Estimation of “True Incidence” of Polio: Some Methodological Issues

A recent report(1) has claimed that the true incidence of polio (due to wild polio virus) in India was 1625 in 2006 and not 674 as officially notified. The authors’ notions of “true incidence” and “misclassification” call for careful examination as they challenge the sensitivity of Acute Flaccid Paralysis (AFP) surveillance. Our methodological objections are as follows:

1. Computation of probability needs to be based on the assumption that the trials (denominator) are independent of each other and the outcomes (numerator) are independent of each other. In this case two stool samples taken from a child is incorrectly considered as independent samples. Therefore, number in the denominator i.e., 1286 which comes from 643 children (i.e., two samples per subject) are not independent; and the outcomes (growth of virus) on two samples from a subject are also not independent. If a child is truly a case of polio then the chances of getting virus grown on both the samples is more, though not always. The authors have considered that “both sample results are independent of each other”. For the 148 cases that had one sample negative for WPV, a sample testing positive for pild polio virus (WPV) in Round I implies that the sample from the same AFP case was negative in Round II and vice versa. Therefore, it is incorrect to consider two stool samples taken from the same child as independent samples(2).

2. For those 148 children where one of the two samples was negative, labelling these 148 samples as ‘false negative’ is incorrect. While labelling a sample as false negative there is always a reference. These 148 samples can be labelled as false negative only when there is a superior method than the method in question to show that these 148 samples actually had the virus that was not grown by the candidate method. It is incorrect to label one of the stool samples as ‘false negative’ by retrospectively considering the virological status of child (which is based on any of the stool samples being positive). For any analysis of the performance of a diagnostic test the units of study/analysis must remain the same i.e. both the test result and the disease status have to be on the same unit of study. In this case, there are two units (child and the stool sample) and the authors have used these two units interchangeably. While labelling a stool sample as false negative they have compared the growth of virus at the stool level in the second sample and the true disease status at the child level. Two stool samples are sent for the culture of polio virus to increase the sensitivity of the test. Other examples of similar approach are: sputum testing in RNTCP and stool examinations to diagnose worm infestation. In the two-by-two analysis, for sensitivity and specificity all four cells, including the one which includes disease negative and test negative subjects/samples, should be considered(3). The authors have not included ‘both negatives’ (24,771 cases); the probability estimates would therefore be biased upwards with compromised validity.

3. The authors have retrospectively computed ‘two’ sensitivity figures—one, if a single sample was received and another, if two samples are received. However, it is not feasible to estimate the sensitivity of the yield of polio virus from the stool collected during AFP surveillance in its current form because no gold standard is used for the purpose. Proxy markers like enterovirus isolation rates indicate well functioning surveillance system.

‘Insensitivity’ is not an appropriate jargon in this context. While all efforts that can enhance our understanding of virological classification are welcome, careful attention needs to be paid to methodological details. The assertions made in the report need careful re-examination.
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REFERENCES


Reply

1. We explicitly stated in our paper that we have assumed that the chance of one of the two stool samples being negative is independent of the result in the other while calculating the ‘false negatives’. Cases of polio may be misclassified as ‘non-polio AFP’ because culture techniques are not perfect, methods used for collection, storage and transport of stool samples are sub-optimal, and viral shedding is not continuous. The fact that the excretion of virus in the stool is intermittent adds credence to our assumption of the independence between two stool specimens.

However, we agree with the correspondents that ‘if a child is truly a case of polio, then the chances of getting virus grown on both the samples is more’. Our assumption of independence of the two samples is, therefore, likely to underestimate (rather than overestimate) the number of polio cases misclassified as non-polio AFP. Dasgupta and Chaturvedi are concerned that our estimates put the number of polio higher than the ‘officially notified’ figure. Their methodology would in fact, erode the credibility of the official figure even more!

2. We agree that where two stool samples are sent for the culture of polio virus it increases the sensitivity of the test. We were concerned that many children had only sent in one sample for testing and in these children the sensitivity of the test is decreased. Inclusion of the ‘24,771 cases when both tests were negative’ in a two by two analysis is necessary if one is interested in calculating the sensitivity, specificity etc., which was not our aim. We tried to derive the true number of polio cases in the community, by estimating the ‘missed’ cases.

3. We agree that it is not feasible to estimate the sensitivity of the yield of polio virus from the stool collected during AFP surveillance in its current form because no gold standard is used for the purpose. However we have our reservations about the proxy markers and here too there is no gold standard estimates for the correspondent to make this claim!

We are as concerned as the correspondents, to ensure that polio is eradicated from our country at the earliest. However, effective program planning needs accurate data and not ‘feel good figures’. We undertook the present exercise only to allow a more realistic post intervention figure to emerge. It is not perfect, but is a conservative estimate. The method suggested by the correspondents would have yielded higher estimates.

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