Letter to the editor

Title: Pre-training inter-rater reliability of clinical instruments in an international psychosis research project.

Running title: Pre-training inter-rater reliability.

Total word count: 999.

Key words: Pre-training inter-rater reliability, psychosis instruments, assessor selection.

Authors: Steven Berendsen¹*, Pim Kapitein¹, Frederike Schirmbeck¹, Mirjam J. van

Tricht¹, Philip McGuire², Craig Morgan³, Charlotte Gayer-Anderson³, Matthew J Kempton²,

Lucia Valmaggia⁴, Diego Quattrone², Marta di Forti², Mark van der Gaag⁵, James B.

Kirkbride⁶, Hannah E Jongsma^{6,7}, Peter B Jones⁷, Maria Parellada⁸, Celso Arango⁸, Manuel

Arrojo⁹, Miguel Bernardo¹⁰, Julio Sanjuán¹¹, José Luis Santos¹⁴, Andrei Szöke¹⁵, Andrea

Tortelli¹⁶, Pierre-Michel Llorca¹⁷, Ilaria Tarricone¹⁸, Giada Tripoli¹⁹, Laura Ferraro¹⁹,

Caterina La Cascia¹⁹, Antonio Lasalvia²⁰, Sarah Tosato²⁰, Paulo Rossi Menezes²¹, Cristina

Marta Del-Ben²², Barnaby Nelson^{23,24}, Anita Riecher-Rössler²⁵, Rodrigo Bressan²⁶, Neus

Barrantes-Vidal^{27,28}, Marie-Odile Krebs²⁹, Merete Nordentoft⁴¹, Stephan Ruhrmann³⁰,

Gabriele Sachs³¹, Bart P. F. Rutten³², Jim van Os^{2,32,33}, EU-GEI High Risk Study, Eva

Velthorst^{1,34,35}, Lieuwe de Haan^{1,36}.

EU-GEI High Risk Study Group not mentioned in main author list: Maria Calem², Stefania Tognin², Gemma Modinos², Sara Pisani², Tamar C. Kraan¹, Daniella S. van Dam¹, Nadine Burger⁴⁴, Patrick McGorry²³, G Paul Amminger²³, Athena Politis²³, Joanne Goodall²³, Stefan Borgwardt³³, Erich Studerus³³, Ary Gadelha²⁶, Elisa Brietzke³⁶, Graccielle Asevedo³⁶, Elson Asevedo³⁶, Andre Zugman³⁶, Tecelli Domínguez-Martínez³⁶, Manel Monsonet²⁶, Lidia Hinojosa ²⁶, Paula Cristóbal-Narváez²⁶, Anna Racioppi²⁶, Thomas R. Kwapil⁴⁰, Mathilde Kazes²⁶, Claire Daban²⁶, Julie Bourgin²⁶, Olivier Gay²⁶, Célia Mam-Lam-Fook²⁶, Dorte Nordholm⁴¹, Lasse Randers⁴¹, Kristine Krakauer⁴¹, Louise Birkedal Glenthøj⁴¹, Birte Glenthøj⁴², Dominika Gebhard³⁰, Julia Arnhold⁴³, Joachim Klosterkötter³⁰, Iris Lasser³¹, Bernadette Winklbaur³¹, Philippe A Delespaul³².

*Corresponding author: Steven Berendsen, MD, UMC Amsterdam, Location AMC. Meibergdreef 9, 1105 AZ Amsterdam. Telephone: +3120 566 9111, email: s.berendsen@amsterdamumc.nl.

¹ Department of Psychiatry, Amsterdam UMC, Amsterdam, the Netherlands.

² Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, England.

³ Department of Health Service and Population Research, Institute of Psychiatry, King's College London, London, UK.

