

Moji Ajeneye and Graeme Tunbridge
Medicines and Healthcare products Regulatory Agency
By email

12 March 2021

Dear Graeme & Moji,

As biostatisticians, we write to alert you to potential harm because PCR-adjudication is absent from the current asymptomatic screening by use of lateral flow tests in secondary schools.

The risk of false positives is a key concern because NHS Test-and-Trace fails to mitigate that risk by confirming LFT-positives by PCR. (As an inherent statistical problem in mass screening in the context of low prevalence, repeated testing of positive results is the usual way to deal with this.) Secondly, the likely low positivity rate **currently** with the INNOVA test in school (and other) settings raises concern about an insufficiently understood need to demonstrate the INNOVA LFT's sensitivity in each new context: specifically for asymptomatic secondary-age children.

As with any test, when disease prevalence drops, positive predictive values drop, which increases the risk of harm (**from unnecessary self-isolation**) in those who screen as LFT-positive. We understand that the original MHRA Emergency Use Approval dates from December 2020 when disease rates were high, and the risk of INNOVA-positive being a false positive was low.

Since the end of January 2021, disease prevalence has been falling, and greater care is needed **currently** to ensure that those who are INNOVA-positive are not false positives. Given that the consequence of LFT-false positivity (ie in the absence of PCR-adjudication) is curtailing individual freedoms, with legal implications not only for the secondary pupil index case but also for family-members and class-mates, the absence of PCR-adjudication needs **urgent** re-consideration.

To mitigate the risk of harm is straightforward: immediately confirm LFT positives with a PCR-test. Self-isolation and contact-tracing are initiated by LFT-positive but are rescinded, tracing rolled-back, if the confirmatory PCR is negative.

Absence of mitigation (dropped by DHSC with effect from 27 January) **is a particular issue for LFT-screening in secondary schools.** In secondary schools, the implications of LFT-false positive extend to the child's or teacher's family and their school bubble; and to the households of the children in the bubble who need to take time out to look after their children who are suddenly back at home. The number of people affected by one false INNOVA-positive could easily extend to 100.

In summary, failure to mitigate at a time of lower infection prevalence as secondary pupils return after weeks of lock-down appears, and is, illogical. Families who have arranged their own PCR-adjudications are astonished: in particular, when parents have experienced INNOVA-screening **with PCR-adjudication** in their workplace.

Such asymptomatic screening of children, with the safeguards (here PCR-adjudication) so blatantly disregarded, is unprecedented. Children shift to twice-weekly at-home-screening soon, which does have PCR confirmation built-in.

However, the 10-day quarantine imposed on pupils and families because of LFT-false positives during 8-19 March will impact on children's schooling for the next two weeks; and on families' willingness for their children to participate in twice-weekly at-home-screening after 19 March 2021.

An immediate requirement by MHRA, as regulator, for secondary pupils' LFT-positive results to be confirmed by PCR and for families' self-isolation to be curtailed on the basis of a timely PCR-negative adjudication would have immediate benefit: potentially, for thousands of families in England with secondary-age pupils.

We note that the low rate of positivity for the INNOVA screening test, particularly in school children, is, in itself, a surprise when considered in light of the prevalence and incidence data from ONS and REACT, as well as the case numbers detected from PCR testing. This a **red flag** that the INNOVA test may be performing at a lower level of sensitivity than expected in school-children, who are not "young adults". The test's sensitivity for screening asymptomatic secondary pupils deserves immediate investigation, as recommended by the Royal Statistical Society's COVID-19 Taskforce, <https://rss.org.uk/RSS/media/File-library/News/2021/RSS-statement-on-surveillance-in-schools-5-March-2021.pdf>.

In summary, an urgent concern – **unless mitigated** - is the potential harm from LFT-false positives when screening secondary pupils. We should be grateful if the MHRA will consider a requirement for PCR confirmation to mitigate the harm that is likely from these tests in screening asymptomatic secondary school children in England.

Yours sincerely,



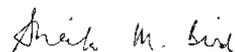
Professor Sylvia Richardson
President



Professor Deborah Ashby
Past President, Co-chair of Diagnostic Testing Working Group



Professor Jon Deeks
Royal Statistical Society, Co-chair of Diagnostic Testing Working Group



Professor Sheila Bird
Royal Statistical Society, Member of COVID-19 Task Force