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Derivation and validation of prognostic models for the risk stratification of childhood infection: a multi-country prospective cohort study in Asia (Spot-Sepsis)

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Introduction

Infections remain the leading cause of preventable child mortality in low-income and middle-income countries. However, reliable guidelines to assist rural practitioners identify children who may benefit from referral to higher-level care are lacking. Whether tools such as pulse oximetry and host biomarker tests can help is unknown. We aimed to develop and validate a clinical prediction model for the triage of febrile children in resource-constrained community settings and evaluate the utility of including pulse oximetry and/or host biomarker tests alongside simple clinical parameters.

Methods

This study recruited children aged 1–59 months presenting with community-acquired acute febrile illnesses to seven hospitals across Bangladesh, Cambodia, Indonesia, Laos, and Viet Nam. Clinical data and biomarker concentrations were measured at presentation. The outcome measure was death or receipt of vital organ support within 2 days of enrolment. We used weighted logistic regression to derive and validate prediction models containing easily ascertainable clinical parameters with and without pulse oximetry and/or host biomarker tests. The models were derived from data from six sites and validated in the held-out dataset from Cambodia. To assess performance of the models, we compared them with the WHO Danger Signs, the existing standard of care for guiding referral of febrile children in resource-constrained community settings. We modelled cost-effectiveness of the triage strategies.

Ethics

This study was approved by the Ethical Review Boards (ERBs) of Médecins Sans Frontières (1967), the University of Oxford (OxTREC 59-19), and each of the participating countries.

Results

From March 2020 to November 2022, we recruited 3,423 children (median age 16.8 months [IQR 8.7–31.0]; 2041/3423 [59.6%] male), of whom 133 (0.4% weighted prevalence) either died or received vital organ support within 2 days of enrolment. Discrimination was similar for all the models (areas under the curve, AUCs, 0.95–0.98) and substantially better than WHO Danger Signs (AUC 0.69; 95% CI 0.61–0.78; p<0.001). While all the models demonstrated good rule-in potential (specificities 0.99–1.0), sensitivity of the models containing pulse oximetry or host biomarkers (sensitivities 0.86–0.89) was considerably better than sensitivity of the model containing clinical parameters only (sensitivity 0.75; 95% CI 0.62–0.87). All of the models were predicted to be substantially more cost-effective than the use of WHO Danger Signs.

Conclusion

This study demonstrates that combining measurements of easily ascertainable clinical parameters outperforms the existing standard of care for risk stratification of febrile children presenting from the community. Further important gains may be realised through the inclusion of pulse oximetry and/or host biomarker tests, and these approaches are likely to be cost-effective. Future work should compare performance to other risk stratification algorithms. Randomised trials are required to evaluate the impact of different triage strategies.

Conflicts of interest

All authors declare no competing interests.