

Validation of app and phone versions of the Control of Allergic Rhinitis and Asthma Test (CARAT)

Jácome C^{1,2}, Pereira AM^{2,3}, Almeida R^{1,2}, Amaral R^{1,4}, Alves Correia M³, Mendes S¹, Vieira-Marques P¹, Ferreira JA⁵, Lopes I⁵, Gomes J⁵, Vidal C⁶, López Freire S⁶, Méndez Brea P⁶, Arrobas A⁷, Valério M⁷, Chaves Loureiro C⁷, Maia Santos L⁷, Couto M³, Araujo L³, Todor Bom A⁸, Pedro Azevedo J⁹, Cardoso J¹⁰, Emiliano M¹⁰, Gerardo R¹⁰, Lozoya C¹¹, Leiria Pinto P¹², Castro Neves A¹², Pinto N¹², Palhinha A¹², Teixeira F¹³, Magalhães M¹³, Alves C¹⁴, Coelho D¹⁴, Santos N¹⁵, Menezes F¹⁶, Gomes R¹⁶, Cidrais Rodrigues JC¹⁷, Oliveira G¹⁷, Carvalho J¹⁷, Rodrigues Alves R¹⁸, Moreira AS¹⁸, Costa A¹⁹, Abreu C²⁰, Silva R²⁰, Morête A²¹, Falcão H²², Marques ML²², Câmara R²³, Cáliz MJ²⁴, Bordalo D²⁵, Silva D²⁶, Vasconcelos MJ²⁶, Fernandes RM^{27,28}, Ferreira R^{27,29}, Freitas P³⁰, Lopes F³¹, Almeida Fonseca J^{1,2,3,31}, INSPIRERS group

¹Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal

²Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS), Faculty of Medicine, University of Porto, Porto, Portugal

³Allergy Unit, Instituto and Hospital CUF, Porto, Portugal

⁴Dept. of Cardiovascular and Respiratory Sciences, Porto Health School, Polytechnic Institute of Porto, Porto, Portugal

⁵Serviço de Imunoalergologia, Vila Nova de Gaia, Portugal

⁶Servicio de Alergia, Complejo Hospitalario Universitario de Santiago, Santiago De Compostela, Spain

⁷Serviço de Pneumologia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

⁸Serviço de Imunoalergologia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

⁹Imunoalergologia, Centro Hospitalar de Leiria, Leiria, Portugal

¹⁰Serviço de Pneumologia, Hospital Santa Marta, Centro Hospitalar Universitário de Lisboa Central, Lisboa, Portugal

¹¹Serviço de Imunoalergologia, Hospital Amato Lusitano, Unidade Local de Saúde de Castelo Branco, Castelo Branco, Portugal

¹²Serviço de Imunoalergologia, Hospital de Dona Estefânia, Centro Hospitalar Universitário de Lisboa Central, Lisboa, Portugal

¹³Serviço de Pediatria, Centro Materno Infantil do Norte, Centro Hospitalar Universitário do Porto, Porto, Portugal

¹⁴Serviço de Pneumologia, Hospital Nossa Senhora do Rosário, Centro Hospitalar Barreiro Montijo, Barreiro, Portugal

¹⁵Serviço de Imunoalergologia, Centro Hospitalar Universitário do Algarve, Portimão, Portugal

¹⁶Serviço de Pneumologia, Hospital Garcia de Orta, Almada, Portugal

¹⁷Serviço de Pediatria, Hospital Pedro Hispano, Unidade Local de Saúde de Matosinhos, Matosinhos, Portugal

¹⁸Unidade de Imunoalergologia, Hospital do Divino Espírito Santo, Ponta Delgada, Portugal

¹⁹Serviço de Pediatria, Hospital da Senhora da Oliveira, Guimarães, Portugal

²⁰Serviço de Imunoalergologia, Hospital São Pedro de Vila Real, Centro Hospitalar De Trás-Os-Montes E Alto Douro, Vila Real, Portugal

²¹Serviço de Imunoalergologia, Hospital Infante D. Pedro, Centro Hospitalar Baixo Vouga, Aveiro, Portugal

²²Serviço de Imunoalergologia, Centro Hospitalar Universitário do Porto, Porto, Portugal

²³Serviço de Imunoalergologia, Serviço de Saúde da Região Autónoma da Madeira, Funchal, Portugal

²⁴Serviço de Pediatria, Hospital de São Teotónio, Centro Hospitalar Tondela–Viseu, Viseu, Portugal

²⁵Serviço de Pediatria, Unidade Hospitalar de Famalicão, Centro Hospitalar do Médio Ave, Vila Nova de Famalicão, Portugal

²⁶Serviço de Imunoalergologia, Centro Hospitalar Universitário de São João, E.P.E., Porto, Portugal

²⁷Departamento de Pediatria, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal

²⁸Farmacologia Clínica e Terapêutica, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal

²⁹Clínica Universitária de Pediatria, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal

³⁰Bloco operatório, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

³¹MEDIDA – Medicina, Educação, Investigação, Desenvolvimento e Avaliação, Porto, Portugal

Corresponding author

Cristina Jácome

Center for Health Technology and Services Research, Faculty of Medicine, University of Porto, Rua Dr.

