

Supplementary tables

Campaigns and interventions

During the conduct of the present trial from 2003 to 2009 many government driven health intervention campaigns occurred as is now usual in Guinea–Bissau and other West African countries (see Table A). We had field assistants who accompanied all the campaign teams in the study area to monitor who received the intervention. After the campaigns we interviewed the mother of children who had not been present to obtain information on whether they had received the intervention elsewhere. There were two measles vaccination campaigns in May 2006 and July 2009. With permission from the Ministry of Health the study participants were excluded from these campaigns. Hence, the field assistants accompanying the vaccination teams had household based lists of all the children in the study area which indicated whether the child was excluded from measles vaccine during the campaign because it participated in the present two dose measles vaccine trial. Only 2-3% of the participants had received an additional measles vaccine outside the study area (Table A).

Subjects in the trial could have taken part in other randomised trials in the area (see Table A). Low birth weight (LBW) children took part in a trial of BCG at birth (ClinicalTrials.gov NCT00146302 and NCT00168610) (30), most normal birth weight children participated in trials of vitamin A supplementation administered at birth with BCG vaccine (ClinicalTrials.gov NCT00168597 and NCT00168610) (31,32) and many were involved in a trial of booster DTP vaccine after 18 months of age (ClinicalTrials.gov NCT00244673).

Table A: Estimated impact in the PP analysis of early two-dose measles vaccine (Group A) compared with measles vaccine at 9 months (Groups B+C) on mortality from 4.5 to 36 months of age in different arms of a concurrent trial or when children were censored for participation in various trials and campaign.

		Mortality rate ratio (MRR) (A vs B plus C)
Overall effect		0.69 (0.51-0.94)
Trials		MRR in different arms of a concurrent trial
VAS-at-birth trials	VAS at birth	0.98 (0.64-1.49)#
	Placebo	0.34 (0.17-0.69)#
DTP booster trial	Booster DTP	0.95 (0.24-3.80)
	No booster	0.75 (0.24-2.40)
Campaigns and health service delivery		MRR after censoring for participation in campaign
BCG at birth		0.67 (0.45-0.99)
Measles vaccine campaign 2006		0.70 (0.52-0.95)
Measles vaccine campaign 2009		0.69 (0.51-0.94)
Bed net distribution 2006		0.70 (0.50-0.96)
Bed net distribution 2007		0.72 (0.53-0.98)
Bed net impregnation 2006		0.71 (0.52-0.96)
Bed net impregnation 2007		0.71 (0.52-0.96)
OPV campaign 2004		0.60 (0.41-0.88)
OPV campaign 2005		0.65 (0.46-0.93)
VAS campaign 2004		0.69 (0.49-0.97)
VAS campaign 2005		0.67 (0.49-0.93)
1 st VAS campaign 2006		0.69 (0.50-0.96)
2 nd VAS campaign 2006		0.69 (0.50-0.95)
1 st VAS campaign 2007		0.73 (0.53-1.00)
2 nd VAS campaign 2007		0.71 (0.52-0.95)
1 st VAS campaign 2008		0.71 (0.52-0.96)
2 nd VAS campaign 2008		0.70 (0.52-0.95)
1 st VAS campaign 2009		0.70 (0.52-0.95)

Notes: Estimates are not adjusted for district; VAS=vitamin A supplementation. From 2006 onwards the vitamin A supplementation campaigns have usually included treatment with mebendazole for children aged 1-4 years. # p=0.012, test of interaction of vitamin A supplementation-at-birth and early measles vaccine.

Table B: The mortality rates and mortality rate ratio of recipients of early two-dose (Group A) compared with measles vaccine at 9 months (Group B). All children

