

Note

Potential conflicts of interest. The author: No reported conflicts of interest. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Peter Baxter

Childrens Hospital,
Sheffield, United Kingdom

References

1. Marais BJ, Heemskerk AD, Marais SS, et al; Tuberculous Meningitis International Research Consortium. Standardized methods for enhanced quality and comparability of tuberculous meningitis studies. *Clin Infect Dis* 2017; 64:501–9.
2. STREPTOMYCIN treatment of tuberculous meningitis. Medical Research Council Lancet 1948; 6503:582–96.
3. Bang ND, Caws M, Truc TT, et al. Clinical presentations, diagnosis, mortality and prognostic markers of tuberculous meningitis in Vietnamese children: a prospective descriptive study. *BMC Infect Dis* 2016; 16:573–582.
4. Misra UK, Kalita J, Maurya PK. Stroke in tuberculous meningitis. *J Neurol Sci* 2011; 303:22–30.
5. Kirkham FJ, Newton CR, Whitehouse W. Paediatric coma scales. *Dev Med Child Neurol* 2008; 50:267–74.

Correspondence: P. Baxter, Ryegate Centre, Sheffield Childrens NHS Foundation Trust, Tapton Crescent Rd, Sheffield S10 5DD, UK (p.s.baxter@sheffield.ac.uk).

Clinical Infectious Diseases® 2019;69(4):735–6

© The Author(s) 2019. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com. DOI: 10.1093/cid/ciz024

Reply to Baxter

TO THE EDITOR—We thank Doctor Baxter for raising 2 important points concerning the prognosis of young children with tuberculous meningitis (TBM). We agree that there is a discrepancy between the original British Medical Research Council (BMRC) TBM grading, which included “gross pareses” in the most severe grade, and the current, widely used, modified BMRC grading, which is primarily defined by coma severity. We also agree that stroke is the likely cause of gross paresis and that clinical experience suggests these children do indeed have a poor prognosis. However, an alternative scoring system, which accommodates paresis

independently from coma, requires derivation from high-quality clinical data and statistical modelling if it is to represent a practice-changing advance to the empirically derived BMRC grade. Unfortunately, the high-quality clinical data required to perform this task are lacking, but we hope that the standardized methodology proposed will encourage future research and enable sharing and merging of the required data sets to more accurately define prognoses in all age groups.

The second point raised was the need to specify that a “modified Glasgow coma scale” should be used in young children, with a clear indication of the best versions to use in relevant age groups. Various modifications to the coma score have been made to accommodate children less than 5 years of age, who are at different phases of language and motor development. Our proposed standardized methodology did not clarify which scale to use beyond infancy [1]. We agree with Doctor Baxter that the unified scale developed by James, together with the Grimace scale for intubated children, as summarized in the article by Kirkham et al [2], provides the most pragmatic approach to a standardized assessment for all children less than 5 years of age. In children older than 5 years of age, the standard adult Glasgow coma scale is appropriate, which implies that this standardized approach can be used across the full age range. However, standardization is not easy in children, with wide variation in practice. Even for a traumatic brain injury, which is the most common cause of acute pediatric neurological impairments worldwide and for which there have been practice guidelines for several years [3], there is no standardization of assessment.

We hope that this clarification will improve the utility of our proposed standardized methods and that more data will accrue over time to substantiate their value and identify the components that require further refinement.

Note

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential

Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Ben J. Marais,¹ Ronald van Toorn,² Tony Figaji,³ and Guy E. Thwaites^{4,5}, on behalf of the Tuberculous Meningitis International Research Consortium

¹Westmead Children's Hospital and the Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, Australia; ²Tygerberg Children's Hospital and the Stellenbosch University, Bellville, and ³Red Cross Children's Hospital and the University of Cape Town, South Africa; ⁴Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam; and ⁵Nuffield Department of Medicine, Centre for Tropical Medicine and Global Health, University of Oxford, United Kingdom

References

1. Marais BJ, Heemskerk AD, Marais SS, et al. Standardized methods for enhanced quality and comparability of tuberculous meningitis studies. *Clin Infect Dis* 2017; 64:501–9.
2. Kirkham FJ, Newton CR, Whitehouse W. Paediatric coma scales. *Dev Med Child Neurol* 2008; 50:267–74.
3. Kochanek PM, Carney N, Adelson PD, et al. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents—second edition. *Pediatr Crit Care Med* 2012; 13(Suppl 1):S1–82.

Correspondence: G. E. Thwaites, Nuffield Department of Medicine, Centre for Tropical Medicine and Global Health, Old Road Campus, Roosevelt Dr, Oxford OX3 7FZ, United Kingdom (gthwaites@oucr.org).

Clinical Infectious Diseases® 2019;69(4):736

© The Author(s) 2019. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com. DOI: 10.1093/cid/ciz026

Symptom-based Scoring for Acute Human Immunodeficiency Virus

TO THE EDITOR—We read with interest the report by Lin et al showing that a simple symptom score consisting of fever, myalgia, and weight loss accurately predicted acute human immunodeficiency virus (HIV) infection (AHI) [1]. We agree with the authors that symptom-based assessment is less prone to limitations inherent to risk-based scores, as “symptoms may be less subject to stigma, and therefore individuals may be more comfortable disclosing symptoms than sexual behaviors” [1]. Our concern is that the symptom score was developed in the United States, and therefore may not optimally identify

AHI in resource-limited countries, as recommended by the authors.

