



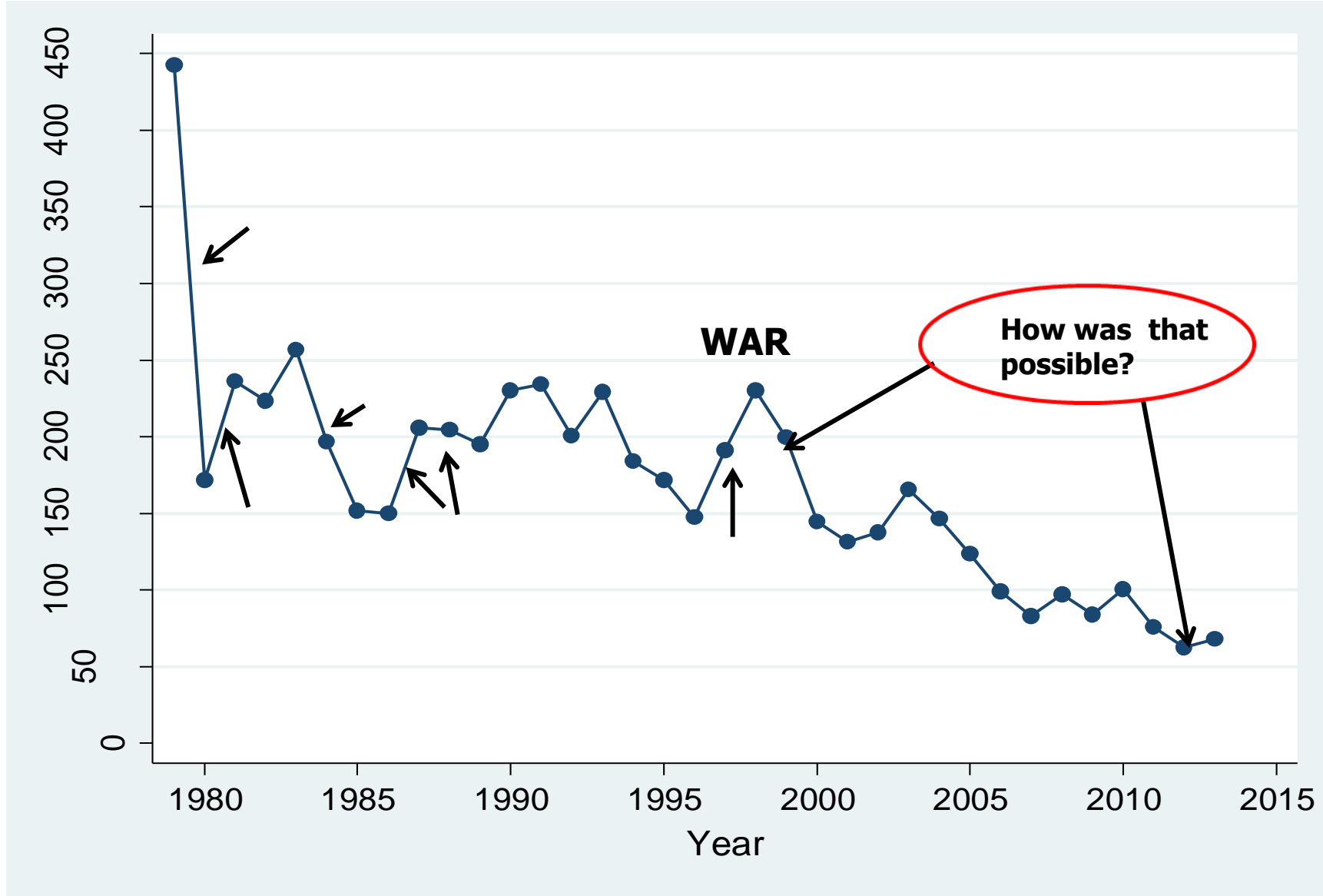
# **National vaccination campaigns with OPV and H1N1: Contrasting effects on overall mortality**

