**Title:** High speed video analysis is accurate in the diagnosis of primary ciliary dyskinesia

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We stand by our study1, demonstrating that high-speed video analysis (HSVA) has good sensitivity and specificity to support PCD diagnosis. We can therefore provide provisional feedback to patients on the day of testing, whilst awaiting further confirmatory tests. Where there were methodological challenges, these are clearly documented in the manuscript; they were not errors. We strongly advocate a combination of several tests to make a diagnosis 1 2. The strengths of HSVA are it (1) can identify likely cases on the day, (2) is a functional test of dyskinesia and (3) adds to the certainty provided by nasal nitric oxide (nNO) that a diagnosis is unlikely. We are uncomfortable with the North American approach of excluding a diagnosis based on nNO alone3; moreover nNO is not easily performed on pre-school children.

To address issues raised by Shapiro et al:

1. Selecting six videos did not introduce bias. As reported, 120 patients were randomly selected. Each had 6-10 videos, difficult or interesting patients had more videos. To blind the scientists to “difficulty or interest”, an independent technician choose six technically acceptable videos (**not** excluded on ‘difficult to diagnose’ criteria).
2. We assessed the accuracy of HSVA on the day of testing, as a means to expedite patients receiving provisional counselling and treatment. Within our paper we advocate further assessment by repeated HSVA and/or reanalysis following culture, TEM, genetics and immunofluorescence testing1. A positive diagnosis of PCD should only be made based on confirmatory genetic or transmission electron microscopy (TEM) analysis as per international guidelines2,3.
3. Since genetic testing fails to identify 20-30% of patients, it cannot exclude a diagnosis2. Similarly TEM fails to identify 20% of patients2. Repeated HSVA identifies patients with dyskinesia associated with normal genetics and TEM. These patients should be considered ‘highly likely’ until further diagnostic advances provide a confirmatory diagnosis2.
4. In the absence of a ‘gold standard’ diagnostic test, we used two imperfect reference standards4,5. The strengths and limitations of each are clearly described in the manuscript.
5. In our hands HSVA can detect *DNAH9*, *GAS8* and *HYDIN* mutations (data not shown). Contrary to Shapiro et al’s letter these all have abnormal beat patterns as described in their original manuscripts. CCNO and MCIDAS are strongly suspected where ciliation is repeatedly poor, particularly following culture. We test genetics where PCD is suspected following HSVA +/- nNO.

In summary, everyone agrees that all current methods for diagnosing PCD and for assessing diagnostic accuracy are imperfect and require further development and scrutiny. We were transparent about diagnostic and statistical methods and their limitations, and confirm our approach was valid. The study is a significant step in the plight to develop an evidence-base to diagnostic testing. Waiting for a ‘gold standard’ will not allow us to move forward in the near future.

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