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- 1 Article category:
- 2 Original research article

- 4 Sub-discipline:
- 5 Sports Medicine (Injury screening)

6

- 7 Sources of outside support:
- 8 There was no specific funding for the research study, though the research was supported by
- 9 World Rugby, which employs some of the author group, as described in Competing Interests

# 10 Competing interests:

- 11 Three of the authors (RT, EF, MH) are full-time and part-time employed by World Rugby in
- 12 roles of research and medicine. JP and GF have served as independent advisors on a
- working group on concussion administered by World Rugby, for which expenses are
- 14 covered.

## 15 Ethics approval and consent to participate

- 16 The research plan for this study was approved by the World Rugby Institutional Ethics
- 17 committee (REF 19007). Players had provided written informed consent for all data
- 18 gathered as part of the World Rugby Concussion management programme to be used for
- 19 research in a de-identified manner

## 20 Availability of data and material

- 21 Original participant data belongs to the players and the clubs/unions that generate such
- 22 data. This may be provided upon request to third parties. World Rugby (the corresponding
- author) may facilitate the provision of that data, in terms of permissions and contacts,
- though there is not a single point of contact, since the data are generated globally from
- 25 multiple teams and Unions.

26

#### Author' contributions and declaration

- 27 MR conceived the study. MR, RT and EF designed the study. RT and MH performed the
- analyses. All authors made substantial contributions to the study design, data processing
- 29 and interpretation. RT drafted the article and all other authors revised it critically for
- 30 important intellectual content. RT is the guarantor. All authors had full access to all of the
- data in the study and can take responsibility for the integrity of the data and the accuracy of
- 32 the data analysis. The manuscript has not been published elsewhere and is not being
- 33 considered for publication elsewhere.

Sport Concussion Assessment Tool: baseline and clinical reference limits for concussion diagnosis and management in elite rugby union Word count: 2985 **Abstract word count**: 247 Number of Figures: 2 Number of Tables: 1 **Supplementary tables and figures**: 3 

## Objectives

Rugby Union has adapted the Sports Concussion Assessment Tool (SCAT) into an abridged off-field concussion screen and the complete SCAT is used during diagnostic screens performed after head impact events. No firm guidelines exist as to what should be considered "abnormal" and warrant further evaluation. This study evaluates SCAT performances in 13479 baseline SCAT assessments, and proposes clear reference limits for each sub-component of the SCAT5. Baseline reference limits are proposed to guide management of baseline testing by identifying abnormal sub-modes, enhancing the clinical validity of baseline screens, while clinical reference limits are identified to support

# Design

62 Cross sectional census sample

concussion diagnosis when no baseline is available.

# Methods

 13 479 baseline SCATs from 7 565 elite adult rugby players were evaluated. Baseline reference limits were identified for each sub-mode as the sub-mode result achieved by approximately 5% of the population, while clinical references limits corresponded to the sub-mode score achieved by as close as possible to 50% of the cohort.

### Results

Players reported symptoms 35% (95% CI 1.29 - 1.42) more frequently during SCAT5 than SCAT3 baseline assessments (mean 1.4  $\pm$  2.7 vs 1.0  $\pm$  2.4). Ceiling effects were identified for many cognitive sub-tests within the SCAT. Baseline and Clinical reference limits corresponding to the worst performing 5<sup>th</sup> percentile and 50<sup>th</sup> percentile were described.

#### Conclusion

Targeted baseline re-testing should be repeated when abnormal sub-modes are identified according to proposed baseline reference limits, while a more conservative clinical reference limit supports concussion diagnosis during screens in diagnostic settings.

## **Keywords:**

84	Concussion, SCAT, Rugby Onion, neurological screening, concussion management, injury
85	
86	Practical implications
87	
88	SCAT5 screening should remain part of the overall management of sports related
89	concussion
90	<ul> <li>The clinical utility of baseline screening can be enhanced if clinicians view such</li> </ul>
91	screening as a means to identify abnormalities as part of annual medical screening
92	<ul> <li>Clinicians who undertake regular baseline screening should use pre-identified</li> </ul>
93	reference limits to identify abnormal tests that warrant further investigation, either
94	repeating tests or investigating contributing factors described here
95	• In the clinical setting, the application of clinical reference limits that correspond to
96	sub-test scores achieved by half the cohort provide a more conservative method of
97	identifying abnormal tests and removing players with suspected concussions
98	
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100	
101	List of abbreviations
101	
102	SCAT – Sports Concussion Assessment Tool
103	HIA - Head Injury Assessment
104	
105	
105	

