A dual point-of-care test strategy to identify treatment-eligible hep B patients in Africa

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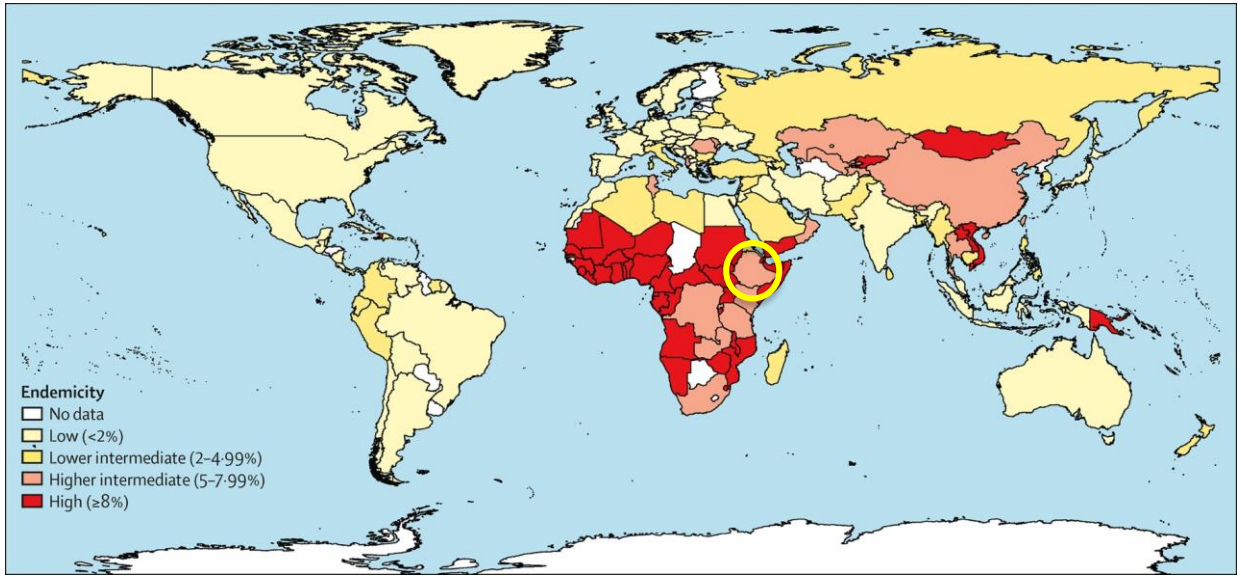
Declaration of interests:

- DA and HV are inventors of the ALT1 test (previously Nanjing BioPoint Diagnostics, now Burnet Institute), HV DA and JH are inventors of the dIgA test (Burnet Institute)
- DA was CEO and Chief Scientist of Nanjing BioPoint Diagnostics until 2022, and is President and Chief Scientist of Nanjing DeShi Diagnostics, China (startup company) brunswickbiotech@gmail.com

Alanine Aminotransferase (ALT) and Fibroscan (cirrhosis) screening are essential in determining Hepatitis B treatment eligibility

- Capacity is highly centralized and/or lacking in many highly endemic regions, which hampers access to antiviral Rx for HBV



Estimations of worldwide prevalence of chronic hepatitis B virus infection. Schweitzer, Aparna et al, The Lancet 2015

Liver disease: Alanine aminotransferase (ALT) and cirrhosis

- ALT (Alanine aminotransferase) is a commonly used marker of liver damage
- ALT enzymatic tests require venous blood, expensive instruments
- Cirrhosis detection via elastography (fibroscan), biopsy (risky), or clinical (too late….)

POC test for ALT1 (first generation, Nanjing BioPoint) *(now Burnet Institute)*

- Measure ALT1 as an antigen (liver-specific ALT1 only, not ALT2), rather than enzymatic
- Lateral flow strip with polyclo
- 40 µl whole blood or 15 µl pl
- Read visually (by compariso
- DA, Huy Van, Mary Garcia, I
- Tests manufactured under IS

Liver INTERNATIONAL

ORIGINAL ARTICLE

Validation of a novel point-of-care test for alanine aminotransferase measurement: A pilot cohort study

