Potential utility of the Genedrive point-of-care test for HCV RNA detection

In an article in *Gut*,[1] Lemoine and Tillman reviewed our recent publication on the development and validation of a novel point-of-care (POC) HCV viral assay.[2] They acknowledge that Genedrive is the only CE-In Vitro Diagnostic-qualified device for HCV detection, and that the

limit of detection (LOD: 1406–3203 IU/mL) permits identification of the vast majority of HCV chronic cases.[3] However, they emphasise some limitations of the study and Genedrive. One limitation highlighted is the need for plasma which is still required for 100% of HCV clinical tests. Nevertheless, recent studies demonstrated microfluidic plasma separation without centrifugation[4] or with low-cost hand-powered paper centrifuges.[5] It is feasible to foresee such devices overcoming the need for conventional centrifuges and facilitating Genedrive testing.

They also question whether 15 µL of plasma can be obtained by fingerprick. Published studies report 20–25 µL per drop of blood,[6] so 1 drop should be sufficient. Furthermore, devices to collect 100 µL of blood from a single fingerstick are now available.[7] Technology evolves rapidly to make new tools available which may further facilitate the use of the Genedrive test. The Xpert technology (Cepheid) illustrates these constant improvements, with the latest version requiring only 100 µL blood,[7] in contrast to the current 1 mL plasma. Whether Genedrive could be used for monitoring treatment responses was not addressed in our initial analysis but is part of ongoing studies. In reference to cartridges surviving extreme temperatures, while formal stability studies are ongoing, test reagents are certified at 2°C–28°C for 12 months, permitting cold chain-free storage. Regarding early separation of plasma being required to prevent HCV RNA degradation, it is stable in EDTA whole blood for 24 hours at room temperature and 4 days at 4°C[8]. Although our study was not designed to test this, a large time between sample collection and testing was reported within African samples. For cases where high haemolysis was observed, there was no loss of performance, but additional studies are required.

Lemoine and Tillmann highlight that 26/1055 samples required retesting with only 16 giving definitive results. If these ambiguous results are included, sensitivity (99.2%) and specificity (98.8%) are still very good. For the 10 samples without a result, 6 were HCV_{pos} with viral loads close to LOD. Because a very small sample volume is used, and 2/3 replicates must be positive, in cases of low viral load, the absence of a viral particle ultimately affects the diagnostic accuracy. For the four HCV_{neg} indeterminate samples, we can speculate on the possible effects of interfering substances. While a number were tested, we did not identify any that impacted Genedrive's performance. Nonetheless, there are many compounds that could potentially affect assay function, as recently encountered for an IL28B single nucleotide polymorphism (SNP) POC assay.[9]

While the authors are enthusiastic for GeneXpert, which has advanced the diagnostics options for HCV, they fail to mention one major limitation: the use of toxic cartridges requiring double cylinder high temperature (≥850°C) incineration, which is challenging to decentralise, in particular in resource-limited settings.[10] In contrast, Genedrive contains non-toxic materials, making waste management much easier.

We agree that a real-life study in POC conditions is required, including a detailed cost analysis. However, as stated in our original discussion, we maintain that this study was a required step for development and validation of the Genedrive HCV test. It has helped to establish global distributions in Africa and Asia generating real-world data and will encourage new developments to address this clinical need. It has resulted in a novel, easy-to-use, portable platform for decentralisation of HCV testing, which may have a positive impact on the continuum of care from diagnosis to treatment.

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