – 96)	0.90 (0.84 – 0.94)
6 ^{th.} Minute			
HR, bpm	113 (100 – 123)	112 (102 – 122)	0.87 (0.82 - 0.93)
SpO_2 , %	94 (90 – 97)	94 (89 – 96)	0.92 (0.87 – 0.95)
Borg d	1 (0 – 3)	$0.5 (0-2.5)^{\sharp}$	0.88 (0.81 - 0.93)
Borg LL	0.5(0-2.5)	0(0-2)	0.93 (0.89 – 0.95)
Distance, m	349 (285 – 419)	363 (288 – 432)	0.97 (0.95 – 0.98)

6MWT-1: first six-minute walk test; 6MWT-2: second six-minute walk test; bpm: beats per minute; Borg d: Borg scale for dyspnea; Borg ll; Borg scale for lower limb fatigue; m: meters. * P<0.0001 for all variables; * P<0.05 in relation to the 6MWT-1.

Table 3. Results for the Glittre ADL-test.

Variables	GT -1	GT – 2	ICC (95% CI)*
Rest			
HR, bpm	90 (78 – 101)	92 (82 – 105)#	0.92 (0.87 - 0.95)
SpO ₂ , %	97 (96 – 98)	97 (96 – 98)	0.83 (0.74 - 0.89)
Borg d	0(0-0.5)	0(0-0.5)	$0.80 \; (0.68 - 0.87)$
Borg LL	0(0-0.5)	0(0-1)	0.67 (0.48 - 0.79)
Final			
HR, bpm	126±19	126±19	0.87 (0.80 - 0.92)
SpO ₂ , %	94 (91 – 97)	94 (91 – 97)	0.88 (0.81 - 0.92)
Borg D	3 (1 – 4)	2 (1 – 4)	0.86 (0.78 - 0.91)
Borg LL	1 (0 – 3)	2(0-3)	0.80 (0.69 - 0.87)
Time, s	286 (220 – 378)	244 (197 − 323) •	0.91 (0.75 - 0.96)

GT-1: first Glittre ADL-test; GT-2: second Glittre ADL-test; bpm: beats per minute; Borg D: Borg scale for dyspnea; Borg LL; Borg scale for lower limb fatigue; s: seconds. * P<0.001 for all variables; • P<0.001 in relation to GT1; * P<0.05 in relation to GT1.

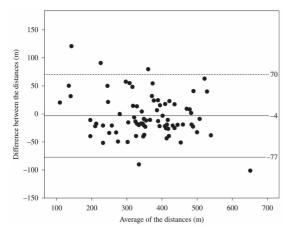


Figure 1. Bland-Altman of the average distance covered in the 6MWT and the difference between the distances in the two tests. The solid horizontal line represents the average polarization. The dashed horizontal lines represent the upper and lower limits of agreement.

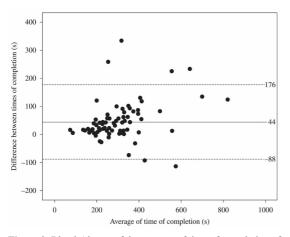


Figure 2. Bland-Altman of the average of time of completion of GT and the difference between the times of completion of the two tests. The dashed horizontal lines represent the upper and lower limits of agreement.

The distance covered in the best 6MWT was greater than 82% of the predicted value in 15 patients (19%) (CAP: 60%, COPD: 27%, Others: 13%) and smaller than 82% of the predicted value in 66 patients (81%) (CAP: 64%, COPD: 18%, Others: 18%). A comparison of these groups, respectively, showed that the older individuals (61±16 and 50±17 years, P<0.05) had higher BMIs (28±4 and 25±5 kg/m², P<0.05) and walked 453±83 and 353±98 m in the 6MWT (P<0.0001) (96±17 and 61±13% of the predicted value, P<0.0001). However, no differences were found in

lung function, period of hospitalization, dyspnea scale or GT (240 ± 69 s and 282 ± 126 s, P=0.08).

There were no significant differences between the 6MWTs in HR and SpO₂. The mean biases (95% CI of the differences) were 0 (-23–23 beats/min⁻¹) and 1 (-5–6%) respectively; for the GT they were -1 (-19–18 beats/min⁻¹) and 0 (-6–5%) respectively.