**Guinea-Bissau has had the highest mortality in the world**

**Lancet 2014**

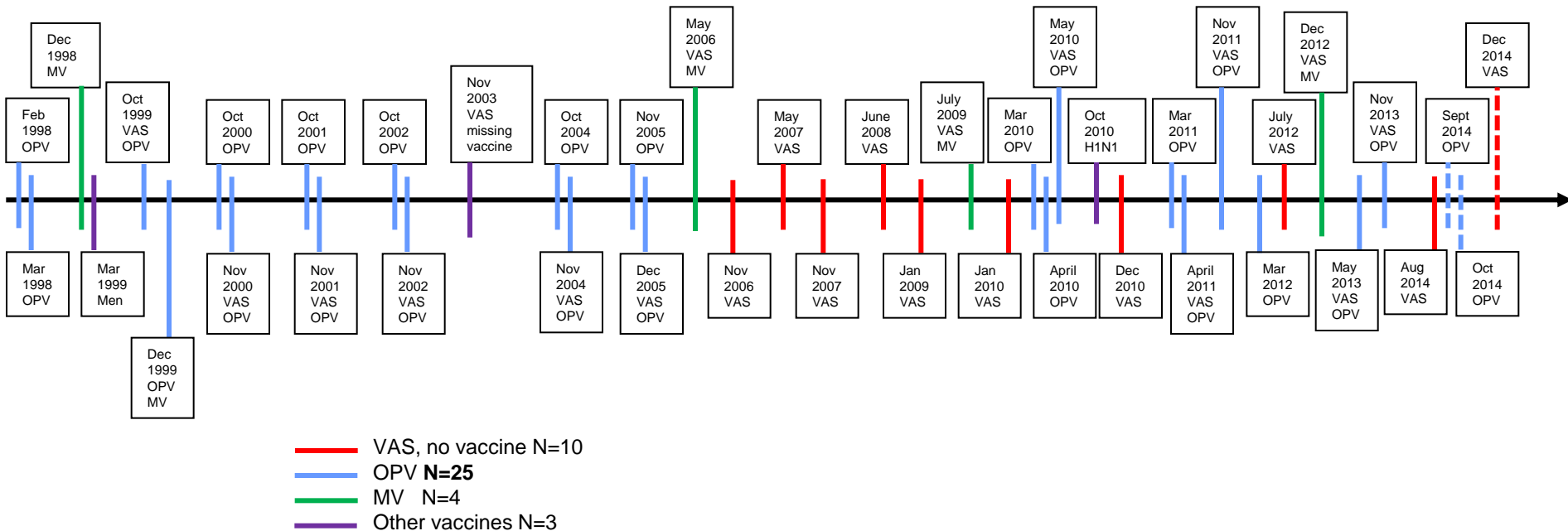
**"In 2013, child mortality rates ranged from 152.5 per 1000 live births in Guinea-Bissau to 2.3 per 1000 in Singapore."**

# But we reached MDG4



**Bissau reached MDG4: 236/1000 in 1990 to 68/1000 in 2013**

# 17 years of campaigns in Guinea-Bissau



**Effects of campaigns have not been measured: Polio and measles are not major killer diseases now so no effect on child survival expected**



## Polio campaigns during the last 15-20 years: No study

### First OPV campaign in Bissau 1998 - Mortality March-Dec 1998

OPV campaign in 1998 – age groups	Mortality for 1-2 doses of OPV	Mortality for No OPV	Mortality rate ratio (MRR)
0-5 months	5.1%(28/553)	8.0%(19/238)	0.56 (0.3-1.0)
0-4 years	3.7%(143/3898)	5.8%(46/798)	0.67 (0.5-0.9)

