John Dharmapalan

**Review comments**:

Reviewer 1;

1.The paper is very relevant to the fields of bioethics and medical ethics in the developing countries.

2.The interpretation is well-developed and could influence practice and policy.

3.Some suggestions for the authors have been added below:

a). Would the authors like to comment on whether the decision to go the OPV way was itself an ethical decision instead of having taken the IPV route? Why are these ethical concerns being expressed at the time of ‘polio endgame’ only?

b). Cuba is one country that has not taken the IPV route at all. How have they justified the ethics of it, will the authors like to explore that?

c). A rate of 4 per million doses of VAPP was perhaps known even early during the use of OPV. Was this figure not high enough to raise enough doubts and forced the GPEI to go the IPV way.

d). The authors have not commented at all on the reported Non-Polio Acute Flaccid Paralysis problem. It was reported that the rates of NPAFP we saw in India were unusually high. Also, they correlated with the rounds of OPV vaccination carried out in the country. It would be fitting if the authors comment on this ignored issue in addition to the problem of VAPP and cVDPV.

e). The authors mention the cVDPV outbreaks in PNG and Syria. Lately there have been several more outbreaks, especially in many countries of Africa such as Nigeria, Congo, Somalia among others and Indonesia in Asia. This merited the WHO to declare Polio as a public health emergency in May 2019 <https://www.who.int/news-room/detail/29-05-2019-statement-of-the-twenty-first-ihr-emergency-committee> . The response from them does not mention speedy replacement of OPV with IPV. Would the authors like to update their paper with this additional information and also comment on the response of the WHO in this entire saga? And their ethical poverty?

f). I suggest that authors discuss the limitations that poor countries face in taking decisions on vaccine choice and coverage as well as the ethics of technical multinational bodies such as WHO and financial- technical bodies such as GAVI and the UNICEF in determining vaccine policies and practice across the world.

--------------------------------------------------------------------------------------------------------------------------------------Reviewer 2:

1.This is a good paper.

2. In the first introductory paragraph, the authors view public health as a venture that benefits many individuals. The benefits are more than just for individuals. There are collective benefits or "common goods" that accrue to more than just individuals. This concept is key to vaccination ethics.

3. The authors should present the idea that OPV is logistically easier to administer than IPV. In pulse polio campaigns, OPV is much easier to administer. This is especially an important consideration in countries like India with severe health human resource crisis.

4. In the cases reported by the author - of outbreaks of vaccine derived polio - the OPV led to outbreaks because of declining coverage of vaccination. Isn’t it important to maintain high coverage rates when the vaccine is at a risk of vaccine derived polio? The authors should consider the argument of - ease of administration attributing a major benefit for a national-wide program - however the important clause being maintaining high coverage rates.

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Response from Authors

Reviewer 1.

We appreciate the first two comments which are encouraging for us as authors.

3.a

The reviewer asks if the decision to go the OPV way was itself an ethical decision. This is a highly relevant question. The sequence of events was that WHO first chose OPV exclusively in EPI in 1974 and continued the same policy as the Resolution for global polio eradication was passed in 1988. We have pointed out the ethical problems of the exclusive use of OPV in EPI in an earlier paper (John TJ, Dharmapalan D. An ethical appraisal of the choice of vaccines against poliomyelitis. IJME 2018; 4: 26-29). In the paper under review we again state that the exclusive use of OPV in eradication was both unethical and unscientific.

The Reviewer asks why these ethical concerns are expressed only now, when End Game is under way. We agree that this paper could have been written earlier, but we believe it is better late than never. This paper is essential now, as we realise that the inordinate delay in achieving eradication is partly due to the choice of exclusive use of OPV. Moreover, as we argue, unless WHO shifts policy, eradication will be further delayed.

3.b

The reviewer is astute in asking about Cuba. By the exclusive use of OPV Cuba had eliminated all wild virus polio decades ago. However, like all other countries using OPV exclusively, Cuba also faces the problem of VAPP (Resik S, Mach O, Tejeda A, Galindo MA, Sutter R. Cuba’s Scientific Contributions to Global Polio Eradication. Int J Environ Res Public Health. 2018 Aug; 15(8): 1755) and remains at risk of vaccine-derived poliovirus emergence and spread if ever OPV use declines for any reason. A lot of research on IPV has come from Cuba, indicating a shift in policy is likely.