106 107	Introduction
108	The Sports Concussion Assessment Tool (SCAT) was first developed in 2004 using tests from
109	eight existing tools by the Concussion in Sport Group, as a standardised assessment tool for
110	acute concussion <sup>1</sup> .
111	Rugby Union has adapted and implemented the SCAT into an abridged off-field concussion
112	screening tool for the professional game (Head Injury Assessment). The complete SCAT5 is
113	used during diagnostic screens performed within three hours of the head impact event
114	(HIA2 screen) and after two nights' rest (HIA3 screen) <sup>2</sup> .
115	World Rugby requires mandatory completion of a baseline SCAT in professional players,
116	usually performed in the pre-season, with subsequent diagnostic results evaluated relative
117	to these uninjured baseline results.
118	A number of sporting organisations have abandoned compulsory baseline testing for use in
119	concussion diagnosis, instead using only normative data <sup>3</sup> . The time required to complete
120	baseline assessments, the possibility that their use may not improve the sensitivity or
121	specificity of concussion diagnosis, and the difficulty of confirming player effort during
122	baseline testing <sup>1,4,5</sup> , are practical and theoretical considerations for those involved in sports
123	concussion diagnosis and management.
124	In the absence of a baseline performance, screen results may be compared to normative
125	data derived from a sport-, sex- and age-matched population <sup>6</sup> . In research published to
126	date, including in rugby players <sup>6,7</sup> , SCAT performances have typically been categorised into
127	ranges as per the Wechsler classification 8, but without commitment to clinically relevant
128	cut-offs that indicate when a concussion diagnosis should be made.
129	While diverging views on the merits of baseline testing for SRC exist, baseline testing is a
130	clinically useful annual interaction between players and team doctors, offering ancillary
131	benefits. One must consider, therefore, whether baseline utility can be improved. This
132	might be achieved by enhancing the validity of baseline SCAT tests through content
133	modification, or by changing the baseline SCAT process to improve clinical utility. Unusually
134	poor sub-mode performances may indicate poor effort or an underlying issue at baseline,
135	perhaps triggering repeat testing. This approach is not unique, with computerised cognitive
136	tests also using normative data to trigger repeat testing and ensure engagement <sup>4</sup> .
137	The primary aim of this study was to analyse SCAT baseline performance in a large (n =
138	13479, from 7565 players) cohort of professional rugby players to identify clear baseline
139	reference limits that indicate abnormal sub-mode performance, and thus require re-testing
140	at haseline. A secondary aim was to apply the haseline cohort data to identify a distinct

clinical reference limit to support concussion diagnosis during the HIA1, HIA2 and HIA3 141 phases in the event that baseline data are absent for a player after a head impact during 142 play. 143 We propose a baseline reference limit that corresponds to the sub-test score or 144 145 performance achieved by the worst-performing 5% of the cohort, while the clinical reference limit is proposed to be the sub-mode score attained by as close as possible to 50% 146 147 of the cohort. Finally, we apply the baseline limits to propose an approach to abnormal sub-component 148 results that will optimize the baseline SCAT collection process (Appendix A). This is intended 149 to improve player effort and baseline validity by ensuring that results falling outside of 150 151 expected ranges are subject to scrutiny at baseline, rather than later. 152 **Methods** 153 154 A cross sectional study was performed using data from the World Rugby Head Injury Assessment (HIA) database, which contains baseline and diagnostic concussion screen 155 156 results from the professional game. In order to use the HIA process, a competition must adhere to mandatory competition player welfare standards [World Rugby Player Welfare 157 158 <u>Site</u>] that ensures a standardised approach to concussion detection and management as 159 well as data collection. The source population thus comprises the majority of eligible 160 professional male players in domestic and international competitions, as well as International Women's squads that underwent mandatory baseline SCAT 161 assessment between 2015 and 2019. 162 163 The SCAT assessments were administered prior to commencement of the relevant 164 competition season or tournament, according to methods described previously <sup>6</sup>. A total of 165 14803 baseline screens from 7630 players were present in the database. 166 For the present analysis, we excluded baseline SCATs performed post-exercise, and thus 167 analysed 13479 resting SCAT assessments (5757 SCAT3 and 7722 SCAT5) from 7565 168 players. We recognise that there may be learning effects in players with multiple tests. 169 These potential effects will be evaluated in subsequent research studies. We chose to 170 include all resting baseline tests to maximize the external validity of the study, since the 171 annual requirement to perform these SCATs means that most players will perform multiple 172 173 SCATs in their careers. 174 Descriptive data for each sub-component are presented as means, standard deviations, 175 medians and ranges. Distributions of continuous variables were visualised using density 176 177 histograms and summarised using mean (M), median (Md), Standard deviation (SD), 178 interquartile range (IQR) and range.