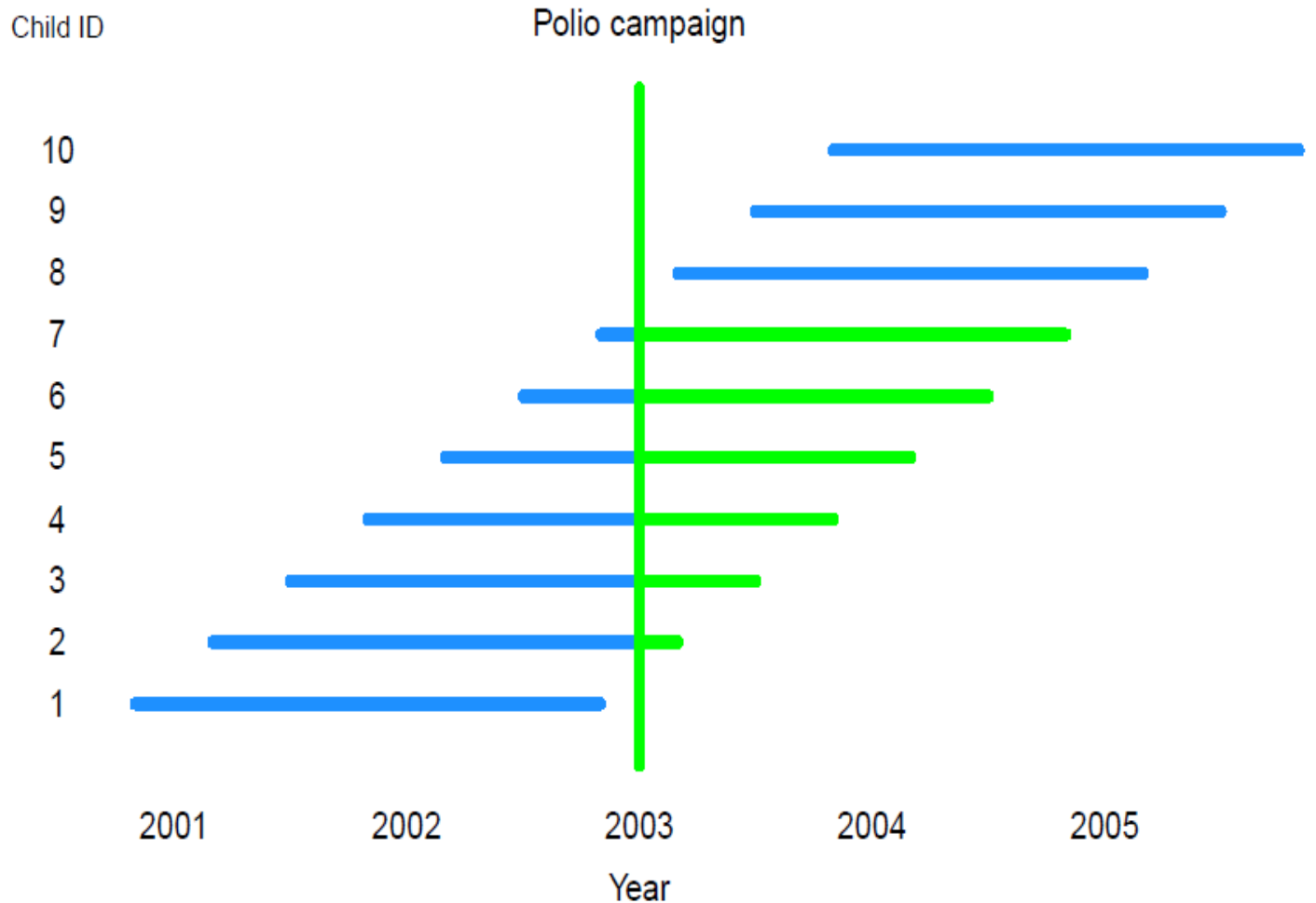


**In this period the Bandim Health Project has conducted 7 randomised clinical trials with mortality as the main outcome:**



- 1. Neonatal vitamin A supplementation (VAS) to low-birth-weight (LBW) children**
- 2. Neonatal VAS to normal birth weight (NBW) children**
- 3. VAS together with routine vaccinations after 6 months of age**
- 4. BCG-at-birth versus delayed BCG to LBW children**
- 5. BCG-at-birth versus delayed BCG to LBW children**
- 6. OPV-at-birth (OPV0) versus no OPV0 to NBW children**
- 7. Early two-dose measles vaccination: 4+9 versus only 9 months**

## Assessing mortality from vaccination campaigns



**We assessed effect of campaigns within RCTs so that children were their own controls – blue time before campaign; green time after campaigns**



# Campaigns

**15 OPV**

**10 VAS**

**1 H1N1**

Randomised Trials	MRR after-OPV vs before-OPV	MRR after-VAS vs before-VAS	MRR after-H1N1 vs before-H1N1
Vitamin A: 3 RCTs	<b>0.75 (0.55-1.01)</b>	<b>1.47 (0.75-2.88)</b>	<b>6.48 (1.42-29.6)</b>
Early MV	<b>0.95 (0.71-1.28)</b>	<b>1.00 (0.70-1.43)</b>	
BCG at birth: 2 RCTs	<b>0.81 (0.63-1.05)</b>	<b>0.68 (0.38-1.20)</b>	<b>2.16 (0.94-4.99)</b>
OPV at birth	<b>0.90 (0.61-1.32)</b>	<b>0.53 (0.16-1.68)</b>	<b>1.44 (0.52-3.96)</b>
All	<b>0.81 (0.70-0.95)</b>	<b>1.04 (0.80-1.35)</b>	<b>1.86 (1.02-3.42)</b>