We have previously developed a symptom-based score with data from at-risk and general populations from Kenya, Malawi, and South Africa [2]. This score assigns 1 point each for age 18–29 years or reported fever, fatigue, body pains, diarrhea, or sore throat, and 3 points for reported genital ulcer disease; individuals scoring ≥ 2 should be tested for AHI [2]. We are using this score to detect AHI with the Xpert HIV-1 Qual assay (Cepheid, Sunnyvale, California) among adults aged 18–39 years seeking urgent care in coastal Kenya (R01AI124968, ongoing). While HIV-1 RNA testing for AHI diagnosis is not supported by policy in sub-Saharan Africa, an exclusive focus on identifying chronic HIV in seropositive adults leads to missed opportunities [3]. This is especially important as preexposure prophylaxis (PrEP) is being scaled up in African settings.

The following case history from a voluntary testing and counseling center affiliated with our research clinic in coastal Kenya illustrates this: A 24-year-old heterosexual man tested negative on 2 HIV rapid antibody tests, whereas his female partner of 3 months tested antibody positive in the same session. He reported diarrhea and fatigue in the preceding 4 days, but no fever, weight loss, or myalgia. He was eligible for PrEP per Kenyan guidelines [4], as he was in a serodiscordant relationship. The patient met 3 of the criteria (young age, fatigue, and diarrhea) from our symptom-based score and was therefore tested with the Xpert HIV-1 Qual assay [2]. He tested positive, as confirmed by a viral load of 5500 copies/mL by Xpert HIV-1 Quant assay. He enrolled in an AHI cohort and started antiretroviral therapy shortly thereafter.

Per Kenyan guidelines, healthcare providers should assess for AHI symptoms prior to PrEP initiation when a recent high-risk exposure is reported [4]. While most front-line healthcare providers in sub-Saharan Africa received no specific training about AHI diagnosis [5, 6], PrEP guidelines offer a glimmer of hope that AHI symptoms will now be assessed in at-risk clients under evaluation for PrEP eligibility. We propose that this symptom screening should be done with our symptom-based score in African settings [2], as limiting AHI screening to those with fever, myalgia, and weight loss will lead to missed opportunities according to our data. As AHI testing should be targeted in resource-limited settings, we applaud the efforts of Lin and colleagues to promote the concept of targeted testing and encourage further research into this important area.

Notes

Disclaimer. The contents of this work are the responsibility of the study authors and do not necessarily reflect the views of the US Agency for International Development (USAID), the National Institutes of Health (NIH), the United States government, or the Wellcome Trust. This report was published with permission from the Kenya Medical Research Institute (KEMRI).

Financial support. This work was partially funded by the International AIDS Vaccine Initiative (IAVI) with the generous support of USAID and other donors; a full list of IAVI donors is available at www.iavi.org. The KEMRI–Wellcome Trust Research Programme is supported by core funding from the Wellcome Trust (grant number 203077/Z/16/Z). E. J. S. receives research funding from IAVI, the NIH (grant R01AI124968), and the Wellcome Trust. S. M. G. and E. J. S. were supported by the NIH (grant number R01AI124968). This work was also supported through the Sub-Saharan African Network for TB/HIV Research Excellence, a DELTAS Africa Initiative (grant number DEL-15-006).

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Eduard J. Sanders,^{1,2,9} Alex Kigoro,¹ Alexander Thiong'o,¹ Eunice Nduati,¹ and Susan M. Graham^{1,3}

¹Kenya Medical Research Institute–Wellcome Trust Research Programme, Kilifi; ²Nuffield Department of Medicine, University of Oxford, United Kingdom; and ³University of Washington, Seattle

References

1. Lin TC, Gianella S, Tenenbaum T, Little SJ, Hoenigl M. A simple symptom score for acute human immunodeficiency virus infection in a San Diego community-based screening program. *Clin Infect Dis* 2018; 67:105–11.
2. Sanders EJ, Wahome E, Powers KA, et al. Targeted screening of at-risk adults for acute HIV-1 infection in sub-Saharan Africa. *AIDS* 2015; 29(Suppl 3):S221–30.
3. Sanders EJ, Chirro O, Oduor C, et al. Point-of-care HIV RNA testing and immediate ART initiation in young adults seeking out-patient care in Kenya. *AIDS* 2019. In press.
4. National AIDS & STI Control Programme (NASCO). Guidelines on use of antiretroviral drugs for treating and prevention HIV infection in Kenya. Nairobi, Kenya: NASCO, 2018.
5. Rafferty H, Chirro O, Oduor C, et al. Pilot testing of an online training module about screening for acute HIV infection in adult patients seeking urgent healthcare. *Int Health* 2018. doi:10.1093/inthealth/ihy077.
6. Prins HA, Mugo P, Wahome E, et al. Diagnosing acute and prevalent HIV-1 infection in young African adults seeking care for fever: a systematic review and audit of current practice. *Int Health* 2014; 6:82–92.

Correspondence: E. J. Sanders, Kenya Medical Research Institute–Wellcome Trust Research Programme, Kilifi, Kenya (esanders@kemri-wellcome.org).

Clinical Infectious Diseases® 2019;69(4):736–7

© The Author(s) 2019. Published by Oxford University Press for the Infectious Diseases Society of America.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

DOI: 10.1093/cid/ciz059