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

This is the final peer-reviewed author's accepted manuscript (postprint) of the following publication:

Published Version:

Pre-training inter-rater reliability of clinical instruments in an international psychosis research project / Berendsen S.; Kapitein P.; Schirmbeck F.; van Tricht M.J.; McGuire P.; Morgan C.; Gayer-Anderson C.; Kempton M.J.; Valmaggia L.; Quattrone D.; di Forti M.; van der Gaag M.; Kirkbride J.B.; Jongsma H.E.; Jones P.B.; Parellada M.; Arango C.; Arrojo M.; Bernardo M.; Sanjuan J.; Santos J.L.; Szoke A.; Tortelli A.; Llorca P.-M.; Tarricone I.; Tripoli G.; Ferraro L.; La Cascia C.; Lasalvia A.; Tosato S.; Menezes P.R.; Del-Ben C.M.; Nelson B.; Riecher-Rossler A.; Bressan R.; Barrantes-Vidal N.; Krebs M.-O.; Nordentoft M.; Ruhrmann S.; Sanchez-Bernardos P.; van Os J.; Veltro J.; Fusco H.; Galen M.; Tognin S.; Modinos G.; Pisani S.; Kraan T.C.; van Dam D.S.; Burger N.; McGorry P.; Amminger G.P.; Politis A.; Goodall J.; Borgwardt S.; Stuberus E.; Gadelha A.; Brietzke E.; Asevedo G.; Asevedo E.; Zugman A.; Dominguez-Martinez T.; Monson M.; Hinojosa J.; Cristofalo M.; Racioppi A.; Kwapil T.R.; Kazes M.; Daban C.; Bourgin J.; Gay O.; Mam-Lam-Fook C.; Nordholm D.; Randers L.; Krakauer K.; Glenthøj L.B.; Glenthøj B.; Gebhard D.; Arnhold J.; Klosterkötter J.; Lasser I.; Winklbaur B.; Delespaul P.A.. - In: SCHIZOPHRENIA RESEARCH. - ISSN 0920-9964 - ELETTRONICO. - 230:(2021), pp. 104-107. [10.1016/j.schres.2020.08.001]

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This is the accepted manuscript of:

Berendsen S, Kapitein P, Schirmbeck F, van Tricht MJ, McGuire P, Morgan C, Gayer-Anderson C, Kempton MJ, Valmaggia L, Quattrone D, di Forti M, van der Gaag M, Kirkbride JB, Jongsma HE, Jones PB, Parellada M, Arango C, Arrojo M, Bernardo M, Sanjuán J, Santos JL, Szöke A, Tortelli A, Llorca PM, Tarricone I, Tripoli G, Ferraro L, La Cascia C, Lasalvia A, Tosato S, Menezes PR, Del-Ben CM, Nelson B, Riecher-Rössler A, Bressan R, Barrantes-Vidal N, Krebs MO, Nordentoft M, Ruhrmann S, Sachs G, Rutten BPF, van Os J, Velthorst E, de Haan L; EU-GEI High Risk Study. Pre-training inter-rater reliability of clinical instruments in an international psychosis research project. *Schizophr Res.* 2020 Nov 23:S0920-9964(20)30429-1

Final peer reviewed version available at : <https://doi.org/10.1016/j.schres.2020.08.001>

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Letter to the editor

Title: Pre-training inter-rater reliability of clinical instruments in a large international multi-center psychosis research project.

Running title: Pre-training inter-rater reliability.

Total word count: 998.

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Acknowledgements

The European Network of National Schizophrenia Networks Studying Gene-Environment Interactions (EU-GEI) Project is funded by grant agreement HEALTH-F2-2010-241909 (Project EU-GEI) from the European Community's Seventh Framework Programme. Additional support was provided by a Medical Research Council Fellowship to M Kempton (grant MR/J008915/1). Further, we would like to thank EU-GEI WP2 Group not mentioned in main author list: Kathryn Hubbard, Stephanie Beards, Simona A. Stilo, Pedro Cuadrado, José Juan Rodríguez Solano, David Fraguas, Álvaro Andreu-Bernabeu, Gonzalo López, Bibiana Cabrera, Juan Nacher, Javier Costas, Mario Matteis, Marta Rapado-Castro, Emiliano González, Covadonga M. Díaz-Caneja, Emilio Sánchez, Manuel Durán-Cutilla, Nathalie Franke, Fabian Termorshuizen, Daniella van Dam, Elles Messchaart, Marion Leboyer⁴, Franck Schürhoff, Stéphane Jamain, Grégoire Baudin, Aziz Ferchiou, Baptiste Pignon, Jean-

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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 with antipsychotic medication[1].

IRR scores without training of raters are typically low, only four studies investigated pre-training IRR [2-5]. The authors reported that the IRR scores of the PANSS, HAM-D or GAF [abbreviations written out 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 [6]. 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 [5, 7].

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 [8]. 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) [9]. According to interpretation guidelines, K-alpha values of >0.8 were considered high, $0.67 - 0.8$ moderate, and <0.67 low [10]. 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 by 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, in light of previous research which noted that rater training was strongly underreported and the impact of unreliability on study outcome [11, 12].