# Campaigns

**15 OPV**

**10 VAS**

**1 H1N1**

Randomised Trials	MRR after-OPV vs before-OPV	MRR after-VAS vs before-VAS	MRR after-H1N1 vs before-H1N1
Vitamin A: 3 RCTs	<b>0.75 (0.55-1.01)</b>	<b>1.47 (0.75-2.88)</b>	<b>6.48 (1.42-29.6)</b>
Early MV	<b>0.95 (0.71-1.28)</b>	<b>1.00 (0.70-1.43)</b>	
BCG at birth: 2 RCTs	<b>0.81 (0.63-1.05)</b>	<b>0.68 (0.38-1.20)</b>	<b>2.16 (0.94-4.99)</b>
OPV at birth	<b>0.90 (0.61-1.32)</b>	<b>0.53 (0.16-1.68)</b>	<b>1.44 (0.52-3.96)</b>
All	<b>0.81 (0.70-0.95)</b>	<b>1.04 (0.80-1.35)</b>	<b>1.86 (1.02-3.42)</b>

**OPV reduced mortality by 19% - additional doses 13% (4-21%) – significant linear trend**  
**Boosting is beneficial**





# Campaigns

**15 OPV**

**10 VAS**

**1 H1N1**

Randomised Trials	MRR after-OPV vs before-OPV	MRR after-VAS vs before-VAS	MRR after-H1N1 vs before-H1N1
Vitamin A: 3 RCTs	<b>0.75 (0.55-1.01)</b>	<b>1.47 (0.75-2.88)</b>	<b>6.48 (1.42-29.6)</b>
Early MV	<b>0.95 (0.71-1.28)</b>	<b>1.00 (0.70-1.43)</b>	
BCG at birth: 2 RCTs	<b>0.81 (0.63-1.05)</b>	<b>0.68 (0.38-1.20)</b>	<b>2.16 (0.94-4.99)</b>
OPV at birth	<b>0.90 (0.61-1.32)</b>	<b>0.53 (0.16-1.68)</b>	<b>1.44 (0.52-3.96)</b>
All	<b>0.81 (0.70-0.95)</b>	<b>1.04 (0.80-1.35)</b>	<b>1.86 (1.02-3.42)</b>

**H1N1 higher mortality:**

**For boys MRR=0.95 (0.23-3.92)**  
**For girls MRR= 2.32 (1.19-4.52)**



# RCT of infant mortality for BCG+OPV0 vs BCG-only

(N=7000; No polio in Bissau)  
Effect of OPV campaigns censored

Group	Mortality rate ratio for OPV0+BCG vs BCG-alone
All children	<b>0.68 (0.45-1.00)</b>
Boys	<b>0.57 (0.33-0.98)</b>
Girls	<b>0.86 (0.48-1.56)</b>
Enrolled day 0-2	<b>0.58 (0.38-0.90)</b>



**OPV1-3 used to be given in Denmark at 2,3, and 4 years of age**

**Hospital admissions at 24-36 months for all children in Denmark for OPV1 as most recent vaccination (1996-2001)**

<b>Most recent vaccination</b>	<b>Rate/100 pyrs (admissions /pyrs)</b>	<b>IRR for all infectious diseases</b>	<b>IRR for Lower Respiratory infections</b>
<b>DTaP-IPV-Hib</b>	<b>7.2 (452/6243)</b>	<b>1 (ref)</b>	<b>1 (ref)</b>
<b>MMR</b>	<b>5.1(1938/37835)</b>	<b>0.86 (0.77-0.95)</b>	<b>0.77 (0.64-0.92)</b>
<b>OPV1</b>	<b>4.5(4040/89919)</b>	<b>0.85 (0.77-0.95)</b>	<b>0.73 (0.61-0.87)</b>

**Study based on 137,403 children**

**OPV2 and OPV 3 associated with further 7%(0-14%) and 13%(4-21%) reductions in admissions between 3 and 5 years of age**



# OPV has modified the negative effect of DTP:

Mortality rate ratio (MRR) for DTP versus unvaccinated

Introduction of DTP and OPV	DTP-only	DTP+OPV	OPV-only
Urban Bissau 1981-1983	<b>10.0 (2.61-38.6)</b>	<b>3.52 (0.96-12.9)</b>	
Rural Bissau 1984-1987 (IJE 2004)	<b>5.00 (0.63-39.7)</b>	<b>1.90 (0.91-3.97)</b>	
Case fatality at hospital (Vaccine 2004)		reference	<b>0.29(0.11-0.77)</b>