179 180	The research plan for this study was approved by the World Rugby Institutional Ethics committee (REF 19007). Players had provided written informed consent for all data
181	gathered as part of the World Rugby Concussion management programme to be used for
182	research in a de-identified manner
183	Patients or the public were not involved in the design, or conduct, or reporting, or
184	dissemination plans of the research.
185	Descriptive statistics for each sub-test were presented as Means, Standard Deviation,
186	Medians and Interquartile Ranges (IQR). A baseline reference limit was identified as that
187	score that was achieved by approximately the worst-performing 5% of players in the cohort.
188	That is, the 5 <sup>th</sup> /95 <sup>th</sup> percentile guided the identification of a sub-test result that would
189	achieve as close to 5% abnormal results as possible.
190	A clinical reference limit was identified using a similar method, but at the 50 <sup>th</sup> percentile,
191	rather than the 5 <sup>th</sup> /95 <sup>th</sup> percentile. Classifications were defined based on direction of
192	scoring for abnormality in each sub-test, with higher symptom scores and modified Balance
193	Error Scoring System (mBESS) errors referred to as abnormally high, and lower cognitive test
194	performances referred to as abnormally low.
195	A modification in SCAT5 compared with SCAT3 involved the method of assessing symptoms.
196	In SCAT5, a player is handed the symptom sheet to read aloud, and instructed to 'rate
197	his/her symptoms based on how he/she TYPICALLY feels'. These have been termed 'trait'
198	symptoms <sup>9</sup> . During SCAT3, and when the SCAT is applied post-injury, the instruction to
199	players is to identify 'how they feel now', so-called 'state' symptoms <sup>10</sup> . We explored
200	whether this change affected symptom results by calculating proportion ratios, with 95%
201	confidence limits calculated according to the delta method. The proportion ratio was
202	calculated as the proportion of players reporting a symptom during SCAT5, divided by the
203	proportion of players reporting that symptom during SCAT3 assessments. Effect sizes for
204	proportion ratios were judged on the following threshold values: trivial – PR <1.11; small
205	$\geq$ 1.11 PR <1.43; moderate $\geq$ 1.43 PR <2.00; large $\geq$ 2.00 PR <3.30; very large $\geq$ 3.30 PR <10.00;
206	and extremely large PR $\geq$ 10.00 $^{11}$ . Z-scores were produced for each comparison to test
207	against the null hypothesis that no difference would exist in symptom reporting frequency
208	between the two SCAT modalities. Statistical significance was accepted at P<0.05.
209	All Statistical analyses were conducted using SPSS (V.23 for Windows, IBM Corp, Armonk,
210	NY, USA). Statistical significance was accepted at $\alpha$ <0.05.
211	

<u>Results</u>

- 214 The sub-component scales, cases, means, standard deviation, medians, interquartile ranges
- and 5<sup>th</sup>/95<sup>th</sup> percentiles for each SCAT components are shown in the supplementary
- 216 materials (Table 1 supplementary material).

- 218 65.2% of players were asymptomatic during baseline testing. Five or more symptoms were
- reported by 9.1% of players, indicative of an "unusually high" number, while
- 220 the 95<sup>th</sup> percentile corresponded to seven symptoms.

221

- The percentage of baseline assessments in which each symptom was reported is shown in
- Table 1. To support clinical management and insight, symptoms are grouped into categories
- of Physical, Cognitive, Vestibulo-ocular and Psychological <sup>3,12</sup>.

225

226 Table 1 here \*

227

- 228 Fatigue, neck pain, trouble sleeping and nervous/anxious were the most commonly
- reported symptoms, accounting for 52.0% of all symptoms reported.