Our findings are in accordance with earlier results concerning insufficient pre-training IRR [2, 3, 5, 13]. 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 [5]. Similarly, another study concerning the CAARMS provided evidence that psychiatry residents produced almost similar IRR scores compared to psychiatrists and psychologists [7]. 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} [14, 15]. 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

1. Berendsen, S., et al., *Burying Our Heads in the Sand: The Neglected Importance of Reporting Inter-Rater Reliability in Antipsychotic Medication Trials*. Schizophr Bull, 2020.
2. Muller, M.J. and A. Dragicevic, *Standardized rater training for the Hamilton Depression Rating Scale (HAM-D-17) in psychiatric novices*. J Affect Disord, 2003. **77**(1): p. 65-9.
3. Muller, M.J. and H. Wetzel, *Improvement of inter-rater reliability of PANSS items and subscales by a standardized rater training*. Acta Psychiatr Scand, 1998. **98**(2): p. 135-9.
4. Rosen, J., et al., *Web-based training and interrater reliability testing for scoring the Hamilton Depression Rating Scale*. Psychiatry Res, 2008. **161**(1): p. 126-30.
5. Loevdahl, H. and S. Friis, *Routine evaluation of mental health: reliable information or worthless "guesstimates"?* Acta Psychiatr Scand, 1996. **93**(2): p. 125-8.

6. Kobak, K.A., et al., *A new approach to rater training and certification in a multicenter clinical trial*. J Clin Psychopharmacol, 2005. **25**(5): p. 407-12.
7. Kollias, C., et al., *Inter-rater reliability of the Greek version of CAARMS among two groups of mental health professionals*. Psychiatriki, 2015. **26**(3): p. 217-22.
8. van Os, J., et al., *Identifying gene-environment interactions in schizophrenia: contemporary challenges for integrated, large-scale investigations*. Schizophr Bull, 2014. **40**(4): p. 729-36.
9. Hayes, A.F. and K. Krippendorff, *Answering the Call for a Standard Reliability Measure for Coding Data*. . Communication Methods and Measures, 2007.
10. Krippendorff, *Agreement and Information in the Reliability of Coding*. Communication Methods and Measures, 2011.
11. Mulsant, B.H., et al., *Interrater reliability in clinical trials of depressive disorders*. Am J Psychiatry, 2002. **159**(9): p. 1598-600.
12. Kobak, K.A., et al., *Why do clinical trials fail? The problem of measurement error in clinical trials: time to test new paradigms?* J Clin Psychopharmacol, 2007. **27**(1): p. 1-5.
13. Vatnaland, T., et al., *Are GAF scores reliable in routine clinical use?* Acta Psychiatr Scand, 2007. **115**(4): p. 326-30.
14. Perkins, D.O., R.J. Wyatt, and J.J. Bartko, *Penny-wise and pound-foolish: the impact of measurement error on sample size requirements in clinical trials*. Biol Psychiatry, 2000. **47**(8): p. 762-6.
15. Kobak, K.A., et al., *Site versus centralized raters in a clinical depression trial: impact on patient selection and placebo response*. J Clin Psychopharmacol, 2010. **30**(2): p. 193-7.

| Table 1. Omnibus test across all groups. | | | | | | | |
|---|----------------------|---------------------|------------------------|----------------------------|--------|----|-------------------|
| | Psychiatrists (N=12) | Psychologist (N=17) | Medical doctors (N=14) | Research assistants (N=13) | F | dF | P-value |
| Mean IRR (SD) | 0.67 (0.14) | 0,60 (0.17) | 0.43 (0.16) | 0.64 (0.09) | 3.905 | 3 | 0.0216 |
| OPCRIT [95% CI] | 0.81 [0.75-0.86] | 0.73 [0.65-0.80] | 0.44 [0.35-0.53] | 0.68 [0.58-0.77] | 16.02 | 3 | <0.0001 |
| SIS-R [95% CI] | 0.75 [0.69-0.82] | 0.66 [0.57-0.74] | 0.32 [0.21-0.42] | 0.74 [0.63-0.83] | 22.92 | 3 | <0.0001 |
| LoTE [95% CI] | 0.78 [0.62-0.91] | 0.66 [0.47-0.82] | 0.62 [0.40-0.79] | 0.67 [0.47-0.85] | 0.6553 | 3 | 0.5819 |
| GAF [95% CI] | 0.64 [0.54-0.73] | 0.49 [0.39-0.56] | 0.27 [0.16-0.37] | 0.53 [0.38-0.63] | 12.53 | 3 | <0.0001 |
| CECA [95% CI] | 0.61 [0.58-0.78] | 0.60 [0.55-0.64] | 0.55 [0.47-0.64] | 0.60 [0.54-0.68] | 0.5124 | 3 | 0.6744 |
| BQ [95% CI] | 0.43 [0.27-0.59] | 0.26 [0.15-0.37] | 0.57 [0.44-0.69] | 0.73 [0.63-0.81] | 16.44 | 3 | <0.0001 |
| CAARMS [95% CI] | - | 0.78 [0.72-0.84] | 0.21 [-0.02-0.42] | 0.53 [0.33-0.70] | 13.82 | 2 | <0.0001 |

