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Cohort profile

Bandim Health Project's (BHP) rural Health and Demographic Surveillance System (HDSS) - A nationally representative HDSS in Guinea-Bissau

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BMJ Open Cohort profile : Bandim Health Project's (BHP) rural Health and Demographic Surveillance System (HDSS) – a nationally representative HDSS in Guinea-Bissau

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ABSTRACT

Purpose Bandim Health Project (BHP) monitors health and survival of women and children in a nationally representative rural Health and Demographic Surveillance System (HDSS) in Guinea-Bissau. The HDSS was set up in 1989–1990 to collect data on health interventions and child mortality.

Participants The HDSS covers 182 randomly selected clusters across the whole country. The cohort is open, and women and children enter the cohort, when they move into the selected clusters, and leave the cohort, when they move out or die, or when children reach 5 years of age. Data are collected through biannual or more frequent household visits. At all village visits, information on pregnancies, vital status, vaccination status, arm circumference, use of bed nets and other basic information is collected for women and children. Today, more than 25 000 women and 23 000 children below the age of 5 years are under surveillance.

Findings to date Research from the BHP has given rise to the hypothesis that vaccines, in addition to their targeted effects, have important non-specific effects altering the susceptibility to other infections. Initially, it was observed that mortality among children vaccinated with the live BCG or measles vaccines was much lower than the mortality among unvaccinated children, a difference, which could not be explained by prevention of tuberculosis and measles infections. In contrast, mortality tended to be higher for children who had received the non-live Diphtheria-Tetanus-Pertussis vaccine compared with children who had not received this vaccine. Since the effect differed for the different vaccines, no bias explained the contrasting findings.

Future plans New health interventions are introduced with little assessment of real-life effects. Through the HDSS, we can describe both the implementation of interventions (eg, the vaccination programme) and their effects. Furthermore, the intensive follow-up allows the implementation of randomised trials testing potential better vaccination programmes.

INTRODUCTION

Bandim Health Project (BHP) implements a health and demographic surveillance system

Strengths and weaknesses

- The Bandim Health Project rural Health and Demographic Surveillance System (HDSS) is a nationally representative HDSS covering women and children below the age of 5 years in 182 village clusters all over Guinea-Bissau.
- Since the inception of the HDSS, registration of pregnancies and follow-up for birth outcomes have been at the core of the data collection.
- Vaccination data are collected at all visits allowing for assessment of the real-life effects of vaccines and changes in vaccination policies.
- Six-monthly visits and individual follow-up means that hard endpoints like deaths are not missed but the precision of dates may be limited to month of event.
- Cause of death is established based on an interview conducted at the time of registering the death, thus classified causes must be interpreted with caution.

(HDSS) in Guinea-Bissau, a small West African country located at the coast to the Atlantic Ocean. Guinea-Bissau borders Senegal in the north and Guinea to the east and south. The climate is tropical with an annual rainfall of approximately 1500 mm¹ during a single rainy season (June to November).

The BHP rural HDSS in its present form was set up in 1989–1990 with support from Unicef to assess the prevalence of neonatal tetanus and to collect data on child mortality to monitor the impact of a Danish International Development Agency (DANIDA)-sponsored project to strengthen primary healthcare.

The surveillance initially comprised randomly selected village clusters in the five most populous rural regions of Guinea-Bissau (Oio, Biombo, Gabu, Cacheu and Bafata), where 83% of the rural Guinean population

lived. The focus was on ensuring accurate data on child mortality and therefore the emphasis was on pregnancy registration, antenatal care and childhood vaccinations. Before the present setup, in 1979–1990, a convenience sample of 20 villages in Biombo, Cacheu, Oio and Tombali was followed; some of the original villages continued as part of the present HDSS.

Cohort description

The BHP rural HDSS covers women of reproductive age and children below the age of 5 years residing in the clusters. Between 1990 and 2006, the HDSS covered 20 clusters in Oio, Biombo, Gabu, Cacheu and Bafata. The clusters were selected using the method recommended by the Expanded Programme on Immunizations for surveys of immunisation coverage. In all, 20 clusters of 100 women per region were selected based on a listing of the population size. The chance of being selected was proportional to the population size. If the village selected had fewer than 100 women, the closest neighbouring village was included. A third village was added if the sample was still below 100 women.