230

- 231 Symptom endorsement was higher during SCAT5 (1.4  $\pm$  2.7) than SCAT3 (1.0  $\pm$  2.4).
- 232 Players report at least one symptom 35% more frequently during the SCAT5 assessment
- than the SCAT3 assessment (proportion ratio 1.35, 95% CI 1.29 1.42, P<0.001, Figure 1). All
- 234 individual symptoms were reported more frequently in SCAT5 than SCAT3 (proportion ratios
- = 1.12 1.55), although effects were small to moderate in size.

236

237 Figure 1 here \*

238

- 239 85.2% of players scored perfectly (five out of five) for Orientation guestions, while 99.9% of
- 240 players answered at least three questions correctly (equating to 9,992 per
- 241 10,000 assessments).

242

- 243 Date was most frequently answered incorrectly (12.7%) followed by Month, Time and
- Day (all 0.8%), with Year least frequently incorrect (0.1%).

245

- 246 Given the change in Immediate Memory assessment from the SCAT3 (a five-word list) to the
- SCAT5 (a ten-word list was added as an option), Immediate Memory performance was
- evaluated separately for SCAT3 and SCAT5 assessments (Figure 1, Supplementary material).

- 250 When using the five-word list (n = 8437), 65.9% of players scored 15 out of 15 (Median 15,
- IQR 14 15), with only 2.9% of players scoring fewer than twelve (Figure 1, Supplementary
- 252 material). The ten-word list (n = 5042) results were more normally distributed (Mean 21.5,
- 253 Median 21, IQR 19 to 24, Table 1 supplementary material). The 5th percentile for the 10-
- word list corresponded to a score of 15 out of 30.

255	
256	The mean concentration score was $4.1 \pm 1.0$ (out of a maximum of five), with $44.2\%$ of
257	players scoring perfectly. The 5th percentile corresponded to a score of two out of 5, with
258	91.7% of players achieving a score of three out of five. Months in reverse was correctly
259	answered in 91.7% of baseline assessments.
260	
261	Delayed Recall was assessed using either the five- or ten-word list. A similar ceiling effect
262	was observed using the five-word list, with 97.5% of players scoring two or more out of
263	five. Using the ten-word list, the 5th percentile corresponded to a score of four out of ten,
264	with 96.6% of players recording at least four correct answers.
265	
266	99.9% of players completed the tandem gait test in under 17 seconds. The 95th percentile
267	corresponded to a time of 13.3 seconds.
268	
269	Errors during double leg balance were rare, with 97.4% of players performing the
270	assessment without any errors. An average of 1.9 errors were made during the single leg
271	balance assessment, with 29.9% of players performing without error. The 95th percentile
272	corresponded to six errors.
273	
274	Tandem stance errors averaged 0.8, with a $95^{\text{th}}$ percentile at three errors. Collectively, total
275	errors ranged between zero and 22, with a mean of 2.8 and a 95 <sup>th</sup> percentile corresponding
276	to eight errors.
277	
278	A schematic summary of the identified baseline and clinical reference limits for each sub-
279	mode in the SCAT5 is shown in Figure 2. The baseline reference limit (top panel) is derived
280	from the 5 <sup>th</sup> and 95 <sup>th</sup> percentiles, and is that score at which as close as possible to 5% of
281	players achieve an abnormally poor result. The clinical reference limit corresponds a sub-
282	mode score as close as possible to the 50 <sup>th</sup> percentile.
283	
284	Figure 2 here *
285	
286	The baseline and clinical reference limits are further summarized into clinical guidelines in
287	Table 2 of the supplementary material, showing the sub-component result that would
288	warrant further investigation (during baseline) and which would support a diagnosis of
289	concussion (during diagnostic settings such as World Rugby's HIA1 off-field screen and the
290	HIA2 and HIA3 assessments).
291	
292	<u>Discussion</u>
293	

This study used a large dataset of baseline SCAT3 and SCAT5 assessments in professional

rugby players to identify reference limits for each sub-component in the SCAT assessment.

294

We propose that the baseline reference limits identified here will enhance the clinical utility of the SCAT baseline testing. Any scores outside of the baseline reference limits indicate that re-testing be undertaken and, if abnormalities persist, further clinical evaluation. In addition, during rugby matches when no player baseline is available, the identified clinical reference limits may be used to support concussion diagnosis and to guide return-to-play decisions.