# The world is switching from OPV to Inactivated polio vaccine (IPV)

Impact of IPV on survival has not been examined

IPV used as comparator vaccine in 3 RCTs in Bissau in the 1980-90s

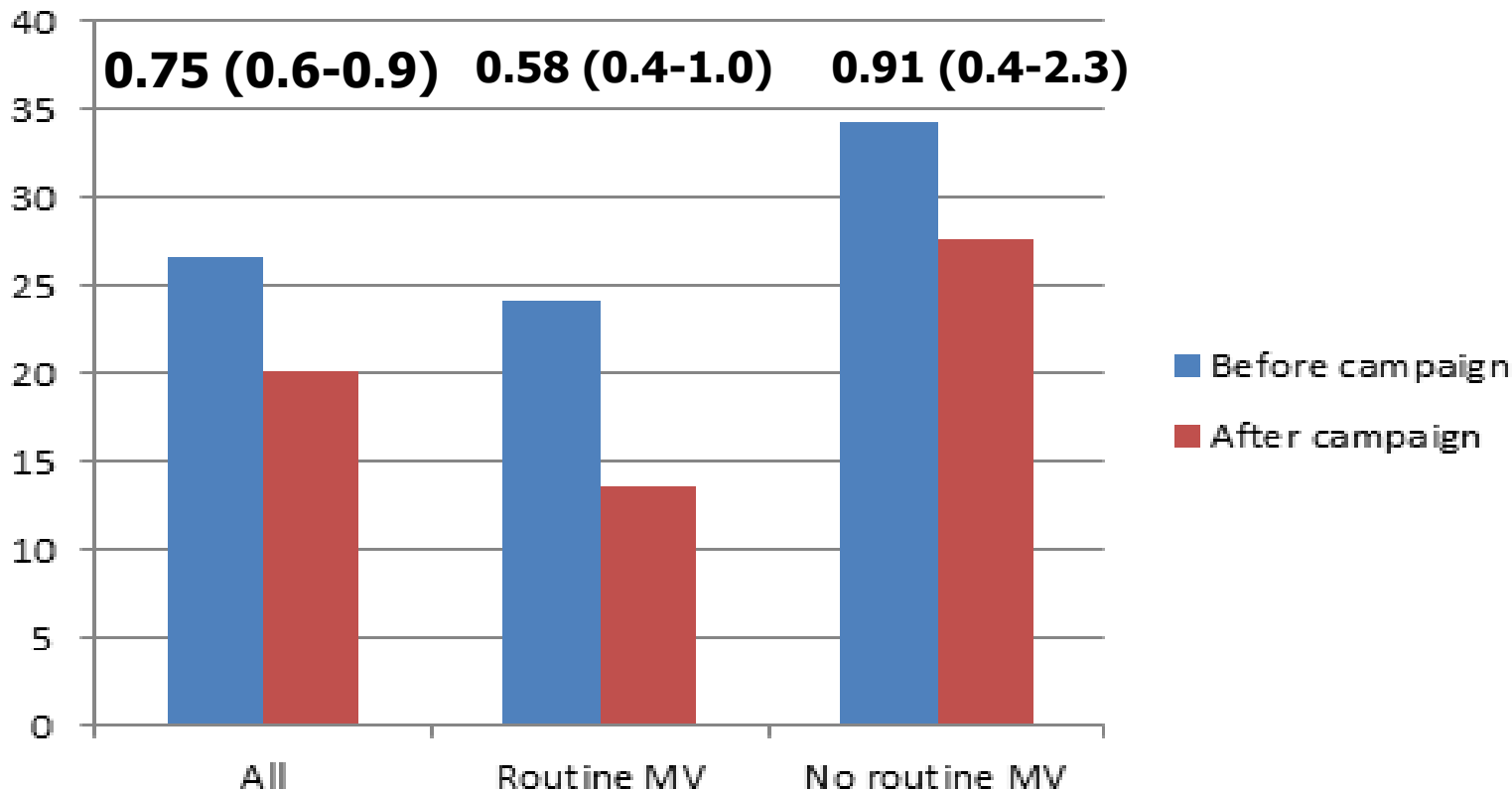
Mortality before receiving measles vaccine	Mortality rate (deaths/pyrs) for girls	Mortality rate (deaths/pyrs) for boys	Mortality rate ratio (MRR)
Randomised to IPV	8.3(60/724)	5.4(39/723)	1.52 (1.02-2.28)