In 2006, with support from World Bank, two additional rural regions (Tombali and Quinara) with 20 clusters and two regions on the islands (Bubaque and Bolama) with 10 and 12 clusters, respectively, were added. The Cacheu health region was split in two health regions (Cacheu and São Domingos) and therefore 20 clusters were added to the already included clusters in Cacheu. Thus, from 2006 and onwards, the rural HDSS consisted of 182 clusters in the nine rural health regions (figure 1). Details of annual population followed are provided in table 1.

The clusters are followed through biannual household visits. The surveillance in the rural HDSS has been uninterrupted, except for slightly longer intervals between visits in 1998–1999, due to a civil war. Since September 2007, a nurse who administers vaccines has accompanied the BHP teams. Since 2012, monthly and bimonthly visits have been conducted in the three health regions closest to Bissau (Oio, Biombo and Cacheu). At these more frequent visits, only pregnancies and children below 12 months of age were registered and followed up (figure 2).

The BHP rural HDSS is an open cohort: Girls who have grown up in the village are registered in the cohort of

women when they reach 13–15 years of age. New women are registered at the first village visit after they are stated to have moved into the village and remain under surveillance until death or out-migration. Women are followed from date of registration and are considered part of the cohort as long as they state that they live in the village (we do not operate with quarantine periods during which an in-migrant has to remain in the area before being registered, as has been done in other HDSS sites). Children are registered already as fetuses. In-migrating children under 5 years of age are registered when they move into the village. All children are followed from birth or date of registration, whichever comes last. Thus, children registered after birth only enter the cohort from date of registration. All children are followed to death, out-migration or 5 years of age.

While key information on pregnancies, births and deaths has been registered throughout, additional information has been collected for shorter periods as displayed in figure 3. When a woman is registered, basic information on ethnicity, age, schooling, obstetric history and vaccination scar status is obtained. Since 2011, we have also registered the name of her mother and whether the woman was born in the village, but linkage to child records has not been performed. At registration and subsequent visits, the woman is asked if she is pregnant, whether she has had any births or miscarriages since last visit and use of bed net (figure 3). On registration of a pregnancy, information on antenatal care and gestational age is obtained, and maternal mid-upper-arm circumference (MUAC) is measured. Information on socioeconomic background factors is collected at the first registration of a pregnancy/child. When registering the pregnancy outcome and at registration of infants, information on antenatal care, tetanus vaccines during pregnancy and place of birth is collected. At all subsequent household visits, information about vaccination status, nutritional status (assessed by MUAC) and hospital admissions is obtained (figure 3). Furthermore, for children under 1 year of age and newly registered children, BCG scar status is assessed. In the regions with shorter intervals between follow-up visits, we also register whether the child has been ill since the last visit, and if the child was taken for outpatient consultation.

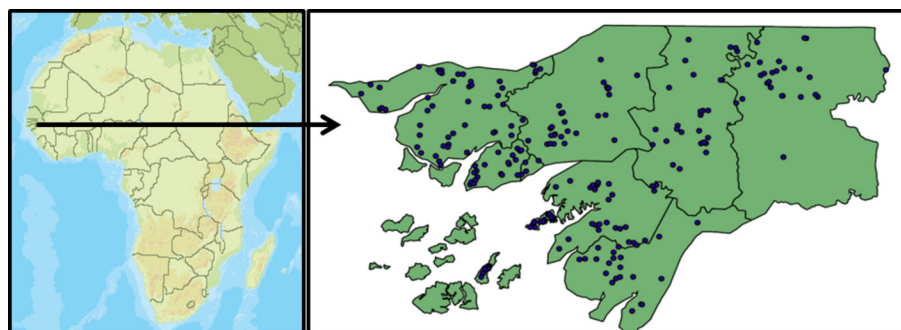


Figure 1 Map of Guinea-Bissau with the HDSS clusters marked as blue dots. HDSS, Health and Demographic Surveillance System.

Table 1 Demographic table with information from the villages under surveillance

Year	Number of pregnancies registered before date of birth	Number of births registered*	Total population under 5 years of age under surveillance	Total population of fertile women under surveillance†
1990	1418	891	1381	8852
1991	1796	1761	3003	9624
1992	1697	1852	4563	10 000
1993	1769	2027	6139	10 479
1994	1774	1928	7445	10 643
1995	1722	2119	8580	11 109
1996	1896	2426	10 963	11 896
1997	1916	2456	11 946	12 395
1998	1013	2143	10 916	12 090
1999	1635	2204	11 368	12 368
2000	1874	2479	11 785	12 556
2001	1786	2382	11 535	12 659
2002	1705	2260	11 698	12 667
2003	1741	2477	11 814	12 949
2004	1785	2457	12 138	13 169
2005	1608	3390	12 161	13 193
2006‡	2850	4114	19 786	22 348
2007	2959	4134	21 502	22 985
2008	2217	3923	20 961	22 419
2009	2734	3908	21 359	22 278
2010	2621	3948	21 483	22 519
2011	3045	4120	21 973	23 247
2012	3444	4462	22 665	23 926
2013	3686	4343	23 581	24 573
2014	3259	4257	23 470	24 588
2015	2717	3996	22 886	24 452
2016	3023	3844	23 174	25 120
2017	2965	3948	23 479	25 649

*Births registered within first 12 months of live.

