Letter to the Editor

Sarah J. Lord*, Andrea Rita Horvath, Phillip J. Monaghan, Sverre Sandberg and Patrick M. Bossuyt, on behalf of the EFLM Committee, Clinical and Analytical Performance Specifications (C-CAPS)

Reply to "Is this quantitative test fit-for-purpose?"

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To the Editor,

We thank Asberg and Bolann [1] for their interest in our paper "Is this test fit-for-purpose? Principles and a checklist for evaluating the clinical performance of a test in the new era of *in vitro* diagnostic (IVD) regulation" [2]. The *In Vitro* Diagnostic Medical Devices Regulation (IVDR) 2017/746 defines clinical performance as "the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user" [3]. The purpose of our paper is to present the principles for evaluating this ability to detect or predict a clinically defined target condition. We explain this entails enrolling a study group that represents the target population and cross-referencing the test results with the presence of the target condition. The distribution of test results in those with and without the target condition expresses its clinical performance. The receiver operating characteristic (ROC) curve and the area under the curve (AUC) are transformations of these distributions, displaying the ability of the test to correctly classify or identify members of the target population, as do sensitivity and specificity for a specific threshold. We refer to these measures as the primary measures of clinical performance and focus our paper on explaining how the same principles apply to tests intended for other purposes, such as prognosis, where the target condition is determined in the future, and key elements for study design for valid estimation. We also describe how clinical performance can be evaluated for any clinically defined criteria, groupings, or risk category relevant to the intended purpose of the test.

In contrast, as Asberg and Bolann explain in their letter [1], likelihood ratios (LR) allow clinicians to estimate the posttest probability of the target condition for an individual with a given test result by applying the LR for that result to an estimate of the pretest probability and thereby aid the interpretation of diagnostic and screening tests results in clinical practice. While we do not wish to detract from Asberg and Bolann's call for reporting functions or tables of LR when reporting clinical performance data, including in package inserts, we do not regard these ratios as primary measures of clinical performance. A likelihood ratio can be calculated for a single result, while our suggested measures of performance apply to the whole target population for whom testing is considered.

We hope our paper [2] will help foster a shared understanding of how clinical performance is defined in this new era of IVDR and the essential elements for study design to provide sound evidence for regulatory assessment.

***Corresponding author: Sarah J. Lord**, National Health and Medical Research Council (NHMRC) Clinical Trials Centre, University of Sydney, Sydney, Australia, E-mail: sally.lord@sydney.edu.au. https://orcid.org/0000-0003-2763-5949
Andrea Rita Horvath, New South Wales Health Pathology Department of Chemical Pathology, Prince of Wales Hospital and School of Medical Sciences, University of New South Wales, Sydney, Australia; and School of Public Health, University of Sydney, Sydney, Australia
Phillip J. Monaghan, Department of Clinical Biochemistry, The Christie NHS Foundation Trust, Manchester, UK; and Division of Cancer Sciences, The University of Manchester, Manchester, UK
Sverre Sandberg, The Norwegian Quality Improvement of Primary Care Laboratories (NOKLUS), Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway; and Laboratory of Clinical Biochemistry, Haukeland University Hospital, Bergen, Norway
Patrick M. Bossuyt, Department of Clinical Epidemiology, Biostatistics & Bioinformatics, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands

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