In the separate evaluations of the reproducibility of the 6MWT in COPD and CAP patients, the results were as follows: COPD: 318±81 and 328±84 m, in the first and second test, respectively (P=0.18), mean bias 10 m (-44–64); ICC: 0.97 (0.91–0.99), P<0.0001; CAP: 368±103 and 366±113 m, in the first and second tests respectively (P=0.84), mean bias 1 s (-78–80); ICC: 0.97 (0.94–0.98), P<0.0001. In relation to the reproducibility of the GT in COPD and CAP patients, the results were as follows: COPD: 378±136 and 302±115 s in the first and second tests respectively (P=0.006), mean bias 77 s (-113–267); ICC: 0.75 (0.15–0.92), P=0.01; CAP: 301±125 and 264±110 s in the first and second tests respectively (P<0.0001), mean bias 37 s (-82–155); ICC: 0.91 (0.76–0.97), P<0.0001.

Comparison of oxyhemoglobin desaturation between the two test types

The comparison between the lowest saturation on the best 6MWT and GT showed no significant differences (P=0.37) and were reproducible (ICC=0.69 (95% CI: 0.51–0.80), P<0.0001). The mean bias (95% CI) of the desaturation between 6MWT and GT was -0.4 (-9–8%).

Discussion

This study examined the reproducibility of the 6MWT and GT in a sample of patients with acute and exacerbated chronic lung diseases. Both tests were reproducible. In the 6MWT, most patients increased the distance covered in the second test (median variation: 14 m, 4% improvement); this was also found in GT, as most patients reduced the time to completion in the second test (median variation: 42 s, 17% lower), suggesting the presence of a learning effect. For both cases, the Bland-Altman analysis confirmed that the second test was better than the first, and the detected limits of agreement were higher than the upper limits of a clinically significant change; that is, changes of 26 m in the 6MWT²⁴ and 53 s in the GT¹³.

While there is interest in the early rehabilitation of patients hospitalized for acute and chronic lung diseases, we were interested in investigating the reproducibility of the 6MWT and the GT since there are no studies on this group. Our results demonstrate that the variability in these conditions is similar to that observed in non-hospitalized patients with chronic lung conditions⁶.

It is common to find a large variability in field tests, which has been credited to the learning effect. In our study, this effect can be identified in the difference in time to perform the GT and the high variability observed by the large limits of agreement in both tests. However, the analysis of this effect is compromised because most studies commonly express the data as mean and SD, showing no variability between tests. In the present study, we employed the Bland-Altman method²⁵, which is considered a better analysis to compare the agreement of two measurements.

Six-minute Walk Test (6MWT)

In the first 6MWT, our patients walked a distance of 349 m (285–419). In the second test, the patients walked 363 m (288–432), representing a 14-m increase in the second test (4% increase). This was less than the difference found in other studies⁶⁻¹², resulting in an excellent correlation coefficient (ICC=0.97-95%, CI 0.95–0.98; P<0.001). The difference found in our study was lower than that suggested by Puhan et al.24, whose study was conducted among patients with stable COPD, suggesting a minimal clinically significant difference of 26 m. The difference in our work was also lower than that suggested by Hernandes et al.6, whose study was also conducted among patients with stable COPD (difference of 27 m). We found a difference of <27 m between tests in 50 patients (62%), which was reported as a clinically important difference by these researchers.

Despite the high test–retest variability by the Bland-Altman analysis (Figure 1), our data showed lower limits of agreement than those previously described using the same method of analysis (-67–120 m in the study by Hernandes et al.⁶ and -77–70 m in our study). The high variability, which was also found in our study, was attributed to the learning effect, and supports the need to perform two 6MWTs. However, the extent to which the test–retest variability is representative of the learning effect remains unclear³⁻¹². To illustrate the magnitude of the variability between the two walking tests carried out on the same day, we also cite a study from Puhan et al.²⁴, which found a mean difference of 20±45 m pre-rehabilitation, which is higher than ours.

In addition to the learning effect already mentioned, we credit the variability found in our study to the heterogeneity of our sample, which comprised patients with several lung diseases. Additionally, there were also acute clinical situations among our patients that could predispose this population to clinical conditions, such as hyperthermia, active infection, cough, chest pain, dyspnea, muscle fatigue, tachycardia, myalgia, sweating, malnutrition, hypoxemia, and adynamia. The patient with chronic lung disease may also present some of these signs and symptoms. However, the patient with acute pulmonary disease presents with this clinical situation without the body, organic, and metabolic adaptations that develop in a patient with chronic disease over his or her lifetime, thereby making this clinical condition quite debilitating with respect to FC and exercise tolerance.