⁴ Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

- ⁵ Amsterdam Public Mental Health Research Institute, Department of Clinical Psychology, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands
- ⁶ PsyLife Group, Division of Psychiatry, UCL, London, England.
- ⁷ Department of Psychiatry, University of Cambridge, Cambridge, England
- ⁸ Department of Child and Adolescent Psychiatry, Institute of Psychiatry and Mental Health, Hospital General Universitario Gregorio Marañón, School of Medicine, Universidad Complutense, Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Spanish Mental Health Research Network (CIBERSAM), Madrid, Spain
- ⁹ Department of Psychiatry, Instituto de Investigación Sanitaria (IDIS), Complejo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, Spain
- ¹⁰ Barcelona Clinic Schizophrenia Unit, Neuroscience Institute, Hospital Clinic of Barcelona, University of Barcelona, Barcelona, August Pi I Sunyer Biomedical Research Institute (IDIBAPS), Spanish Mental Health Research Network (CIBERSAM), Spain
- ¹¹Department of Psychiatry, Hospital Clínico Universitario de Valencia, School of Medicine, Universidad de Valencia, Valencia, Spain
- ¹²Department of Psychiatry, University of Oviedo, Spanish Mental Health Research Network (CIBERSAM), Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Mental Health Services of Principado de Asturias (SESPA), Oviedo, Spain
- ¹³Neurobiological Research Group, Institute of Technology, Universidad de Castilla-La Mancha, Cuenca, Spain
- ¹⁴Department of Psychiatry, Hospital "Virgen de la Luz", Cuenca, Spanish Mental Health Research Network (CIBERSAM), SpainINSERM, U955, Créteil, France
- ¹⁵Etablissement Public de Santé Maison Blanche, Paris, France
- ¹⁶Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, France
- ¹⁷Department of Medical and Surgical Sciences, Psychiatry Unit, Alma Mater Studiorum Università di Bologna, Bologna, Italy
- ¹⁸Department of Biomedicine, Neuroscience and advanced Diagnostics, University of Palermo, Palermo, Italy
- ¹⁹Section of Psychiatry, Department of Neuroscience, Biomedicine and Movement, University of Verona, Verona, Italy
- ²⁰Department of Preventive Medicine, Faculdade de Medicina, Universidade of São Paulo, São Paulo, Brazil
- ²¹Ribeirão Preto Medical School, University of São Paulo, Brazil
- ²²Orygen, Parkville, Victoria, Australia
- ²³Centre for Youth Mental Health, The University of Melbourne, Parkville, Victoria, Australia
- ²⁴Medizinische Fakultät, Universität Basel, Basel, Switzerland
- ²⁵LiNC-Lab Interdisciplinar Neurociências Clínicas, Depto Psiquiatria, Escola Paulista de Medicina, Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil
- ²⁶Departament de Psicologia Clínica i de la Salut, Universitat Autònoma de Barcelona, Barcelona, Spain
- ²⁷Fundació Sanitària Sant Pere Claver, Spanish Mental Health Research Network (CIBERSAM), Spain
- ²⁸University of Paris, GHU-Paris, Sainte-Anne, C'JAAD, Inserm U1266, Institut de Psychiatrie (CNRS 3557), Paris, France
- ²⁹Department of Psychiatry and Psychotherapy, Faculty of Medicine and University Hospital, University of Cologne, Cologne, Germany
- ³⁰Department of Psychiatry and Psychotherapy, Medical University of Vienna, Vienna, Austria

- ³¹Department of Psychiatry and Neuropsychology, School for Mental Health and Neuroscience, Maastricht University Medical Centre, Maastricht, the Netherlands
- ³²Department of Psychiatry, Brain Centre Rudolf Magnus, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands
- ³³Seaver Center for Research and Treatment, Icahn School of Medicine at Mount Sinai, NY, USA
- ³⁴Department of Psychiatry, Icahn School of Medicine at Mount Sinai, NY, USA
- ³⁵Arkin Institute for Mental Health, Amsterdam, the Netherlands
- ³⁶University of Basel, Basel, Switzerland
- ³⁷Department of Psychiatry, Escola Paulista de Medicina, Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil
- ³⁸CONACYT-Dirección de Investigaciones Epidemiológicas y Psicosociales, Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz, México
- ³⁹Department of Psychology, University of Illinois at Urbana-Champaign, IL, USA
- ⁴⁰Mental Health Center Copenhagen and Center for Clinical Intervention and Neuropsychiatric Schizophrenia Research, CINS, Mental Health Center Glostrup, Mental Health Services in the Capital Region of Copenhagen, University of Copenhagen, Copenhagen, Denmark
- ⁴¹Centre for Neuropsychiatric Schizophrenia Research (CNSR) & Centre for Clinical Intervention and Neuropsychiatric Schizophrenia Research (CINS), Mental Health Centre Glostrup, University of Copenhagen, Glostrup, Denmark
- ⁴²Psyberlin, Berlin, Germany
- ⁴³Parnassia Psychiatric Institute, Department of Psychosis Research, Zoutkeetsingel 40, 2512 HN The Hague, The Netherlands.

