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Short communication

Campaigns with oral polio vaccine may lower mortality and create unexpected results

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ABSTRACT

Three studies from Guinea-Bissau found conflicting effects of OPV-at-birth (OPV0) on child survival. One study from 2004 suggested excess male mortality among children receiving OPV0 compared with children receiving NoOPV0 during a period of shortage of OPV. However, two subsequent studies showed beneficial effects of OPV0. In 2004, two national OPV-campaigns had been conducted in Guinea-Bissau. In a reanalysis of the 2004-study, in a survival analysis the age-adjusted mortality rate of study participants was 67% (95% CI = 42–81%) lower after the OPV-campaigns than before the campaigns. In the OPV0 group only 22% (655/3031 person-years (pyrs)) of follow-up time was "after" the OPV-campaigns whereas 55% (473/859 pyrs) of the time in the NoOPV0 group was post-campaign ($p < 0.0001$, Chi^2). Censoring for OPV-campaigns in the original study removed excess male mortality and made the three studies more homogeneous. Overall, there is now considerable evidence that OPV, like other live vaccines, has important beneficial non-specific effects.

1. Introduction

In 2004, within a randomised controlled trial (RCT) of neonatal vitamin A supplementation (NVAS) versus placebo in Guinea-Bissau, West Africa [1], we experienced several periods in which oral polio vaccine (OPV) was missing. For all trial children it was registered whether they received OPV-at-birth (OPV0) or no OPV0 (NoOPV0). We previously analysed this "natural experiment" to explore the effect of OPV0 on overall infant mortality. Receiving OPV0 was associated with increased mortality for males (OPV0 versus NoOPV0, Hazard ratio (HR) = 2.82 (95% CI = 1.41–5.65), whereas it made little difference for females (HR = 0.87 (0.53–1.44), p = 0.006 for interaction) [2].

We subsequently tested this observation in another "natural experiment" when OPV was missing in 2007 [3], and in an RCT of OPV0 from 2008 to 2011 [4]. These subsequent studies did not confirm a negative effect of OPV0 in males. In the second "natural experiment" the HR comparing OPV0 versus NoOPV0 in males was 0.63 (0.24–1.67) [3], and in the RCT it was 0.72 (0.47–1.10) [4], the three results being statistically heterogeneous (Fig. 1A).

We subsequently observed that OPV campaigns have strong beneficial effect on survival. In an analysis of 15 OPV campaigns from 2002 to 2014, the mortality rate was lower after OPV-only campaigns than before, the age-adjusted HR being 0.81 (95% CI = 0.68–0.95). With each additional dose of campaign-OPV, the mortality rate declined further (0.87 (0.79–0.96) per dose) (submitted).

Therefore, we speculated that the heterogeneous effects of OPV0 observed in the three Guinean studies could be due to differences in the intensity of OPV campaigns [4]. In 2004, national OPV campaigns took place in October and November 2004. Some periods with missing OPV0 presumably occurred because the Guinean immunization programme saved OPV for the campaigns; hence, many children, who did not receive OPV0, subsequently received several doses of campaign-OPV. During the "natural experiment" in 2007 [3], there were no OPV campaigns. During the conduct of the RCT of OPV0 [4], there were many OPV-campaigns; if we censored for these campaigns, the HR comparing OPV0 versus NoOPV0 in males became more pronounced, changing from 0.72 (0.47–1.10) to 0.55 (0.32–0.95), suggesting that the OPV-campaigns had masked a beneficial effect of OPV0 in males [4].