# MV campaigns should have little effect on mortality

Many MV campaigns during last 15 years  
We compared mortality 1-yr after MV campaign with 2 yrs before

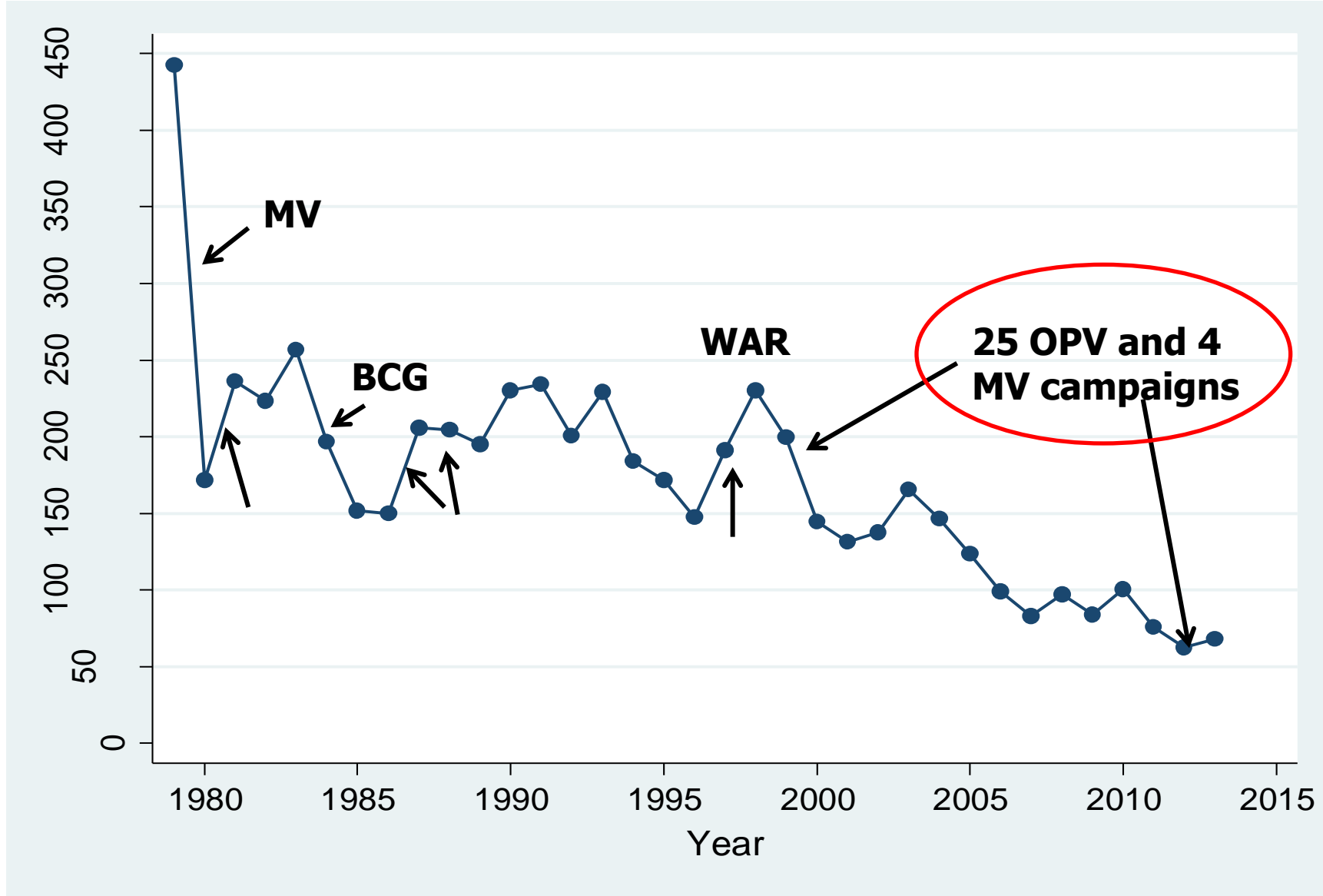
Age 1-4 years



Fisker PIDJ  
2015



# Under-5 mortality in Guinea-Bissau: The road to MDG4 has been paved with OPV and MV campaigns



# Conclusions

**Campaigns have had a much larger effect on mortality than usually assumed**

**Expected future negative effects for immune training:**

- **OPV campaigns will be removed**
- **OPV will no longer reduce the negative effect of DTP**
- **IPV is likely to have a negative effect for girls**
- **Measles vaccination campaigns will eventually be removed**