Dear Editor,

Inter-rater reliability (IRR) is an important component of methodology to establish valid results and prevent large measurement errors. However, only a minority of reports in psychiatric research present information concerning assessor training or reliability of applied instruments. For example, a recent study found that IRR coefficients and training procedures were strongly underreported in double-blind RCTs of antipsychotic medication(Berendsen et al., 2020).

IRR scores without training of raters are typically low, with only four studies investigated pre-training IRR (Muller and Dragicevic, 2003, Muller and Wetzel, 1998, Rosen et al., 2008, Loevdahl and Friis, 1996). ROSEN VERWIJDEREN The authors reported that the IRR scores of the PANSS, HAM-D or GAF [full titles available in the supplement] before training were generally moderate to poor, other observational instruments were not investigated. On the other hand, the authors reported significant improvement of the IRR after assessors were trained.

Selection of assessors based on their clinical backgrounds and assessment experience may also lead to improved pre-training IRR scores. However, merely three studies addressed the topic of assessor selection and pre-training reliability. The first study of Kobak et al. provided evidence that assessors with a PhD or medical degree showed significantly higher HAM-D clinical assessment skills necessary to conduct reliable assessments compared to assessors with lower educational degrees (Kobak et al., 2005). In contrast, Loevdahl et al. and Kollias et al. found no differences in pre-training reliability of the GAF or the CAARMS between psychiatrists, residents, psychologists and nurses (Loevdahl and Friis, 1996, Kollias et al., 2015).

This raises the question whether acceptable IRR scores can be achieved without assessor training or selection. Therefore, we aimed to determine the pre-training IRR of seven observational instruments that capture different aspects of psychosis in a large international multi-center research project by scoring video-taped interviews. In addition, we investigated the effect of assessor characteristics on pre-training IRR scores.

Assessors of the large multi-center study EU-GEI were instructed to rate participants on seven instruments via an online training platform (van Os et al., 2014). These instruments were chosen to measure predictors and outcome in psychosis. Ratings were based on videotaped assessments of interviews with actors playing the role of the patient. Demographic characteristics (age and gender), professional background (psychiatrists, psychologists, medical doctors or research assistants) and assessment experience (in months) of assessors were collected. The pre-training IRR of the following instruments were evaluated: CAARMS, SIS-R, LoTE, BQ, CECA, OPCRIT and GAF.

Pre-training IRR was calculated by Krippendorff's alpha (K-alpha) (Hayes and Krippendorff, 2007). According to interpretation guidelines, K-alpha values of >0.8 were considered high, 0.67 - 0.8 moderate, and <0.67 low (Krippendorff, 2011). For each K-alpha 95% confidence intervals were computed based on 10.000 bootstraps. Differences in age, assessment experience and IRR between different professional groups were analyzed for each assessment instrument using analysis of variance (ANOVA), followed by Bonferroni corrected pair-wise post-hoc comparisons.

**Table 1*.

In total 12 psychiatrists, 17 psychologists, 14 medical doctors and 13 research assistants participated in the online training platform. Mean age [30.18 years, F=13.43, p<0.001; see supplement table 1] and assessment experience (F=5,76, p=0.002; see supplement figure 1)

were significantly higher for psychiatrists compared to medical doctors and research assistants, and at trend level compared to psychologists.

Observed pre-training IRR score was moderate for LoTE (K-alpha =0.67), low for GAF (K-alpha=0,45), BQ (K-alpha=0.47), SIS-R (K-alpha=0.55), CAARMS (0,57), CECA (K-alpha=0.60) and OPCRIT (K-alpha=0.64).

IRR scores of subgroups are shown in Table 1. Overall mean IRR scores were significantly higher for psychiatrists compared to medical doctors (F=3,905, p= 0.0216). Comparisons for separate instruments showed significantly higher IRR scores for psychiatrists, psychologists and research assistants compared to medical doctors on the OPCRIT (F=18,38, p=<0.001), SIS-R (F=20,66, p=<0.001), GAF (F=12,53, p=<0.001) and CAARMS (F=13,34, p=<0.001). Additionally, medical doctors and research assistants scored significantly higher IRR scores compared to psychiatrists and psychologists on the BQ (F=16,75, p=<0.001). For detailed information on pair-wise comparisons of IRR scores between professionals and assessment experience see supplement figures 2a-2f.

