Analysing the effects of OPV campaigns

Executive summary

At the Bandim Health Project HDSS, we have studied the effects of the national campaigns with Oral Polio Vaccine (OPV) and found very beneficial non-specific effects; the OPV campaigns have the reduced all-cause mortality rate by 15-25%. We have subsequently confirmed this observation in collaboration with HDSS sites in Ghana, Burkina Faso and Bangladesh. We have developed a generic protocol for analysing HDSS data. The present proposal describes the main outline of the analyses and seeks collaboration with other HDSS sites interested in participating in these analyses.

If your HDSS is interested in collaborating, please contact Sebastian Nielsen (senielsen@health.sdu.dk) and Peter Aaby (p.aaby@bandim.org).

Introduction

The world has experienced a major decline in child mortality of more than 50% in low-income countries in the last 2-3 decades. In Guinea-Bissau, in the period 2002-2014, the Bandim Health Project (BHP) has found a 25% (95% confidence interval: 15-33%) reduction in all-cause child mortality after Oral Polio Vaccine campaigns (C-OPV) among children below 3 years of age and that C-OPV had a far better effect than other campaigns (1). Studies from Burkina Faso and Ghana have also shown reduced child mortality after C-OPV (2,3). The results from Bandim have recently been confirmed in data from Chakaria, Bangladesh, with a reduction in mortality rate of 32% (10-49%); again the effect of C-OPV was much stronger than the effects of other campaigns (4). Since

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there has been no polio infection in Guinea-Bissau, Ghana and Burkina Faso, and very little in Bangladesh, these studies strongly suggest beneficial non-specific effects of OPV.

As polio is soon to be eradicated and OPV subsequently stopped (or replaced with IPV), it is urgent that we investigate the effects OPV campaigns and find ways to remedy the potential negative effects of stopping the use of OPV. **We would therefore like to know whether you and your site is interested in collaborating in an analysis of the impact of C-OPVs on child mortality levels.**

We have attached the analysis from Bandim and Chakaria to give you an idea of what kind of analysis we would like to do.

Below we have defined the main features of the analysis and which variables it is necessary to have to conduct the analysis.

Methods

Intention-to-treat campaign participation

The main analysis will be an intention-to-treat analysis of campaigns where all eligible children in the HDSS will be assumed to have received the vaccine on the first day of the campaign.

Secondary we may also consider data on individual campaign participation if that has been collected at any site. We will use the landmark approach, only including children from the first day they have been registered, secondary sensitivity analyses may include children followed retrospectively.

Outcomes

All-cause mortality will be the primary outcome. Secondary outcomes will include censoring for accidents and by cause of death. If available, we may later also consider using morbidity data, i.e. hospitalisations and consultations.

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Analysis period

The main analysis will include all available data from the period where the site has mortality data. Should there be any major changes during the study period, the analysis may be stratified accordingly;e.g. the Bangladesh data collection changed in 2012, and data was analysed stratified for the two periods (4).

Statistical analyses

All analyses will be conducted using multivariable Cox-proportional hazards models adjusting for differential trends of outcomes variables within age groups (e.g. 0-5 months, 6-11 months, 12-23 months 24-35 months, and 36-59 months if children were followed to 5 years of age) and mortality trends over calendar time.

Main analysis will be the effect of OPV-alone campaign adjusted for other campaigns and include all children aged 1 day to 3 years or 5 years of age.

Secondary analyses include stratification by sex, the effect of OPV co-administered with VAS, effect within different age groups, by season at risk, socio-economic risk factors, the number of campaigns received, other campaigns, strain of OPV, most recent campaign, by most recent received routine vaccine, etc.

Campaign information

We will use the first date of all health interventions for children below 3 years (or 5 years) of age conducted in the analysis period within the HDSS site. We will need information on which campaigns were conducted and to which age groups of children. This can usually be obtained at the HDSS site, or with the local or national health authorities. Please see in the papers from Bandim and Chakaria for lists of such campaigns.

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We will use information on OPV campaign from the international WHO office databases to verify campaign dates. If no information is available from the HDSS site, local or national health authorities, then we will use the information from these global databases in the main analysis.

Data and variables

With campaign dates and the following few variables, the main analysis of changes in child mortality rates can be performed:

Main variables		
Name of variable	Description	Type
ID	Identification number of individual	Integer
DOB	Date of birth	Date
SEX	Sex of the child: 1 = Male 2 = Female	Integer
REGDATE	Date of the first registration of the child	Date
EXITDATE	Date of censoring (whichever comes first of migration, death or end of follow-up)	Date
STATUS	Vital status at EXITDATE: 1 = Alive 2 = Moved 3 = Dead	Integer

Publication strategy

Any collaborators from the HDSS will be invited to join publications on data from their own HDSS and for site specific publications the main collaborator will be invited to be last author. For potential future combined meta-analyses of data, the primary collaborator(s) will be invited to participate in the publications.

All publications will be submitted to international peer-reviewed journals.

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References

1. Andersen A, Fisker AB, Rodrigues A, Martins C, Ravn H, Lund N, Biering-Sørensen S, Benn CS, Aaby P. National immunization campaigns with oral polio vaccine (OPV) reduce the general all-cause mortality rate: An analysis of the effect of campaign-OPV on child mortality within seven randomised trials. Front Public Health 2018;6:13
2. Schoeps A, Nebié E, Fisker AB, Sié A, Zakane A; Müller O, Aaby P, Becher H. No effect of an additional early dose of measles vaccine on hospitalization or mortality in children: a randomized controlled trial. Vaccine 2018, 36: 1965-71
3. Welaga P, Oduro A, Debpuur C, Aaby P, Ravn H, Andersen A, Binka F, Hodgson A. Fewer out-of-sequence vaccinations and reduction of child mortality in Northern Ghana. Vaccine 2017 Apr 25;35(18):2496-2503
4. Nielsen S, Khalek MA, Benn CB, Aaby P, Hanifi SMA. National immunisation campaigns with oral polio vaccine may reduce all-cause mortality: An analysis of demographic surveillance data in rural Bangladesh from 2004 to 2019. (Submitted)
5. Chumakov K, Benn CS, Aaby P, Kottilli S. Gallo R. Can existing live vaccines prevent COVID-19? Science 2020;368:1187-9

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