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Digitally targeted testing for blood-borne viruses: Systematic review and and meta-analysis of predictive risk algorithms (TARGET-ID)

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Background

High quality predictive algorithms to digitally identify people living with blood-borne viruses (BBVs) in care settings exist but require development and validation.

Methods

We conducted a systematic review and meta-analysis of published predictive algorithms on the BBVs HIV, hepatitis B (HBV) and hepatitis C (HCV). We searched the Web of Science, MEDLINE, EMBASE, and CENTRAL databases from 1946 to 2023.

Eligible papers were extracted using the CHARMS (CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies) and appraised using the PROBAST (Prediction model Risk Of Bias ASsessment Tool). Studies were classified as high-risk if any of the four PROBAST signalling domains were rated as high-risk.

Two researchers independently evaluated risk of bias. The first used ChatGPT (OpenAI) and Claude (Anthropic) for semi-automated classification per PROBAST, while the second manually assessed risk. An independent statistician resolved ambiguous results. Following consensus, risk ratings from the AI-assisted and manual methods were statistically compared.

Forest plots were generated for each individual BBV and a meta-analysis of the Area Under the Receiver Operating Characteristic Curve (AUC) was conducted. The performance of the algorithms was considered acceptable in distinguishing cases if the AUC was between 0.7 and 0.8 and excellent, if between 0.8 and 0.9.

Results

After removing duplicates, 33,901 articles were screened, 310 assessed in full, 72 included in the final analysis, and 238 excluded. 31,296,475 people at risk of BBVs were screened, and 65,269 were diagnosed with at least one BBV.

BBVs studied included HIV only (n=52), HCV only (n=13), HBV only (n=5), all BBVs, and HBV and HCV combined (n=1 each). No study investigated BBV co-infection in the general population.

Study settings: Forty-one studies were conducted in low-to middle-income countries, while 31 were conducted in high-income countries. The studies were conducted in eight different settings: sexual health (n=30), secondary care (n=14), community settings (n=8), registry (n=6), paediatric (n=5), primary care (n=5), drug centres (n=2), and electronic health record (n=2) (Figure 1 (a)).

Study populations: Studies reported general population (n=26), men who have sex with men (MSM) (n=19), cisgender-women (n=7), people with HIV (n=5), children/adolescents (n=5), substance users (n=4), patients with tuberculosis (n=3), haemodialysis/malignancy/HBV risk (n=1 each); one study reported separately for MSM, female sex workers, and drug users.

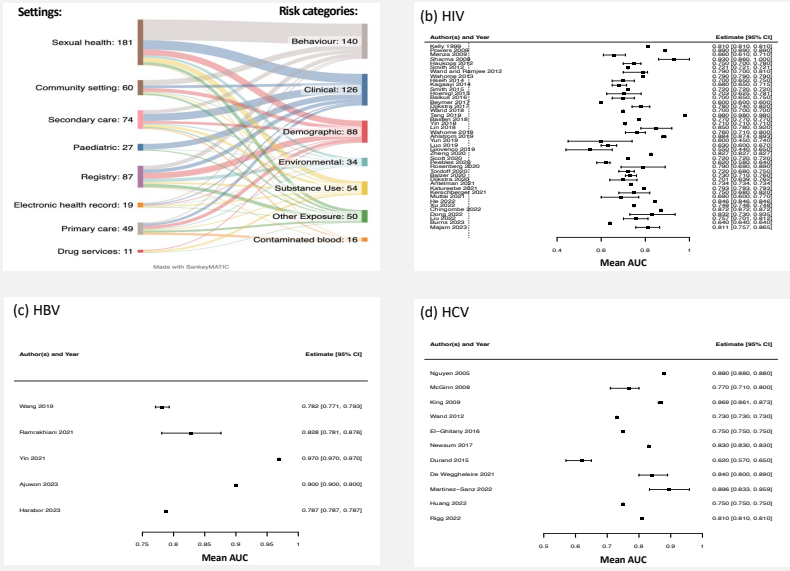

Figure 1: (a-d): Sankey diagram showing distribution for 508 predictors incorporated in the final algorithms over eight study settings (a), and Forest plots of AUC values for prediction algorithms on HIV (b), HBV (c), and HCV (d).

Results continued…

Predictor mapping: Data were obtained from a total of 61 studies. These studies utilized 508 predictors that were incorporated into the final algorithms. Predictors were categorised as behavioural (n=140), clinical (n=126), demographic (n=88), substance use (n=54), environmental (n=34), contaminated blood (n=16) , and other exposure (n=50) (Figure 1 (a)).

Top predictor use differed by setting: sexual health - behavioural (n=82); secondary care - clinical (n=29); registry - demographic (n=23); community - behavioural (n=21); primary care - demographic (n=12); paediatric - clinical (n=22).

Algorithm type, development and validation: The statistical methods included regression analysis (n=51), machine learning (n=17) and other (n=4). The studies included both development and internal validation (n=34), development only (n=13), external validation only (n=9), and eight each on combinations of development with external validation and on development with both internal and external validation.

Internal validation types included split sample analysis (n=34), cross-validation (n=14), bootstrapping (n=14), and other (n=2).

Risk of bias analysis: AI-assisted and manual assessment were 88% concordant. With consensus, 65 studies were considered high-risk and seven (all HIV) were low-risk.

Statistical analysis: Thirty-two studies reported AUC means and ranges: 25 HIV studies with a mean AUC of 0.75 (range 0.44-0.98), five HCV studies with a mean AUC of 0.80 (range 0.57-0.96), and two HBV studies with a mean AUC of 0.85 (range 0.77-0.97) (Figure 1 (b-d)).

Conclusion

Prediction algorithms for BBVs showed acceptable performance for HIV and excellent performance for HBV and HCV. However, there was substantial variability in the reported AUC ranges across different studies, populations, and settings. The limited research with low-risk of bias, along with the lack of improvement in algorithm performance, indicates that advancements in machine learning have not yet resulted in consistently better reporting or more accurate BBV predictions. A refined algorithm, tailored for diverse populations and tested on different datasets and settings, is crucial for effective BBV testing and elimination.

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