Our study demonstrated that only one instrument showed moderate pre-training IRR, whereas the observed reliability scores of all other instruments were insufficient. Furthermore, medical doctors demonstrated significantly lower reliability scores compared to other professional subgroups in mean IRR ratings and several investigated instruments. These findings are important, particularly in light of previous research noting that rater training was strongly underreported and the impact of unreliability on study outcome (Mulsant et al., 2002, Kobak et al., 2007).

Our findings are in accordance with earlier results concerning insufficient pre-training IRR (Vatnaland et al., 2007, Muller and Dragicevic, 2003, Muller and Wetzel, 1998, Loevdahl and Friis, 1996). Differences in mean IRR scores between professions could be explained by the

significantly higher assessment experience of psychiatrists compared to the other professions. However, observed IRR scores of separate instruments were also different between psychologists and research assistants compared to medical doctors, while the latter two subgroups did not significantly differ in assessments experience. Our hypothesis concerning the latter variation is that research assistants and psychologist probably received more training in psychopathology scales such as the CAARMS or SIS-R during their general education, in comparison to medical doctors.

Our findings concerning differences between professionals seem to contrast with previous literature, which found no significant differences in pre-training IRR of GAF scores between psychiatrists and psychologists, compared to psychiatric nurses (Loevdahl and Friis, 1996). Similarly, another study concerning the CAARMS provided evidence that psychiatry residents produced almost similar IRR scores compared to psychiatrists and psychologists (Kollias et al., 2015). Possible explanations for these inconsistent findings could be that psychiatry residents have more experience with observational instruments and psychiatric diagnosis compared to medical doctors.

Of note, we evaluated *pre-training* IRR in this report. All included researchers achieved high IRR scores after training before permitted to perform assessments. However, we should acknowledge an important limitation of our study: we do not have data concerning previous training or clinical background of raters.

In conclusion, our study emphasizes the importance of rater training and assessor selection for research in psychiatry. Without rater training, reliability is generally insufficient. This has potentially major implications for the interpretation of study-results because of decreased power and higher placebo-response*see supplement (Perkins et al., 2000, Kobak et al., 2010). Future research should focus on specific assessors characteristics that predict higher IRR

scores after training. Finally, considering its importance, we propose training procedures and reliability coefficients should be reported in all studies.