Plácido da Costa, Porto 4200-450, Portugal

E-mail: cjacome@med.up.pt

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi:

10.18176/jiaci.0640

Keywords: Asthma. Control. Mobile health. Patient-reported outcome measure.

Palabras clave: Asma. Control. Saludmóvil.

Assessment of asthma control at every opportunity is recommended[1]. Control of Allergic Rhinitis and Asthma Test (CARAT) is a patient-reported outcome measure commonly used to assess asthma control in clinical practice[2-4]. It includes ten questions answered in a 4-point Likert scale that address upper and lower airway symptoms, sleep interference, limitation of activities, and the need to increase medication over a 4-week period[5]. CARAT is frequently administered on paper during medical visits, but digital versions through website[6] and mobile apps are available[7, 8].

With the COVID-19 pandemic, the European Respiratory Society recommends the use of phone screening to monitor patients with asthma[9] as face-to-face contacts are to be minimized. So, clinicians need to rely on CARAT versions (digital or phone) that can be used outside medical facilities to gain insight into patients' health status and allow better strategic planning during the period between visits. So far, four apps integrate CARAT (implementing questions on ten consecutive screens with bullet-point responses)[7, 8] and their usefulness is being increasingly reported[10, 11]. An app version of CARAT with 1-week recall has been previously validated[7] and other was used in an interventional study with adolescents [12]. Yet, validation of the app version considering the 4-week recall period is still needed. A previous study applying CARAT by phone showed its feasibility, but not its validity[13].

CARAT collected through a mobile app or phone interview is a convenient alternative to the paper version. Yet, before widespread implementation, we need to ensure these versions are equally reliable and valid. We compared the psychometric properties of three CARAT versions (paper, phone and app) in patients with asthma.

We analyzed data collected between 03/2018 and 01/2020 from prospective observational studies conducted by the authors about the feasibility of Inspirer Mundi app[14]. Patients were recruited during a medical visit at 23 secondary care centres from Portugal and Spain. Patients were included if they had persistent asthma, were ≥ 13 years, were able to use apps, had access to a mobile device with Internet and were prescribed an inhaled controller medication. During medical visits, physicians reported patients' asthma treatment, asthma control according to the Global Initiative for Asthma[1], number of exacerbations and of unscheduled medical visits. Patients filled in a sociodemographic and clinical questionnaire, including the CARAT paper version (pCARAT). Patients were invited to complete the CARAT in the following days using the Inspirer Mundi app[8](mCARAT). After approximately 1-week (3-10 days), CARAT was collected through a telephone interview (tCARAT) (Supplementary Figure S1). A total of 144 patients participated in the studies, but only those completing the three versions within 10 days were analyzed. CARAT total (CARAT-T, 0-30), upper airways (CARAT-UA, 0-12) and lower airways (CARAT-LA, 0-18) scores were calculated. Scores >24 on CARAT-T, >8 on CARAT-UA, and ≥ 16 on CARAT-LA defined good disease control. The internal consistency (Cronbach's α), convergent validity (Spearman correlation- r_s), reliability (intraclass correlation coefficient-ICC, Bland-Altman analysis), and agreement (% agreement, Cohen's kappa-k) were determined.

Sixty-seven patients with a median [percentile 25-percentile 75] of 20 [17-33] years were analyzed (Supplementary Table S1). mCARAT was completed in the same day of pCARAT by 85% of patients (median 0 [0-2] days), while tCARAT was completed after a median of 6 [5-7] days. The median pCARAT total score was 20 [16-23], the mCARAT 20 [18-24], and the tCARAT 22 [18-26]. The median CARAT-UA and CARAT-LA scores were 5 [4-8] and 15 [12-17] in pCARAT, 6 [4-8] and 15 [12-17] in mCARAT and 7 [4-8] and 16 [13-17] in tCARAT, respectively.

Internal consistency of the CARAT scores was good (pCARAT $\alpha=0.71-0.79$, mCARAT $\alpha=0.72-0.81$ and tCARAT $\alpha=0.71-0.80$). The scores obtained with pCARAT were significantly correlated with the mCARAT scores ($r_s=0.64-0.82$) and tCARAT scores ($r_s=0.55-0.64$). The correlation between

mCARAT and tCARAT scores was also significant ($r_s=0.59-0.69$)(Supplementary Table S2). Differences in CARAT-T between methods were significantly correlated with time interval between the assessments ($r_s=0.22$, Supplementary Figure S2).