†Women aged 13–49 years are considered of reproductive age. Information on age is missing for 380 women.

‡Upscaling from 100 to 182 village clusters.

At all visits, vital status is updated for both women and children and a simple verbal autopsy is conducted on registration of a death. The verbal autopsy seeks to distinguish deaths due to accidents and natural causes, and to describe symptoms in the period leading up to death.

The data are collected on paper questionnaires and entered in the BHP offices in Bissau city. Data are entered into tables using a platform build in dBaseV. Following data entry, data are checked for consistency and required corrections are made by consulting the original forms. The data on children under surveillance and registered pregnancies are used to create lists for the next visit with pre-printed of identifying information for pregnant

women and all children including their already collected vaccination information. Since we allow neighbours to provide information for women and children who cannot be localised in the villages, our loss to follow-up is very low, but 1/5 children are registered to have migrated out of the village before 5 years of age.

Patient and public involvement

The communities were involved in locating households, when the HDSS was setup and contributed information allowing tracing of internal migrants within and to some extent between villages. No participants were involved in setting the research question or the outcome measure, nor were they involved in developing plans for recruitment, design or implementation of the study. No participant was asked to advise on interpretation or writing up the results. The results of studies carried out within the HDSS are disseminated to the national public health institute. There are no plans to disseminate results of the research to study participants or the community.

Findings to date

The rural HDSS has made it possible to obtain accurate estimates of mortality and to evaluate factors related to both maternal^{2 3} and child mortality^{4–11} in a nationally representative sample of the rural population in Guinea-Bissau. A list of papers based on the rural HDSS data is provided in the online supplementary appendix.

Vaccines and child mortality: non-specific effects of vaccines

Vaccines are given to protect against targeted diseases, but research from the BHP has given rise to the hypothesis that vaccines, in addition to their targeted effects, have important non-specific effects (NSEs) altering the susceptibility to other infections. Using data from the first years of data collection during the early 1990s, while the vaccination programme was still being rolled out, a surprising finding was made⁴: The live BCG and measles vaccination (MV) were associated with beneficial NSEs. The mortality among children vaccinated with BCG or MV was much lower than the mortality among unvaccinated children, a difference, which could not be explained by prevention of tuberculosis and measles infections. In contrast, the opposite tendency was seen for the non-live Diphtheria-Tetanus-Pertussis (DTP) vaccine. Since the effect was different for the different vaccines, no bias explained the contrasting findings.

Following the surprising finding on DTP, WHO reviewed the data collection and the data management, and found no sources of bias that could invalidate the study.¹² To further examine the possible deleterious effects of DTP, WHO sponsored a series of re-analyses of existing datasets on vaccinations from other cohorts.^{13–17} All studies found beneficial effects of DTP on child survival. Unfortunately, these studies introduced major bias in the analyses. First, children were not excluded for lack of information on vaccination status; in a setting with no public registers, information is not available for all children. A reason

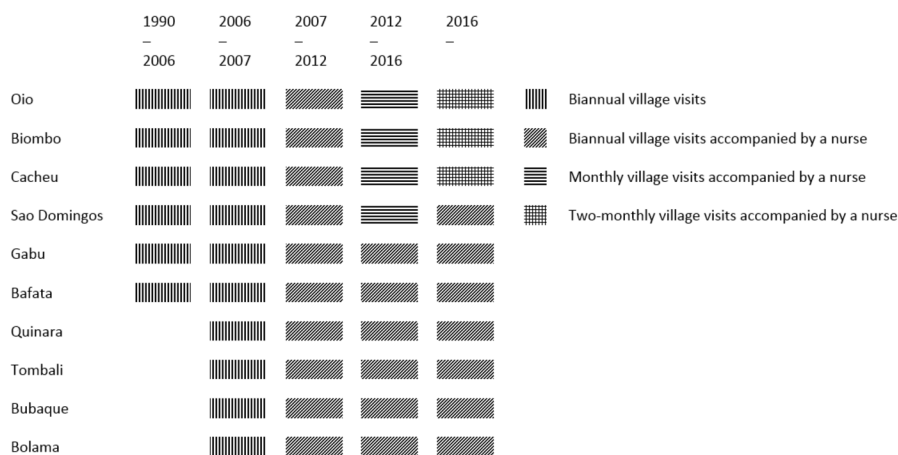


Figure 2 Visit frequency by period and health region.