Cuba is an island country of 10 million people. They give OPV twice every year, 6 months apart, in nationwide simultaneous campaigns. Coverage is near 100%. If any VDPV emerges, the next campaign will interrupt it. So Cuba is not a replicable model.

As we explored ethics, we realise that no country had been advised by WHO for an ethical assessment of choice between OPV and IPV. We assume that as a dictator-ruled country, ethics was not applied in Cuba. Probably they also believed that public health need not examine ethics.

3.c

The reviewer asks why the high frequency of VAPP was not taken into account while making an exclusive OPV policy. We believe that was most probably because ethics was not applied, perhaps under the belief that ethics did not apply in public health as we point out in Introduction. We thank the reviewer for raising this pertinent question, which reinforces the necessity of a study on ethics of vaccine choice in polio eradication.

3.d

This is a very relevant question, if truly the increase in non-polio AFP in India is “caused by” OPV campaigns. The causality has not been proved. Therefore we did not want to put in our paper something about which controversy can arise. All our arguments are non-controversial.

3.e

We thank the reviewer for highlighting the magnitude of cVDPV problem. We know that cVDPV outbreaks have occurred in the last many years in some 30 plus countries – in some repeatedly – and we wondered how to handle that in an ethics paper.

We chose to highlight the problem and count the numbers of vaccine-related polio versus wild virus polio, and for ease of understanding we created the graph. The vaccine-related polio subsumes cVDPV cases in many countries. WHO does put out cVDPV cases in the public domain but not VAPP numbers. We believe that the graph will suffice to illustrate the “consequences of going the unethical way”.

3.f

The reviewer has touched a sensitive issue – that poor countries trust WHO and such international bodies, and for that reason they should be doubly cautious. If poor countries were autonomous in decision making, and had good leadership, global polio eradication would have had a different course in history. However, focusing on ethics, we have not considered it necessary to bring in this extraneous issue – important issue but extraneous to the ethics of public health.

In summary, we appreciate all comments and we believe we have covered all ethics-related concerns in the paper itself.

Reviewer 2

We very much appreciate the first two comments. The second comment reinforces the premise on which we wrote the paper.

3.

This is an interesting viewpoint. OPV is easier to give than IPV. That is the common perception. That is true only if IPV is given by separate injection and not as quadrivalent (DPT plus IPV) or pentavalent (DPT+Hib+IPV) or hexavalent (DPT+Hib+HBV+IPV). Be that as it may, when ethics is violated, ease of giving cannot be used as an argument for choosing an unethical product.

Regarding cost, no one has done a cost-benefit or cost-effectiveness analysis for IPV versus OPV. Two national pulse campaigns have been suggested among experts, as costing equal to full IPV based programme. Dose for dose OPV is much cheaper but 10-20 doses versus 2 or 3 doses make IPV cheaper overall for the programme. The global programme is consuming 1 billion US dollars every year for the exclusive OPV policy. An IPV based eradication programme might have saved not only time but also money.

If the ethical product is unaffordable, for argument’s sake, but unethical product is affordable, how does one choose? “Relativity applies to physics – not to ethics”, so said Einstein.

4.

The reviewer is right in pointing out the need for high coverage and sustained campaigns even after wild viruses are eliminated. If the community immunity drops due to some problem – including fatigue, pockets of under-immunisation etc, cVDPV will emerge. That is why we illustrated with Syria and Papua New Guinea with cVDPV outbreaks. In other words, OPV is like tiger’s tail – can’t let go. So the world will be forced to continue polio eradication for ever. That of course is untenable, continuously creating VAPP in the polio eradicated world.

In summary we appreciate all comments, and believe that the pertinent issues have already been covered in the paper.

If the Editor wishes that we expand the paper in some particular aspect, we will be happy to do so.

We believe the paper is complete in itself and is a forceful spotlight on a blind spot in this major public health programme.