Given that the baseline reference limit is identified at the sub-mode score as close as possible to the 5<sup>th</sup>/95<sup>th</sup> percentile, while the clinical reference limits correspond to scores near the 50<sup>th</sup>percentile, every sub-mode score requirement during clinical settings is more challenging than during baseline (Figure 2). For example, six or more single leg errors constitutes an abnormal baseline test, whereas an abnormal clinical screen at HIA1, HIA2 or HIA3 occurs at two or more errors (Figure 2 and Table 2 Supplementary material). We recognize that this will produce more abnormal clinical tests than previously, since the thresholds have been reduced compared to historical thresholds. However, since baseline testing is now mandatory, the real impact of this change will be small because normative data should rarely be applied. We also deem it to be more conservative, and thus preferable, because fewer false negatives will occur. Thus, despite the risk of increased cases of false positives, we deem the proposed clinical reference limits to be preferred in cases where no baseline screen is present.

The baseline reference limits that guide re-testing of abnormal baseline screens are based on the premise that these scores are achieved by the worst-performing 5% of players (Figure 2). We then propose specific guidance to evaluate these results (Appendix A), with advice on repeating any abnormal baseline sub-components, followed by clinical steps that may identify contributing factors and possible confounders for persistent abnormal results.

The process we outline here will also address concerns such as player effort, effective implementation and data reliability, since repeating tests that are identified using the baseline reference limits will ensure greater concentration and performance. This approach also supports concussion education, allows the physician to obtain a better understanding of individual player's medical profiles and ensures more accurate post-injury diagnosis. Player welfare will also be improved with the recommendation to investigate reported baseline 'trait' symptoms. Each sub-component outcome is described briefly.

We found that symptom endorsement is greater using SCAT5 than SCAT3 (Figure 1), possibly as a result of different instructions for how symptoms should be collected.

The distinction between a trait and a state symptom is key to the collection and diagnostic utility of valid and reliable baseline SCAT5 symptoms, which should be recorded only

if typically present. After a head impact, only symptoms that are new or altered should indicate a concussive event.

For this reason, symptom reference limits have not been proposed (Figure 2). In return-to-play and diagnostic settings, clinicians should interpret the presence of new symptoms as indicative of a concussion, while symptoms claimed by the player to be typically present (trait symptoms) should be questioned to identify if these symptoms have changed. A 'trait' symptom that has worsened should be interpreted as indicative of a concussion.

In the general population, a variety of medical conditions may cause concussion-like symptoms. For example, headaches may be cervicogenic in origin, dizziness may be related to viral infection or cardiac disease, and sleep disorders may relate to underlying depression or anxiety <sup>12</sup>. The most commonly endorsed symptom, fatigue (19.6% of SCAT5s, Table 1), is often load-related, but the clinician should also consider illness (e.g. anaemia), and psychologically-related fatigue. These may require investigation using tests such as Profile of Mood States (POMS) <sup>13</sup>, medical work-up and endocrinological review considered if mood is unaffected.

Neck pain, reported in 16.3% of baseline SCAT5 tests, warrants further investigation due to a possible role in prolonged concussion recovery and persistent post-concussion symptoms <sup>14,15</sup>. Cervical muscles are thought to play a significant role in chronic headaches <sup>16,17</sup>. Mechanical neck pain is common but other causes such as cervical disc pathology, shoulder pathology and medical conditions require exclusion.

Trouble falling asleep may be considered as a sign of heavy training load and functional over-reaching <sup>18</sup>, possible increased use of ergogenic agents such as caffeine and taurine <sup>19</sup> or a potential indicator for undiagnosed mental health issues. Sleep hygiene assessment should be considered because quality and quantity of sleep are recognised components of an athlete's recovery and preparation <sup>20</sup>.

Finally, anxiety was reported in 9.7% of SCAT5 tests at rest and may be a potential indicator of a mental health condition. This symptom requires further investigation which may include specific neuro-psychological screen or immediate referral for psychological evaluation.

We found that the use of the ten-word lists at least partly overcomes ceiling effects <sup>1,21</sup> during Immediate Memory and Delayed Recall sub-tests (Figure 2, supplementary material). This may improve the clinical performance of these sub-components for concussion diagnosis.