References

- BERENDSEN, S., VAN, H. L., VERDEGAAL, L. M. A., VAN TRICHT, M. J., BLANKERS, M. & DE HAAN, L. 2020. Burying Our Heads in the Sand: The Neglected Importance of Reporting Inter-Rater Reliability in Antipsychotic Medication Trials. *Schizophr Bull*.
- HAYES, A. F. & KRIPPENDORFF, K. 2007. Answering the Call for a Standard Reliability Measure for Coding Data. . *Communication Methods and Measures*.
- KOBAK, K. A., KANE, J. M., THASE, M. E. & NIERENBERG, A. A. 2007. Why do clinical trials fail? The problem of measurement error in clinical trials: time to test new paradigms? *J Clin Psychopharmacol*, 27, 1-5.
- KOBAK, K. A., LEUCHTER, A., DEBROTA, D., ENGELHARDT, N., WILLIAMS, J. B., COOK, I. A., LEON, A. C. & ALPERT, J. 2010. Site versus centralized raters in a clinical depression trial: impact on patient selection and placebo response. *J Clin Psychopharmacol*, 30, 193-7.
- KOBAK, K. A., LIPSITZ, J. D., WILLIAMS, J. B., ENGELHARDT, N. & BELLEW, K. M. 2005. A new approach to rater training and certification in a multicenter clinical trial. *J Clin Psychopharmacol*, 25, 407-12.
- KOLLIAS, C., KONTAXAKIS, V., HAVAKI-KONTAXAKI, B., SIMMONS, M. B., STEFANIS, N. & PAPAGEORGIOU, C. 2015. Inter-rater reliability of the Greek version of CAARMS among two groups of mental health professionals. *Psychiatriki*, 26, 217-22.
- KRIPPENDORFF 2011. Agreement and Information in the Reliability of Coding. *Communication Methods and Measures*.
- LOEVDAHL, H. & FRIIS, S. 1996. Routine evaluation of mental health: reliable information or worthless "guesstimates'? *Acta Psychiatr Scand*, 93, 125-8.
- MULLER, M. J. & DRAGICEVIC, A. 2003. Standardized rater training for the Hamilton Depression Rating Scale (HAMD-17) in psychiatric novices. *J Affect Disord*, 77, 65-9.
- MULLER, M. J. & WETZEL, H. 1998. Improvement of inter-rater reliability of PANSS items and subscales by a standardized rater training. *Acta Psychiatr Scand*, 98, 135-9.
- MULSANT, B. H., KASTANGO, K. B., ROSEN, J., STONE, R. A., MAZUMDAR, S. & POLLOCK, B. G. 2002. Interrater reliability in clinical trials of depressive disorders. *Am J Psychiatry*, 159, 1598-600.
- PERKINS, D. O., WYATT, R. J. & BARTKO, J. J. 2000. Penny-wise and pound-foolish: the impact of measurement error on sample size requirements in clinical trials. *Biol Psychiatry*, 47, 762-6.
- ROSEN, J., MULSANT, B. H., MARINO, P., GROENING, C., YOUNG, R. C. & FOX, D. 2008. Web-based training and interrater reliability testing for scoring the Hamilton Depression Rating Scale. *Psychiatry Res,* 161, 126-30.
- VAN OS, J., RUTTEN, B. P., MYIN-GERMEYS, I., DELESPAUL, P., VIECHTBAUER, W., VAN ZELST, C., BRUGGEMAN, R., REININGHAUS, U., MORGAN, C., MURRAY, R. M., DI FORTI, M., MCGUIRE, P., VALMAGGIA, L. R., KEMPTON, M. J., GAYER-ANDERSON, C., HUBBARD, K., BEARDS, S., STILO, S. A., ONYEJIAKA, A., BOURQUE, F., MODINOS, G., TOGNIN, S., CALEM, M., O'DONOVAN, M. C., OWEN, M. J., HOLMANS, P., WILLIAMS, N., CRADDOCK, N., RICHARDS, A., HUMPHREYS, I., MEYER-LINDENBERG, A., LEWEKE, F. M., TOST, H., AKDENIZ, C., ROHLEDER, C., BUMB, J. M., SCHWARZ, E., ALPTEKIN, K., UCOK, A., SAKA, M. C., ATBASOGLU, E. C., GULOKSUZ, S., GUMUS-AKAY, G., CIHAN, B., KARADAG, H., SOYGUR, H., CANKURTARAN, E. S., ULUSOY, S., AKDEDE, B., BINBAY, T., AYER, A., NOYAN, H., KARADAYI, G., AKTURAN, E., ULAS, H., ARANGO, C., PARELLADA, M., BERNARDO, M., SANJUAN, J., BOBES, J., ARROJO, M., SANTOS, J. L., CUADRADO, P., RODRIGUEZ SOLANO, J. J., CARRACEDO, A., GARCIA BERNARDO, E., ROLDAN, L., LOPEZ, G., CABRERA, B., CRUZ, S., DIAZ MESA, E. M., POUSO, M.,

JIMENEZ, E., SANCHEZ, T., RAPADO, M., GONZALEZ, E., MARTINEZ, C., SANCHEZ, E., OLMEDA, M. S., DE HAAN, L., VELTHORST, E., VAN DER GAAG, M., SELTEN, J. P., VAN DAM, D., VAN DER VEN, E., VAN DER MEER, F., MESSCHAERT, E., KRAAN, T., BURGER, N., LEBOYER, M., SZOKE, A., SCHURHOFF, F., LLORCA, P. M., JAMAIN, S., TORTELLI, A., FRIJDA, F., VILAIN, J., GALLIOT, A. M., BAUDIN, G., FERCHIOU, A., et al. 2014. Identifying gene-environment interactions in schizophrenia: contemporary challenges for integrated, large-scale investigations. *Schizophr Bull*, 40, 729-36.

VATNALAND, T., VATNALAND, J., FRIIS, S. & OPJORDSMOEN, S. 2007. Are GAF scores reliable in routine clinical use? *Acta Psychiatr Scand*, 115, 326-30.