Test-retest relative reliability of CARAT scores was acceptable for all versions, although better for pCARAT-mCARAT ($ICC_{2,1}=0.65-0.85$) and mCARAT-tCARAT ($ICC_{2,1}=0.71-0.76$) in comparison with pCARAT-tCARAT ($ICC_{2,1}=0.59-0.71$). There was reasonable agreement between versions, with bias close to zero and reasonable limits of agreement. A slightly better agreement is seen between pCARAT-mCARAT in comparison with tCARAT-mCARAT and pCARAT-tCARAT (Figure 1, Supplementary Figure S3).

Disease was not controlled in 81% of patients (based on pCARAT), in 78% (mCARAT) and in 67% (tCARAT). The agreement on CARAT-T control classification was higher between tCARAT and mCARAT (81%; $k=0.52$ [95%CI 0.30-0.74]), in comparison with pCARAT and mCARAT (76%; $k=0.28$ [95%CI 0.01-0.55]) and with pCARAT and tCARAT (72%, $k=0.28$ [95%CI 0.04-0.52]). Not controlled UA and LA symptoms were present in 81% and 58% of patients based on pCARAT, 76% and 36% based on mCARAT, and 76% and 55% based on tCARAT. The agreement for CARAT-UA and CARAT-LA control classification (75%-85%; $k=0.51-0.64$) followed the same pattern as CARAT-T.

Comparison of paper and app versions obtained better results, followed by app and phone versions and lastly by paper and phone versions. This finding is likely related to the time interval between the assessments rather than with the collection method. Most patients answered the app version on the same day they filled in the paper version, while the phone version was collected one week later. During this period and considering the possible effect of the medical visit (and related interventions), patients may have changes in symptoms or in other CARAT-assessed domains; or may perceive them differently. A previous study showed that recent weeks play a more prominent role in the assessment of the patient's control than the initial weeks considering the 4-week recall period[7]. In an additional analysis

(Supplementary Table S2) with patients answering the 3 versions within 7 days, slightly better results were found, compared to those answering with 10-day difference. Nevertheless, a better agreement between paper and app versions was noticeable for both time-lags. It is possible that the slightly larger differences observed between tCARAT and the other versions may also relate with the distinct nature of phone interview, involving an interviewer, in comparison with patients' self-completion in paper and app versions. Future studies should collect the three methods during a shorter period (<48h) and in a random order to clarify this.

The internal consistency of the CARAT scores, regardless of the collection method, were above the 0.7 threshold[15]. Also, the correlation coefficients between CARAT scores obtained were found to be moderate[7]. Most ICCs were above 0.7[15], so we can rely in the test-retest reliability of CARAT using the three methods. The only ICCs that were below this cut-off were CARAT-T and CARAT-UA between paper and phone versions and CARAT-UA between paper and app versions. This may be linked to the high variability of UA symptoms in our sample.

This study was based on a small sample, mostly of adolescents/young adults followed at secondary care. Future studies should include an adequate powered sample of patients with an extended age range recruited also from primary care. This study showed that both mHealth and phone versions of CARAT are acceptable tools to assess disease control in adolescents and young adults with persistent asthma.

Conflicts of interest

The authors have declared that they have no competing interests in relation to this study.

Funding

This work was funded by ERDF (European Regional Development Fund) through the operations: POCI-01-0145-FEDER-029130 ("mINSPIRERS—mHealth to measure and improve adherence to medication in chronic obstructive respiratory diseases - generalization and evaluation

of gamification, peer support and advanced image processing technologies”) cofounded by the COMPETE2020 (Programa Operacional Competitividade e Internacionalização), Portugal 2020 and by Portuguese Funds through FCT (Fundação para a Ciência e a Tecnologia).

Acknowledgements

We thank the participants and centers involved in the project Inspirers.