Age interval	ITT Mortality rate per 100 person-years (deaths/person-days) [N]		ITT Mortality rate ratio (A/B)	ITT Mortality rate ratio (A/B) (with censoring for measles infection)	PP Mortality rate ratio (A/B)	PP Mortality rate ratio (A/B) (with censoring for measles infection)
	Early two-dose measles vaccine (Group A)	Measles vaccine at 9 months (Group B)				
4.5 to 9 months						
Boys	2.6 (10/142341) [1084]	2.0 (8/144740) [1091]	1.26 (0.50-3.19)	1.42 (0.54-3.74)	1.26 (0.50-3.19)	1.42 (0.54-3.74)
Girls	1.6 (6/137245) [1045]	3.4 (13/139281) [1062]	0.51 (0.19-1.35)	0.60 (0.22-1.65)	0.51 (0.19-1.35)	0.60 (0.22-1.65)
All	2.1 (16/279586) [2129]	2.7 (21/284021) [2153]	0.80 (0.42-1.55)	0.94 (0.48-1.84)	0.80 (0.42-1.55)	0.94 (0.48-1.84)
9 to 36 months						
Boys	1.2 (26/762500) [1047]	1.3 (26/757189) [1055]	0.99 (0.58-1.71)	1.05 (0.60-1.83)	0.81 (0.46-1.44)	0.83 (0.46-1.47)
Girls	1.1 (23/744638) [1012]	1.8 (35/723179) [1017]	0.64 (0.38-1.08)	0.67 (0.39-1.13)	0.58 (0.33-1.02)	0.61 (0.35-1.08)
All	1.2 (49/1507138) [2059]	1.5 (61/1480368) [2072]	0.79 (0.54-1.15)	0.83 (0.56-1.21)	0.69 (0.46-1.02)	0.71 (0.47-1.06)
4.5 to 36 months						
Boys	1.5 (36/904841) [1084]	1.4 (34/901929) [1091]	1.06 (0.66-1.69)	1.13 (0.70-1.83)	0.92 (0.56-1.49)	0.95 (0.58-1.56)
Girls	1.2 (29/881883) [1045]	2.0 (48/862460) [1062]	0.60 (0.38-0.95)	0.64 (0.40-1.03)	0.55 (0.34-0.90)	0.60 (0.37-0.98)
All	1.3 (65/1786724) [2129]	1.7 (82/1764389) [2153]	0.79 (0.57-1.09)	0.84 (0.61-1.18)	0.71 (0.50-1.00)	0.75 (0.53-1.07)

Table C: The mortality rates and mortality rate ratio of recipients of early two-dose (Group A) compared with measles vaccine at 9 months (Group C). All children

Age interval	ITT Mortality rate per 100 person-years (deaths/person-days) [N]		ITT Mortality rate ratio (A/C)	ITT Mortality rate ratio (A/C) (with censoring for measles infection)	PP Mortality rate ratio (A/C)	PP Mortality rate ratio (A/C) (with censoring for measles infection)
	Early two-dose measles vaccine (Group A)	Measles vaccine at 9 months (Group C)				
4.5 to 9 months						
Boys	2.6 (10/142341) [1084]	3.4 (13/138192) [1060]	0.76 (0.33-1.74)	1.09 (0.44-2.68)	0.76 (0.33-1.74)	1.09 (0.44-2.68)
Girls	1.6 (6/137245) [1045]	3.6 (14/140118) [1075]	0.43 (0.17-1.13)	0.46 (0.17-1.22)	0.43 (0.17-1.13)	0.46 (0.17-1.22)
All	2.1 (16/279586) [2129]	3.5 (27/278310) [2135]	0.59 (0.32-1.10)	0.72 (0.38-1.37)	0.59 (0.32-1.10)	0.72 (0.38-1.37)
9 to 36 months						
Boys	1.2 (26/762500) [1047]	1.4 (28/749182) [1025]	0.91 (0.54-1.56)	0.94 (0.55-1.60)	0.75 (0.42-1.31)	0.76 (0.43-1.35)
Girls	1.1 (23/744638) [1012]	1.4 (28/752870) [1036]	0.83 (0.48-1.44)	0.82 (0.47-1.42)	0.72 (0.40-1.28)	0.71 (0.40-1.26)
All	1.2 (49/1507138) [2059]	1.4 (56/1502052) [2061]	0.87 (0.59-1.28)	0.88 (0.60-1.29)	0.73 (0.49-1.10)	0.74 (0.49-1.10)
4.5 to 36 months						
Boys	1.5 (36/904841) [1084]	1.7 (41/887374) [1060]	0.86 (0.55-1.35)	0.97 (0.61-1.54)	0.75 (0.47-1.19)	0.84 (0.52-1.36)
Girls	1.2 (29/881883) [1045]	1.7 (42/892988) [1075]	0.70 (0.44-1.12)	0.71 (0.44-1.14)	0.63 (0.38-1.02)	0.63 (0.39-1.03)
All	1.3 (65/1786724) [2129]	1.7 (83/1780362) [2135]	0.78 (0.57-1.08)	0.83 (0.60-1.16)	0.69 (0.49-0.96)	0.73 (0.52-1.03)

Table D: Mortality rates and mortality rate ratios by district and health centre.