Hernandes et al.⁶ also investigated the determinants for a >42 m distance covered in the second 6MWT. They concluded that a poor first 6MWT (<350 m), Charlson index <2 points, or a BMI<30 kg/m² were determinants. Sciurba et al.⁷ found that participants with higher maximal inspiratory pressures showed more marked improvements in the second walk.

Glittre ADL-test (GT)

Patients performed the first GT in a median of 286 s (220-378) and the second test in a median of 244 s (197–323), with a time difference of 42 s (17% decrease) and a good correlation (ICC=0.91–95%, CI: 0.75–0.96; P<0.001). The time to completion of the second test was closest to the time found in the study by Skumlien et al. 13 conducted in patients with stable COPD (median 250 s). In this study, 52 patients underwent two GTs to test its reproducibility. The test-retest difference was 22 s (7% decrease), which was attributed to the learning effect. As observed in our study, there were no differences in dyspnea and SpO₂. It was not possible to compare our limits of agreement with this study because this type of analysis was not performed. It is interesting to note that, in another group of COPD patients that performed a pulmonary rehabilitation program, there was an improvement of 53 s in the test duration¹³, a post-treatment difference higher than ours (42 s).

Few studies beyond the original¹³ have used the GT as a field test. However, none of these studies provided test–retest measurements, therefore this test's reproducibility and variability was not established²⁶⁻²⁸.

We can raise the hypothesis of the learning effect to explain the great variability found in our study in addition to what has been previously described with the heterogeneity and the acute clinical condition of our sample. Just as it is common to find differences between the 6MWT that can be credited to the learning effect, the GT may also be influenced by this effect, as considered in another study¹³. This effect can be greater when compared with the effect shown in the 6MWT because this test has additional and more complex activities.

Oxyhemoglobin desaturation between the two test types

We also found that the changes in oxygen saturation measured by pulse oximeter were reproducible in both the 6MWT and GT. When comparing the lowest pulse oximetric saturation in the best 6MWT and best GT, we also found good equivalence; however, although the analysis using the Bland-Altman method showed a small mean of the differences, we observed large limits of agreement (-9–8%). This wide dispersion of results can be credited to the heterogeneity of the studied sample, whose physiopathological changes may limit the individual's activities in different ways. For example, some patients may experience great difficulty in exercising the upper limbs, bending down and carrying weights (COPD), whereas others do not have much difficulty performing these activities (CAP and other diseases).

Potential and implications of the study

Although the reproducibility of the 6MWT has already been widely studied in the literature and the GT has already been described in COPD, our study was the first to assess the reproducibility of these tests in patients hospitalized for acute lung diseases, which are routinely found in hospital wards. Our study also showed a statistical analysis that yielded results of clinical importance, and it constituted not only the data of averages and differences but also the limits of agreement between the assessments.

The clinical implications of the findings in this study relate to the fact that the differences found in the clinical field tests may lead to erroneous interpretations of the FC examination of these patients. Our findings demonstrate that the results were better in the second test of both examinations surveyed, meaning that interpretations based on a first test would be inaccurate for the patient assessment, prescription, or responsiveness of a training program. Therefore, we recommend that at least two 6MWTs, as recommended by American Thoracic Society (ATS)², and two GTs should be performed in patients hospitalized for acute or exacerbated chronic lung diseases.

Limitations of the study

This study has some limitations. First, the tests were not always performed by the same examiner; however, the testing was standardized^{2,13} and these examiners were trained. Moreover, to represent an acute pulmonary situation, the results are applicable to patients who were hospitalized at up to 48 h. Nevertheless, we know that a patient can seek hospital care at the first symptoms of the disease while others wait until they have a significant worsening of symptoms, which could lead to a variability in clinical conditions among the sample population. Finally, we had to adjust the distance of the 6MWT for 20 m due to space constraints in the hospital environment.

Conclusions

The 6MWT and GT were reproducible in patients hospitalized for acute lung diseases, and most patients improved their scores on the second test. The detected variability was large and the limits of agreement exceeded the minimal clinically significant difference. Desaturation was similar between 6MWT and GT; therefore, the GT can be used to detect exercise-induced desaturation, and we speculate that the GT could also be used to identify patients who would present desaturation during ADL.

Our study showed that, in the evaluation of the FC of this group of patients, at least two tests of each examination are needed to obtain reliable and valid assessments.

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