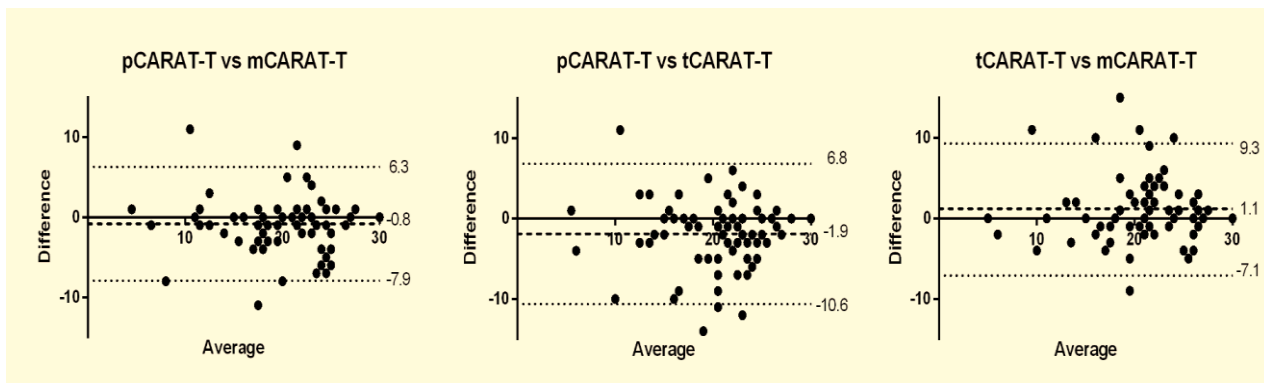
References

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for prevention, diagnosis and management of COPD. URL: <https://goldcopd.org/gold-reports/>. 2020.
2. Calderón MA, Casale TB, Demoly P. Validation of Patient-Reported Outcomes for Clinical Trials in Allergic Rhinitis: A Systematic Review. *The Journal of Allergy and Clinical Immunology: In Practice*. 2019;7:1450-61.e6.
3. Azevedo P, Correia de Sousa J, Bousquet J, Bugalho-Almeida A, Del Giacco SR, Demoly P, et al. Control of Allergic Rhinitis and Asthma Test (CARAT): dissemination and applications in primary care. *Prim Care Respir J*. 2013;22:112-6.
4. van der Leeuw S, van der Molen T, Dekhuijzen PN, Fonseca JA, van Gemert FA, Gerth van Wijk R, et al. The minimal clinically important difference of the Control of Allergic Rhinitis and Asthma Test (CARAT): cross-cultural validation and relation with pollen counts. *NPJ Prim Care Respir Med*. 2015;25:14107.
5. Fonseca JA, Nogueira-Silva L, Morais-Almeida M, Azevedo L, Sa-Sousa A, Branco-Ferreira M, et al. Validation of a questionnaire (CARAT10) to assess rhinitis and asthma in patients with asthma. *Allergy*. 2010;65:1042-8.
6. Control of Allergic Rhinitis and Asthma Test [Available from: <http://www.caratnetwork.org/>].
7. Flokstra-de Blok BMJ, Baretta HJ, Fonseca JA, van Heijst E, Kollen BJ, de Kroon J, et al. Control of Allergic Rhinitis and Asthma Test with 1-week recall: Validation of paper and electronic version. *Allergy*. 2018;73:2381-5.
8. Jácome C, Almeida R, Teixeira J, Vieira-Marques P, Vilaça R, Fernandes J, et al., editors. Inspirers: An app to measure and improve adherence to inhaled treatment. *International Conference e-Health*; 2017; Lisbon.
9. European Respiratory Society. COVID-19 and asthma. URL: <https://www.ersnet.org/the-society/news/covid-19-and-asthma> (accessed on 27.05.2020). 2020.
10. Pereira AM, Jacome C, Almeida R, Fonseca JA. How the Smartphone Is Changing Allergy Diagnostics. *Curr Allergy Asthma Rep*. 2018;18:69.
11. Mazzoleni S, Turchetti G, Ambrosino N. The COVID-19 outbreak: From "black swan" to global challenges and opportunities. *Pulmonology*. 2020;26:117-8.
12. Kosse RC, Bouvy ML, Belitser SV, de Vries TW, van der Wal PS, Koster ES. Effective Engagement of Adolescent Asthma Patients With Mobile Health—Supporting Medication Adherence. *JMIR Mhealth Uhealth*. 2019;7:e12411.
13. Sá-Sousa A, Amaral R, Morais-Almeida M, Araújo L, Azevedo LF, Bugalho-Almeida A, et al. Asthma control in the Portuguese National Asthma Survey. *Pulmonology*. 2015;21:209-13.

14. Jácome C, Guedes R, Almeida R, Teixeira JF, Pinho B, Vieira-Marques P, et al. mINSPIRERS - Estudo da exequibilidade de uma aplicação móvel para medição e melhoria da adesão à medicação inalada de controlo em adolescentes e adultos com asma persistente. Protocolo de um estudo observacional multicêntrico. Revista Portuguesa de Imunoalergologia. 2018;26:47-61.
15. Mookkink LB, Prinsen CA, Patrick DL, Alonso J, Bouter LM, Vet HCd, et al. COSMIN methodology for systematic reviews of Patient-Reported Outcome Measures (PROMs): user manual. URL: https://www.cosmin.nl/wp-content/uploads/COSMIN-syst-review-for-PROMs-manual_version-1_feb-2018.pdf. 2018.

Accepted Article

Figure 1. Bland-Altman plots of Control of Allergic Rhinitis and Asthma Test (CARAT) total scores obtained through paper (pCARAT), app (mCARAT) and telephone (tCARAT)



* The dashed lines represent the bias and the dot-dashed lines the 95% limits of agreement