Intention-to-treat analysis

District	MR per 100 person-years (deaths/person-days)	Mortality rate ratio (A/(B+C))	Health Centre	MR per 100 person-years (deaths/person-days)	Mortality rate ratio (A/(B+C))
Bandim 1	1.8 (79/1595873)	0.90 (0.56-1.46)	Bandim	1.8 (113/2272576)	0.78 (0.52-1.17)
Bandim 2	1.8 (34/676703)	0.54 (0.24-1.18)			
Belem	1.0 (17/640095)	1.37 (0.52-3.60)	Belem & Mindara	1.0 (26/972399)	1.68 (0.78-3.64)
Mindara	1.0 (9/332304)	2.48 (0.66-9.22)			
Cuntum 1	1.6 (63/1425578)	0.81 (0.47-1.40)	Cuntum	1.6 (91/2086500)	0.61 (0.37-0.99)
Cuntum 2	1.5 (28/660922)	0.25 (0.07-0.81)			
Combined estimate	Adjusting for district	0.78 (0.59-1.05)		Adjusting for health centre	0.78 (0.59-1.04)
Main estimate	Without adjusting for district	0.78 (0.59-1.04)			

Notes: Interaction tests: Districts: p-value=0.11; Health centres: p-value=0.09

Per-protocol analysis

District	MR per 100 person-years (deaths/person-days)	Mortality rate ratio (A/(B+C))	Health Centre	MR per 100 person-years (deaths/person-days)	Mortality rate ratio (A/(B+C))
Bandim 1	1.9 (77/1499671)	0.86 (0.53-1.40)	Bandim	1.9 (108/2128808)	0.70 (0.46-1.07)
Bandim 2	1.8 (31/629137)	0.40 (0.16-0.98)			
Belem	1.0 (17/601260)	1.31 (0.50-3.45)	Belem & Mindara	1.0 (25/909983)	1.48 (0.67-3.27)
Mindara	0.9 (8/308723)	1.92 (0.48-7.66)			
Cuntum 1	1.6 (57/1332768)	0.69 (0.38-1.25)	Cuntum	1.6 (84/1931891)	0.52 (0.31-0.88)
Cuntum 2	1.6 (27/599123)	0.23 (0.07-0.77)			
Combined estimate	Adjusting for district	0.70 (0.52-0.94)		Adjusting for health centre	0.70 (0.51-0.94)
Main estimate	Without adjusting for district	0.69 (0.51-0.94)			

Notes: Interaction tests: Districts: p-value=0.11; Health centres: p-value=0.10

Table E: The mortality rates and mortality rate ratio of recipients of early two-dose measles vaccine (Group A) compared with measles vaccine at 9 months (Groups B+C). Only children who had received vitamin A supplementation at birth in the vitamin A supplementation-at-birth trials

Age interval	ITT Mortality rate per 100 person-years (deaths/person-days) [N]		Mortality rate ratio (A/(B+C)) Intention-to-treat	Mortality rate ratio (A/(B+C)) Per-protocol
	Early two-dose measles vaccine (Group A)	Measles vaccine at 9 months (Groups B and C)		
4.5 to 9 months				
Boys	3.7 (7/68738) [526]	1.6 (6/135473) [1021]	2.38 (0.80-7.09)	2.38 (0.80-7.09)
Girls	2.2 (4/65286) [496]	3.7 (13/126919) [972]	0.63 (0.21-1.96)	0.63 (0.21-1.96)
All	3.0 (11/134024) [1022]	2.6 (19/262392) [1993]	1.20 (0.57-2.53)	1.20 (0.57-2.53)
9 to 36 months				
Boys	1.5 (15/361254) [507]	1.4 (27/723239) [994]	1.13 (0.60-2.12)	0.91 (0.47-1.76)
Girls	1.0 (10/357695) [481]	1.1 (20/681546) [936]	0.96 (0.45-2.06)	0.96 (0.43-2.14)
All	1.3 (25/718949) [988]	1.2 (47/1404785) [1930]	1.05 (0.65-1.71)	0.92 (0.55-1.54)
4.5 to 36 months				
Boys	1.9 (22/429992) [526]	1.4 (33/858712) [1021]	1.34 (0.78-2.29)	1.16 (0.66-2.01)
Girls	1.2 (14/422981) [496]	1.5 (33/808465) [972]	0.82 (0.44-1.53)	0.80 (0.42-1.53)
All	1.5 (36/852973) [1022]	1.4 (66/1667177) [1993]	1.07 (0.71-1.61)	0.98 (0.64-1.50)

Table F: The mortality rates and mortality rate ratio of recipients of early two-dose measles vaccine (Group A) compared with measles vaccine at 9 months (Groups B+C). Only children who had received placebo at birth in the vitamin A supplementation-at-birth trials