for getting no information is that the child has already died, thus some dead, vaccinated children will be selectively misclassified as ‘unvaccinated’, skewing the results. Second, whereas the BHP studies had only counted survival time from the day the vaccination card had been inspected, the WHO-sponsored studies retrospectively updated vaccination status from the date of vaccination, thus allocating risk-free survival time to children from date of vaccination until the day the vaccination card was inspected. The implications of these methodological flaws were major; BHP could show that if we analysed our own data the same way as WHO-sponsored studies had done, we would get the same ‘faulty’ beneficial effects of DTP.¹⁸ This led to a discussion on prospective follow-up,

which has defined the standard for later studies of the impact of vaccinations on child survival.^{18–21}

The findings of beneficial NSEs of BCG and MV and negative NSEs of DTP have later been confirmed in many other settings²² including the clusters followed in rural Guinea-Bissau before 1990.²³ A key feature of the NSEs is that the effects frequently differ for boys and girls, with girls obtaining larger benefit from receiving live MV,^{6,22,24,25} but also stronger negative effects of receiving DTP.^{26,27} This emphasises the need to assess effects of health interventions by sex. Studies of the NSEs of vaccines and other health interventions have defined much of the research agenda at the BHP.

Declining mortality levels and possible explanations: vaccination campaigns

Mortality for children in the rural HDSS has declined by almost two-thirds between 1990 and 2013, and according to the verbal autopsies performed since 2005, the main cause of death is malaria.⁹ Part of the reduction may be ascribed to vaccination campaigns conducted with short intervals during the last two decades. MV campaigns are conducted to ensure that children receive the second dose of MV. We used the HDSS data to assess the effects of a general MV campaign in rural Guinea-Bissau,⁷ and found that the MV campaign was associated with a 20% (95% CI: 4% to 34%) reduction in mortality rate.

Mortality of women of reproductive age

In contrast to the marked reduction in child mortality, mortality of women of reproductive age has declined little over the past 28 years³. Research with a focus on levels and causes of death indicate that mortality of women below the age of 50 years remains high at around 750/100 000 person years; one-third of these deaths is related to pregnancy and childbirth.^{28–30}

Implementation and evaluation of the vaccination programme

Vaccines are available at the government health centres and since 2008 frequently also through outreach to

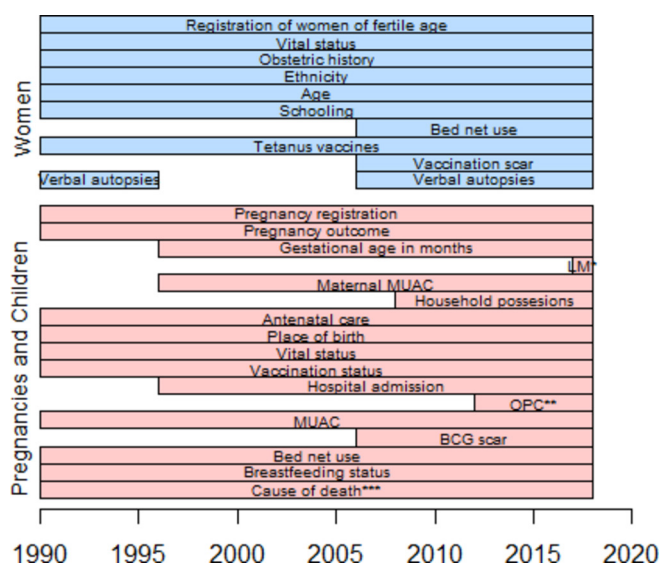


Figure 3 Gantt diagram of data collected through the BHP rural HDSS Note: *LM: last menstrual period **OPC: outpatient consultations *** symptoms of disease leading up to death registered throughout. Further details collected through a verbal autopsy since 2005. BHP, Bandim Health Project; HDSS, Health and Demographic Surveillance System.

villages further away from the health centres.⁶ The HDSS enables us to describe both the implementation of the vaccination programme and its effect. Vaccination coverage estimates are commonly based on number of vaccines given to children below 12 months divided by the estimated population of infants surviving past infancy. The estimated target population of children based on projected census data carries much uncertainty, and coverage estimates are therefore not very precise and may exceed 100%. Using the rural HDSS data, we have been able to precisely measure vaccination coverage^{6 31 32} based on vaccination coverage among those with assessed vaccination status (seen vaccination card or never vaccinated).