Clinically abnormal cognitive tests that persist at re-test baseline SCAT indicate further assessments, either via computerised psychometric assessment or formal neuropsychological assessment. In players with a history of previous concussions, post-concussion syndrome should be considered. In all instances medical illnesses need to be considered.

Numbers of balance errors are higher than previously identified, with a 95<sup>th</sup> percentile corresponding to six errors for single leg stance, and 4.6% of players making four errors during tandem stance.

Abnormal balance results that persist on retesting may indicate chronic ankle ligamentous instability, a common complaint in field sport populations <sup>22</sup>. Many such athletes regularly strap their ankles, in this case, baseline testing should be repeated under similar conditions. Further lower limb orthopaedic causes should be investigated and if indicated, vestibular-ocular assessment, and a thorough neurological examination is also recommended.

Among the strengths of this study are its size, among the largest documented number of baseline assessments in athletes, allowing for robust conclusions and normative ranges and reference limits to be created. The method of collection, using the CSx platform, allows immediate data collection with minimal missing data. Study conduct and reporting is consistent with STROBE guidelines for observational studies <sup>23</sup>

There are some limitations to the present study. The inclusion of multiple tests per player may introduce learning effects, which we acknowledge. However, we chose to include these tests because during the diagnostic screens after head impacts, those same learning effects are present, and thus any normative limits derived from baseline testing should be generated using all tests for external validity. The potential for learning effects will be explored in future research.

We also cannot account for individual player circumstances and characteristics, including previous concussions and other injuries, and acknowledge that these may affect baseline performances and thus normative ranges. Future research will also explore how head impact events and diagnosed concussions affect subsequent baseline performance. Finally, intra- and inter-observer reliability was not assessed.

Our recommendation is that individual baseline SCAT be retained as part of the overall management of sports related concussion. We have identified what we propose as reference limits for abnormal sub-test results during baseline and during clinical settings when baseline data are absent. We recommend that the baseline reference limits guide the re-testing of abnormal sub-modes, and possible investigation of persistent abnormal performances. This approach should ensure collection of a more reliable and valid

- individual baseline SCAT test and allows the clinician to use baseline testing as a screening 417 tool for both concussive and non-concussive related injury. 418 419 420 Recognising that this new approach will add to the workload of the team medical staff our next analysis will investigate the necessity for annual baseline SCAT by reviewing cases 421 422 where multiple baseline SCATs are available over time. This analysis will also review the 423 impact of previous concussive events on baseline SCAT modes and identify if exercise and 424 rest influence each SCAT mode. This subsequent analysis will support recommendations regarding the necessity for annual part or full baseline SCAT collection. 425 426 427 Acknowledgements We would like to acknowledge and sincerely thank the team doctors and medical 428 practitioners for their help in facilitating collection of Sports Concussion Assessment Tool 429 (SCAT) data. 430 431 References 432 1. Echemendia RJ, Meeuwisse W, McCrory P, et al. The Sport Concussion Assessment Tool 433 5th Edition (SCAT5): Background and rationale. Br J Sports Med 2017;51:848–850. 434 435 2. Raftery M, Kemp S, Patricios J, et al. It is time to give concussion an operational definition: a 3-step process to diagnose (or rule out) concussion within 48 h of injury: World Rugby 436 437 guideline. Br J Sports Med 2016;50:642–643. 438 3. Harmon KG, Drezner JA, Gammons M, et al. American Medical Society for Sports Medicine position statement: concussion in sport. Br J Sports Med 2013;47:15–26. 439 4. Walton SR, Broshek DK, Freeman JR, et al. Valid but Invalid: Suboptimal ImPACT Baseline 440 Performance in University Athletes. Med Sci Sport Exerc 2018;50:1377–1384. 441 5. Chin EY, Nelson LD, Barr WB, et al. Reliability and Validity of the Sport Concussion 442
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Figure titles and legends Figure 1: Proportion ratios ( $x/\div$  95% confidence intervals) for symptoms reported in SCAT5 relative to symptoms reported in SCAT3 symptoms. Effect sizes and P-values also shown. Figure 2: Schematic representation of the identified baseline (top panel) and clinical (bottom panel) reference limits for SCAT5 sub-modes. Baseline reference limits are to be applied at baseline testing, indicating abnormal sub-modes that require re-testing. Clinical reference limits are applied during screens when baseline data are absent in clinical settings, and correspond to a sub-mode score nearest the 50<sup>th</sup> percentile