Age interval	ITT Mortality rate per 100 person-years (deaths/person-days) [N]		Mortality rate ratio (A/(B+C)) Intention-to-treat	Mortality rate ratio (A/(B+C)) Per-protocol
	Early two-dose measles vaccine (Group A)	Measles vaccine at 9 months (Groups B and C)		
4.5 to 9 months				
Boys	0 (0/46578) [350]	1.9 (5/96630) [733]	0 (p=0.120)*	0 (p=0.120)*
Girls	0 (0/42893) [329]	3.1 (8/94217) [715]	0 (p=0.066)*	0 (p=0.066)*
All	0 (0/89471) [679]	2.5 (13/190847) [1448]	0 (p=0.009)*	0 (p=0.009)*
9 to 36 months				
Boys	0.8 (6/258906) [344]	1.3 (18/520760) [711]	0.67 (0.26-1.68)	0.44 (0.15-1.31)
Girls	0.9 (6/235657) [320]	1.7 (24/504044) [691]	0.54 (0.22-1.31)	0.43 (0.17-1.14)
All	0.9 (12/494563) [664]	1.5 (42/1024804) [1402]	0.59 (0.31-1.12)	0.43 (0.21-0.89)
4.5 to 36 months				
Boys	0.7 (6/305484) [350]	1.4 (23/617390) [733]	0.52 (0.21-1.29)	0.35 (0.12-1.02)
Girls	0.8 (6/278550) [329]	2.0 (32/598261) [715]	0.40 (0.17-0.96)	0.33 (0.13-0.85)
All	0.8 (12/584034) [679]	1.7 (55/1215651) [1448]	0.45 (0.24-0.84)	0.34 (0.17-0.68)

Note: * log-rank test.

Table G: The mortality rates and mortality rate ratio of recipients of early two-dose measles vaccine (Group A) compared with measles vaccine at 9 months (Groups B+C). Only children who had not participated in the vitamin A supplementation-at-birth trials

Age interval	ITT Mortality rate per 100 person-years (deaths/person-days) [N]		Mortality rate ratio (A/(B+C))	Mortality rate ratio (A/(B+C))
	Early two-dose measles vaccine (Group A)	Measles vaccine at 9 months (Groups B and C)	Intention-to-treat	Per-protocol
4.5 to 9 months				
Boys	4.1 (3/27025) [208]	7.2 (10/50829) [397]	0.57 (0.16-2.07)	0.57 (0.16-2.07)
Girls	2.5 (2/29066) [220]	3.8 (6/58263) [450]	0.66 (0.13-3.27)	0.66 (0.13-3.27)
All	3.3 (5/56091) [428]	5.4 (16/109092) [847]	0.61 (0.22-1.66)	0.61 (0.22-1.66)
9 to 36 months				
Boys	1.3 (5/142340) [196]	1.3 (9/262372) [375]	1.02 (0.34-3.06)	1.04 (0.34-3.16)
Girls	1.7 (7/151286) [211]	2.4 (19/290459) [426]	0.71 (0.30-1.68)	0.61 (0.24-1.54)
All	1.5 (12/293626) [407]	1.8 (28/552831) [801]	0.81 (0.41-1.59)	0.74 (0.36-1.49)
4.5 to 36 months				
Boys	1.7 (8/169365) [208]	2.2 (19/313201) [397]	0.79 (0.35-1.80)	0.76 (0.33-1.76)
Girls	1.8 (9/180352) [220]	2.6 (25/348722) [450]	0.71 (0.33-1.51)	0.63 (0.28-1.40)
All	1.8 (17/349717) [428]	2.4 (44/661923) [847]	0.74 (0.42-1.30)	0.69 (0.39-1.22)

Table H: The mortality rates and mortality rate ratio of recipients of early two-dose measles vaccine (Group A) compared with measles vaccine at 9 months (Groups B). Only children who had not received vitamin A supplementation at birth