The coverage of the third dose of the DTP-containing vaccine by 12 months of age is one of the main indicators of the vaccination programme. This indicator may not contribute to the optimal implementation of the vaccination programme: When the pentavalent vaccine (DTP, Hepatitis B and *Haemophilus Influenzae* type B) was introduced in the vaccination programme,⁶ we evaluated the impact. The introduction of the new vaccine was accompanied by increased vaccination outreach services and a more restrictive wastage policy. We found that the proportion of fully vaccinated children did not change (risk ratio 1.00; 95% CI: 0.89 to 1.11), but interestingly the coverage of DTP3 increased from 73% in 2007 to 81% in 2009, whereas the MV coverage declined from 71% in 2007 to 66% in 2009. Bearing in mind that previous research had shown beneficial NSEs of MV, whereas DTP-containing vaccine was associated with negative NSEs, this shift may have had important negative consequences.⁶

In 2014, a WHO commissioned review evaluated the evidence of NSEs of BCG, MV and DTP, and concluded that the live BCG and MV were associated with beneficial NSEs.²² No alterations to the vaccination programme were recommended, but a call for more research was issued.²² Though vaccinations are recommended at specific ages, BHP data demonstrate that there is a large gap between the recommendations and the implemented vaccination programme. Part of the explanation is the focus on *vaccine wastage* as a performance indicator complementing the 12-month vaccination coverage. This has led to a national policy of not opening a vial of BCG or MV unless sufficient children are present for vaccination because the vaccines come in multi-dose vials, which have to be discarded within 6 hours after reconstitution. We have shown that disregarding the policy of only opening a vial if sufficient children are present for vaccination can increase vaccine coverage.^{32 33} We have furthermore been able to show that it is highly cost-effective to open a multi-dose vial of MV even for one child³³: already at a wastage rate of 88% it was cost saving to vaccinate all children with MV.

Building on to our assessment of the measured real-life effects of vaccines, we have investigated alternative indicators of vaccination programme effectiveness. Based on our findings, the programme should emphasise timeliness of vaccines, especially of the live vaccines

that are administered as one dose in the routine vaccination programme. Furthermore, post-vaccination BCG scar should be an indicator: If BCG vaccines are given correctly, then they result in the formation of a BCG scar in approximately 90% of cases.^{34–36} Using data from the rural HDSS, we found that only 52% of children vaccinated through the routine vaccination programme in Guinea-Bissau had a BCG scar, and we could show that among BCG-vaccinated children, having a BCG scar was associated with lower mortality.⁸

Randomised trials in the BHP rural HDSS

The HDSS setup allows the nesting of individually and cluster-randomised trials. In 2007–2011, we tested the effect of vitamin A supplementation at vaccination contacts.⁵ Subsequently, we have implemented cluster-randomised and individually randomised trials testing potential benefits of altering the vaccination schedule and its implementation^{37 38} (table 2). Since we have no control areas with no trial implementation, we cannot make strong conclusions on the impact of the trials on the child mortality level in the villages. However, in the past trials, only a small subset of children has been enrolled.^{5 38}

At present, less than half of the children in rural Guinea-Bissau receive BCG vaccine in the first month of life.³² We are conducting a cluster-randomised trial of providing BCG and oral polio vaccination (OPV) vaccines within 3 days of birth to children in rural Guinea-Bissau.³⁹ The study will evaluate the effect of BCG and OPV on early infant mortality, and will furthermore be a proof-of-concept of whether it is possible to deliver vaccines at birth in a rural setting, where many women do not deliver at health centres.

We are also testing the effects of campaigns with live MV and OPV in randomised trials.⁴⁰ Polio and measles infections are about to be eradicated and the vaccination campaigns are therefore likely to be stopped. Since the vaccination campaigns may be associated with survival benefits beyond what can be explained by the prevention of polio^{41 42} and measles,^{7 43} we conduct two cluster-randomised trials assessing the campaign effects. In these trials, HDSS villages have been randomised to receive a vaccination campaign or not receiving a vaccination campaign. The first trial assesses the effect of OPV campaigns among children aged 0–8 months of age, and the second trial is assessing the effect of measles campaigns among children aged 9–59 months of age.⁴⁰

Strengths and limitations

The emphasis on pregnancy registration throughout the data collection period allows accurate data on early mortality over the past 28 years, but we do not presume to have information on the exact number of births, which have occurred in the registered households. The nationally representative village clusters, and the individual-level registration of preventive health interventions received, enable us to evaluate the real-life implementation and effects of new interventions.

