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COMMENTARY

Next-generation diagnostic instruments in haematology

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Gallo et al. assessed the impact of implementing a clinical decision support tool in a multi-hospital setting. This is one of three important points to unlock the capabilities of the next-generation of diagnostic instruments: (a) integrating diagnostic information from various sources, (b) ensuring accurate development and validation in well-designed clinical studies and (c) seamlessly integrating them into clinical practice.

Commentary on: Gallo et al. Clinical decision support to reduce unnecessary diagnostic testing for heparin-induced thrombocytopenia. Br J Haematol 2023 (Online ahead of print). doi: 10.1111/bjh.18902.

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decision support system, diagnostic accuracy, diagnostic haematology, sensitivity and specificity

In the current issue of the British Journal of Hematology, Gallo, and colleagues report on the retrospective evaluation of a clinical decision support (CDS) system implemented in the electronic health record of a 30-hospital healthcare system in the United States.[1] The heparin-induced thrombocytopenia (HIT) computerized risk (HIT-CR) scoring system, developed by the same group, determines the pretest probability of HIT, thus serving as a diagnostic test to rule out HIT.[2,3] Hence, the HIT-CR represents a step from classical laboratory tests towards the next-generation of diagnostic instruments in haematology.

Laboratory test and other classical diagnostic tests have not yet reached their full potential and three reasons are responsible for this. First, a single source of information is used (e.g. the presence of heparin/PF4 antibodies), often with a categorical interpretation (positive/negative), thus neglecting the complexity of the human body as a multifactorial, interconnected system. New computational techniques, however, such as machine-learning algorithms, may revolutionize diagnostics by integrating diagnostic information from multiple sources into one model and taking complex interactions into account (Figure 1). A second problem is the unclear diagnostic efficacy of many tests in clinical practice, as well as the meaning of the results of the tests for individual patients. This is because high-quality clinical studies are missing. However, a conceptual framework for a phased approach ensuring a complete and sound methodology is available (Table 1).[4] As a third point, if not used in clinical practice, even the most accurate diagnostic tool will be of no

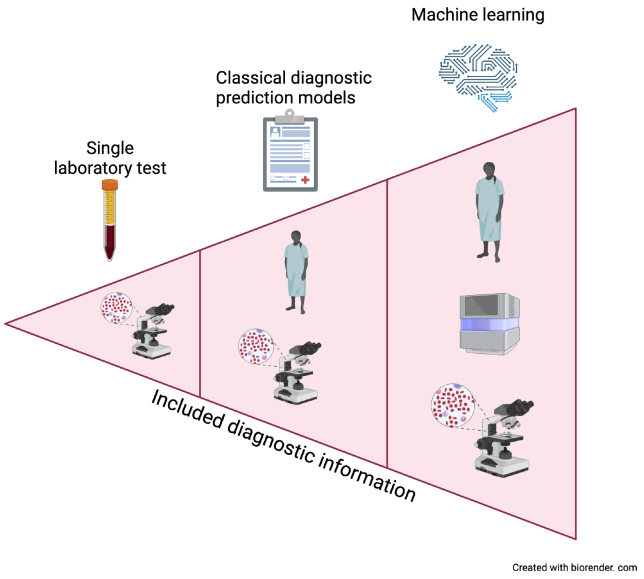

FIGURE 1 Illustration demonstrating the increasing diagnostic information and complexity of data linkage in different generations of diagnostic instruments.

TABLE 1 A conceptual framework for the development and implementation of new diagnostic tests.[4]

Phases	Objectives	Study design
Conceptualization	Assessment of current practice and identification of clinical needs	Observational research, literature review, health services research
	Biomarker discovery and identification of candidate variables	Case–control studies, observational research, literature review
Development	Development of measuring instruments and detailed assessment of analytical characteristics (e.g. calibration, technical performance, linearity, analytical sensitivity, precision)	Adapted to the individual measuring instrument
	Identification of influencing factors (e.g. patient characteristics, material)	Adapted to the individual measuring instrument
Validation	Assessment of the diagnostic or prognostic accuracy	Adequately designed cross-sectional or prospective cohort studies (population, index test, reference standard, flow and timing)
	External validation in other settings and populations	Adequately designed cross-sectional or prospective cohort studies (population, index test, reference standard, flow and timing)
Implementation	Regulatory approval and integration in healthcare delivery processes	Adapted to the individual measuring instrument
Impact evaluation	Clinical and healthcare outcomes including adoption and barriers of implementation	Health services research

value. Hence, seamless integration into healthcare delivery processes is essential for widespread adoption and utilization. One example of an impactful tool is the estimated glomerular filtration rate, which is often seamlessly integrated into the hospital information system (HIS).

The last point is the great strength of the present paper by Gallo et al. assessing the impact of implementing a CDS in a multi-hospital HIS. For 319 advisories presented within a 20-week period in an institution of 30 hospitals, the immunoassay test order was cancelled in 25% of the cases. Analysing the cases retrospectively, a negative predictive value of 98.8% was calculated. The HIT-CR, automatically calculating the pretest probability of HIT using the degree and timing of thrombocytopenia in patients treated with heparin, was developed and validated in previous studies of the same group.[2,3]

Other DSC have been proposed for patients with suspected HIT. The 4Ts score is an expert-opinion-based score allocating points to several clinical variables. It has been validated in various studies, claiming a high negative predictive value.[5] However, the accuracy and reproducibility is observer dependent and studies conducted in routine clinical practice found a relevant number of patients missed. More recently, another pretest probability score was proposed by a French group but validation in a representative (external) population is pending.[6] The diagnostic algorithm recommended by the American Society of Hematology is an expert-based decision tree based on the categorical interpretations (positive/negative) of the 4Ts score and a subsequent immunoassay test result.[7] Two other groups followed a similar approach, but combined the 4Ts score and the immunoassay in a stratified manner following a Bayesian approach.[8,9] Our group recently published a machine learning-based algorithm for the diagnosis of HIT that was derived from a prospective, multicentre cohort of patients with suspected HIT in clinical practice.[10] The model was implemented as a web application to facilitate its use (https://toradi-hit.org).

In spite of recent advances in highly sensitive laboratory tests, we have yet to fully exploit diagnostic information. In order to unlock the capabilities of the next-generation of diagnostic instruments, it is vital to (a) integrate diagnostic information from various sources, (b) ensure accurate development and validation in well-designed clinical studies and (c) seamlessly integrate them into clinical practice.

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