Age interval	ITT Mortality rate per 100 person-years (deaths/person-days) [N]		ITT Mortality rate ratio (A/B)	ITT Mortality rate ratio (A/B) (with censoring for measles infection)	PP Mortality rate ratio (A/B)	PP Mortality rate ratio (A/B) (with censoring for measles infection)
	Early two-dose measles vaccine (Group A)	Measles vaccine at 9 months (Group B)				
4.5 to 9 months						
Boys	1.5 (3/73603) [558]	2.4 (5/74789) [567]	0.55 (0.13-2.32)	0.52 (0.12-2.24)	0.55 (0.13-2.32)	0.52 (0.12-2.24)
Girls	1.0 (2/71959) [549]	3.4 (7/75769) [578]	0.31 (0.06-1.56)	0.45 (0.08-2.40)	0.31 (0.06-1.56)	0.45 (0.08-2.40)
All	1.3 (5/145562) [1107]	2.9 (12/150558) [1145]	0.42 (0.15-1.19)	0.49 (0.17-1.45)	0.42 (0.15-1.19)	0.49 (0.17-1.45)
9 to 36 months						
Boys	1.0 (11/401246) [540]	1.3 (14/392211) [548]	0.78 (0.35-1.71)	0.88 (0.39-1.98)	0.63 (0.27-1.48)	0.66 (0.28-1.57)
Girls	1.2 (13/386943) [531]	2.3 (24/389429) [554]	0.55 (0.28-1.08)	0.59 (0.30-1.17)	0.45 (0.22-0.93)	0.49 (0.24-1.00)
All	1.1 (24/788189) [1071]	1.8 (38/781640) [1102]	0.63 (0.38-1.05)	0.69 (0.41-1.16)	0.51 (0.30-0.89)	0.54 (0.31-0.95)
4.5 to 36 months						
Boys	1.1 (14/474849) [558]	1.5 (19/467000) [567]	0.73 (0.37-1.46)	0.79 (0.39-1.61)	0.62 (0.30-1.29)	0.64 (0.30-1.33)
Girls	1.2 (15/458902) [549]	2.4 (31/465198) [578]	0.50 (0.27-0.92)	0.56 (0.30-1.06)	0.42 (0.22-0.81)	0.48 (0.25-0.93)
All	1.1 (29/933751) [1107]	2.0 (50/932198) [1145]	0.59 (0.37-0.93)	0.65 (0.41-1.04)	0.50 (0.31-0.80)	0.54 (0.33-0.88)

Table I: The mortality rates and mortality rate ratio of recipients of early two-dose measles vaccine (Group A) compared with measles vaccine at 9 months (Groups C). Only children who had not received vitamin A supplementation at birth

Age interval	ITT Mortality rate per 100 person-years (deaths/person-days) [N]		ITT Mortality rate ratio (A/C)	ITT Mortality rate ratio (A/C) (with censoring for measles infection)	PP Mortality rate ratio (A/C)	PP Mortality rate ratio (A/C) (with censoring for measles infection)
	Early two-dose measles vaccine (Group A)	Measles vaccine at 9 months (Group C)				
4.5 to 9 months						
Boys	1.5 (3/73603) [558]	5.0 (10/72670) [563]	0.30 (0.08-1.10)	0.49 (0.12-1.95)	0.30 (0.08-1.10)	0.49 (0.12-1.95)
Girls	1.0 (2/71959) [549]	3.3 (7/76711) [587]	0.30 (0.06-1.44)	0.34 (0.07-1.68)	0.30 (0.06-1.44)	0.34 (0.07-1.68)
All	1.3 (5/145562) [1107]	4.2 (17/149381) [1150]	0.30 (0.11-0.82)	0.42 (0.15-1.18)	0.30 (0.11-0.82)	0.42 (0.15-1.18)
9 to 36 months						
Boys	1.0 (11/401246) [540]	1.2 (13/390921) [538]	0.80 (0.36-1.78)	0.84 (0.37-1.91)	0.65 (0.27-1.55)	0.69 (0.29-1.67)
Girls	1.2 (13/386943) [531]	1.7 (19/405074) [563]	0.71 (0.35-1.44)	0.69 (0.34-1.39)	0.62 (0.29-1.32)	0.61 (0.29-1.28)
All	1.1 (24/788189) [1071]	1.5 (32/795995) [1101]	0.74 (0.44-1.26)	0.74 (0.44-1.27)	0.63 (0.36-1.11)	0.63 (0.36-1.12)
4.5 to 36 months						
Boys	1.1 (14/474849) [558]	1.8 (23/463591) [563]	0.59 (0.30-1.14)	0.73 (0.36-1.47)	0.50 (0.25-1.01)	0.62 (0.30-1.30)
Girls	1.2 (15/458902) [549]	2.0 (26/481785) [587]	0.60 (0.32-1.13)	0.60 (0.32-1.15)	0.53 (0.27-1.04)	0.54 (0.27-1.06)
All	1.1 (29/933751) [1107]	1.9 (49/945376) [1150]	0.59 (0.37-0.94)	0.65 (0.41-1.05)	0.51 (0.32-0.84)	0.57 (0.35-0.94)