Table 2 Trials implemented in the Bandim rural HDSS

Trial	Objective	Year of trial	Enrolment ages and criteria	Number of children enrolled/ planned to be enrolled	Trial registration ID at clinicaltrials.gov
Evaluation of the impact on mortality and morbidity of the WHO recommended vitamin A supplementation at first immunisation contact after 6 months of age ⁵	To assess the effect of providing vitamin A supplementation at vaccination contacts after 6 months of age	2007–2011	6–23 months, missing one or more routine vaccines	7587	NCT00514891
The effect on overall mortality of a national policy of limiting MV to children below 12 months of age ^{33 37}	To assess the effect on mortality and hospitalisations of providing MV to all MV-unvaccinated children between 9 and 35 months of age disregarding the national policy of restricting the opening of MV vials	2011–2016	9–35 months, measles unvaccinated	4476	NCT01306006
A two-site-randomised trial of an additional measles vaccine at 4 months of age to reduce child mortality in rural areas of Burkina Faso and Guinea-Bissau ³⁸	To assess the effect on child survival of a two-dose MV schedule by providing an additional dose of Edmonston-Zagreb measles vaccine as soon as possible after 4 months of age as well as the standard measles vaccine at 9 months of age.	2012–2016	4–7 months, received penta3 at least 4 weeks previously	3750	NCT01644721
Can earlier BCG vaccination reduce early infant mortality? A cluster-randomised trial ³⁹	To assess the effect of BCG and OPV provided at a single home visit within 72 hours after birth on early infant mortality and morbidity.	2015–2020	0–3 days, BCG unvaccinated, registered in the HDSS during pregnancy	6666	NCT02504203
The effect of a MV campaign on morbidity and mortality among children aged 9–59 months in rural Guinea-Bissau—a cluster-randomised controlled trial ⁴⁰	To assess the effect of a MV campaign on mortality and morbidity	2016–2019	9–59 months, not enrolled in the OPV campaign trial	18000	NCT03460002
A cluster-randomised controlled trial of the effect of oral polio vaccine campaigns on child morbidity and mortality ⁴⁰	To assess the effect of OPV campaigns on morbidity and mortality in Guinea-Bissau in a context with no polio	2017–2020 (anticipated)	0–8 months	10000	NCT03460002

HDSS, Health and Demographic Surveillance System; MV, measles vaccination; OPV, oral polio vaccination.

The data are collected through household visits by experienced fieldwork assistants, many of whom have worked for the BHP for years; thus, they are very familiar with all aspects of data collection. The close collaboration with the local and national health authorities ensures that findings from the BHP rural HDSS are passed on to the health authorities. The long-standing relation with the population under surveillance enables the collection of important and at times sensitive information.

Conducting demographic surveillance in a highly mobile population is possible because family members provide information on the whereabouts of the travelling individuals. Not operating with periods of quarantine allows unbiased mortality estimates, also for migrants.

Only a quarter of the deaths occur in health facilities, and even for deaths in facilities, the diagnostic information is limited. Hence, in a rural population where many do not seek healthcare even for severe illness, and where little information is provided by the health staff to those who do, we seldom obtain diagnosis for admissions or causes of death. We seek to assess the cause of death based on the described symptoms obtained from a short interview conducted when a death is registered, but classified causes must be interpreted with caution.

With 6-monthly visits, the recall period becomes long, and dates may be subject to some uncertainty. We rarely are able to obtain full information on, for example, vaccines received for children who have died between two rounds of visits. To avoid selectively misclassifying observation time, we therefore only rely on the landmark approach¹⁸ in our analyses, emphasising the prospective follow-up from the date of registration of vaccination rather than retrospective update of vaccination status.

The 6-monthly visits make it unlikely that hard endpoints like death should be subject to bias, but other endpoints could be influenced by bias. More frequent visits in some regions increase the precision.

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Contributors PA established the surveillance and implemented the original census in collaboration with MF, SMT and ABF now manage the surveillance and drafted the article. MF, CSB and PA were involved in critical revision of the article. All authors were involved in final approval of the article.

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Data sharing statement Data from the BHP's rural HDSS can be made available on a collaborative basis (www.bandim.org).

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