Jessica Howell ✉, Huy Van, Minh D. Pham, Rohit Sawhney, Fan Li, Purnima Bhat, John Lubel, William Kemp, Stephen Bloom, Avik Majumdar, Geoffrey W. McCaughan, Samuel Hall, Timothy Spelman, Joseph S. Doyle, Margaret Hellard, Kumar Visvanathan, Alexander Thompson, Heidi E. Drummer, David Anderson ... See fewer authors

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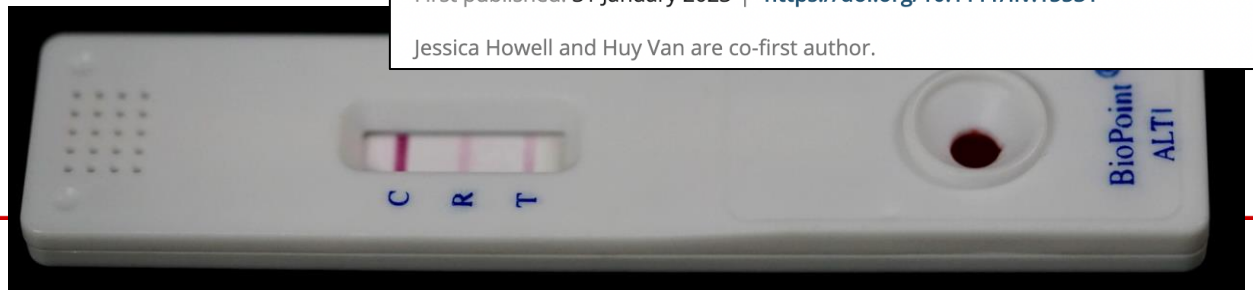
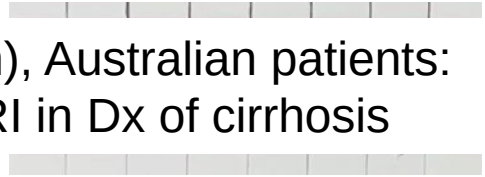
Jessica Howell and Huy Van are co-first author.

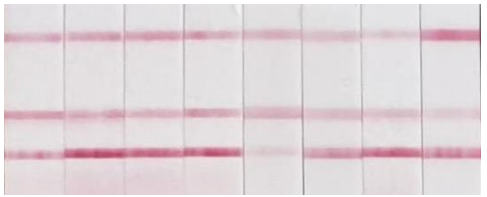


POC test for dIgA and IgA2 – cirrhosis (or >F2 fibrosis) (Burnet Institute)

- Dimeric IgA (dIgA) recognized as a marker of cirrhosis in the 1980s – hard to test
  - Our approach - Measure relative amount of dimeric IgA and total IgA; and total IgA2
- Lateral flow strip with **Chimeric Secretory Component (CSC)** (dIgA), anti-IgA2, and protein L (total IgA) test lines, colloidal gold anti-IgA detection
- 5 µl whole blood, add buffer; wait 10 min add buffer; wait 20 minutes
- Read with AX-2X instrument reader (future test will hopefully be visual)
- **Huy Van**, DA, Jess Howell (Burnet).

Howell *et al* (under revision), Australian patients: similar performance to APRI in Dx of cirrhosis





Healthy

Cirrhotic

Clinical studies in chronic hepatitis B patients in Addis Ababa, Ethiopia

- Ongoing clinical study and treatment program with full laboratory testing
- Targeted retrospective cohort (n=200, plasma stored in Norway) used to determine relative (local) cutoffs
- Validation cohort (n=105, plasma - retrospective samples stored in Ethiopia)
- Prospective cohort (n=290) performed on **whole blood** by **local technicians** in Ethiopia

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- Prospective cohort (n=290) performed on **whole blood** by **local technicians**
- ALT1 POC: Sensitivity for ALT >40 IU/l was 67-90%
- dIgA/IgA2 POC: Sensitivity for >F2 fibrosis was 70-82%
- Dual-POC approach (either/or) identified treatment-eligible HBV patients with 87-88% sensitivity, 32-34% specificity, 42-49% PPV, 75-82% NPV.
- **Among those who had a high viral load, sensitivity for Rx eligibility was 94-97%**

Conclusions

- Dual POC approach with ALT1 and dIgA/IgA2 tests shows promise in screening for treatment eligibility in Ethiopia
- May require optimis
  - Confounder of
- Very high sensitivity - so the patients who ar
  - Viral load is ex
- Future studies warr