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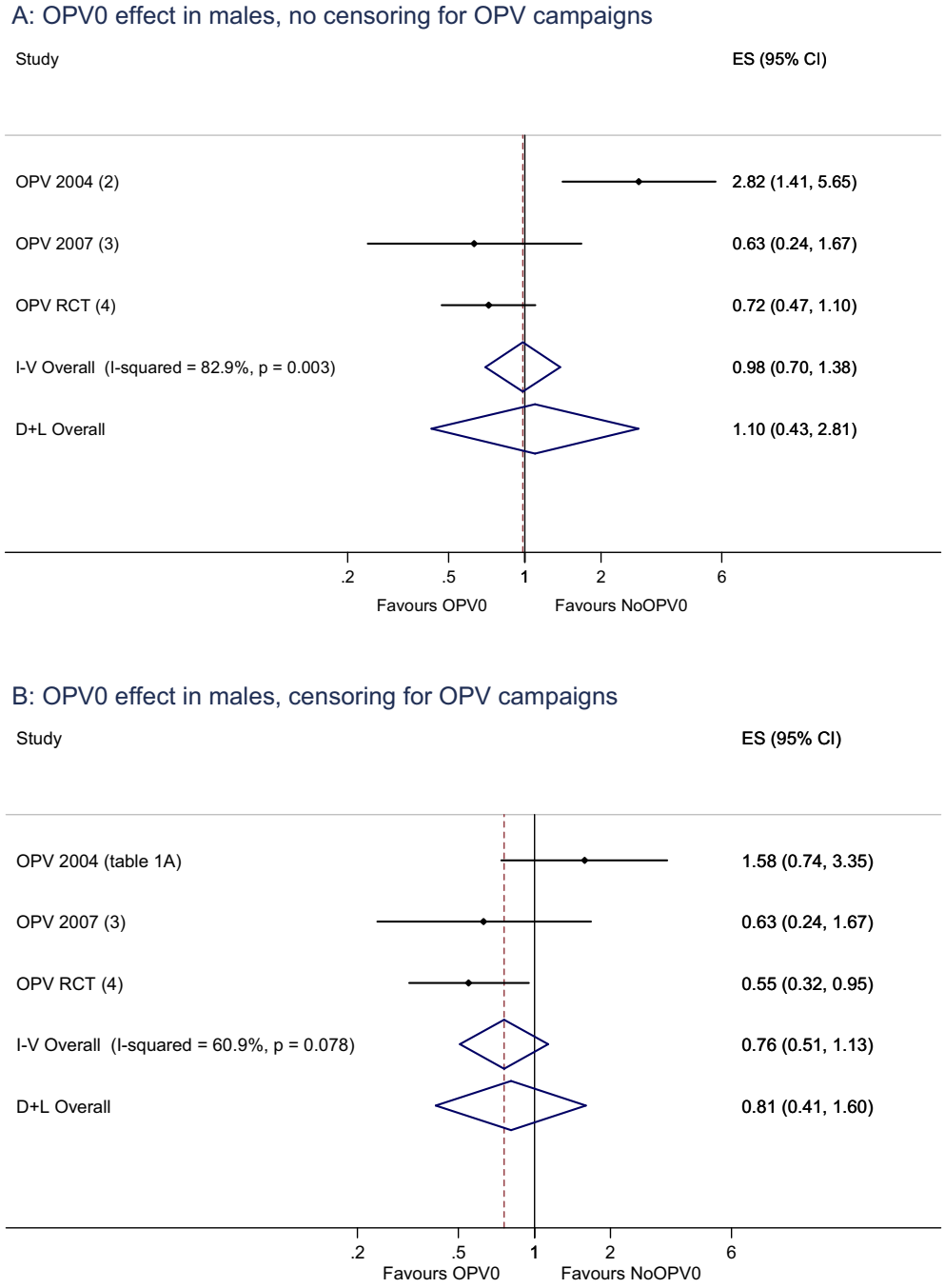

Fig. 1. The effect of receiving OPV-at-birth (OPV0) or not (NoOPV0) in males in three studies (A) without and (B) with censoring for subsequent OPV campaigns. Fixed and random meta-estimates presented.

In the present reanalysis of the "natural experiment" in 2004, we explored whether the OPV-campaigns could explain the observed increased mortality after OPV0 in males.

2. Methods

The NVAS trial was conducted at the Bandim Health Project's Health and Demographic Surveillance System (HDSS) site (www.bandim.org) in Bissau, Guinea-Bissau from 13 November 2002 to 29 November 2004. The trial has been described in detail elsewhere [1]. Briefly, normal-birth-weight newborns were randomised to NVAS or placebo together with BCG vaccination. At the time of randomisation, it was noted whether the child received OPV0 or not. Children were followed through the HDSS and at a special home visit at age 12 months.

2.1. Original analysis of OPV0 [2]

OPV was missing in Bissau during several periods of 2004: (1) from early-February 2004 to early-June 2004, (2) briefly in late-June 2004, and (3) from mid-October 2004 to the trial enrolment ended on 29 November 2004. Two national OPV campaigns took place 18–21 October 2004 and 18–21 November 2004. During the first campaign, OPV was given alone to all children <5 years