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HEALTH AND DEMOGRAPHIC SURVEILLANCE SYSTEM PROFILE

Profile: Manhiça Health Research Centre (Manhiça HDSS)

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The Manhiça Health Research Centre, established in 1996 in a rural area of southern Mozambique, currently follows around 92 000 individuals living in approximately 20 000 enumerated and geo-positioned households. Its main strength is the possibility of linking demographic data and clinical data to promote and conduct biomedical research in priority health areas. Socio-demographic data are updated twice a year and clinical data are collected on a daily basis. The data collected in Manhiça HDSS comprises household and individual characteristics, household socio-economic assets, vital data, migration, individual health history and cause of death, among others. Studies conducted in this HDSS contributed to guide the health authorities and decision-making bodies to define or adjust health policies such as the introduction of Mozambique's expanded programme of immunization with different vaccines (*Haemophilus influenzae* type b, *Pneumococcus*) or the development of the concept of Intermittent Preventive Treatment for Infants (IPTi) that led to the World Health Organization recommendation of this method as best practice for the control of malaria among infants. Manhiça's data can be accessed through a formal request to Diana Quelhas (diana.quelhas@manhica.net) accompanied by a proposal that will be analysed by the Manhiça HDSS internal scientific and ethics committees.

Keywords Rural Southern Mozambique, HDSS, households, population, health, mortality, morbidity, migration, fertility, cause of death

Why was the Manhiça HDSS set up?

The Manhiça Health Research Centre (Centro de Investigação em Saúde de Manhiça, CISM) was established in 1996 to promote and conduct biomedical research in those diseases representing a major morbidity and mortality burden for the local population (malaria, tuberculosis, HIV/AIDS and bacterial disease), targeting primarily the two most vulnerable population groups, namely children under the age of 5 years and pregnant women. The centre was also set up with the aim of promoting the training in biomedical research of young Mozambican graduates from all

fields, so as to increase the critical mass of national scientists. Since its creation, the centre has developed its activities under a bilateral cooperation programme between the governments of Mozambique and Spain and with the support of the Hospital Clínic/Universitat de Barcelona in Spain. However, since 2008 the centre has been fully managed by the Manhiça Foundation,[1] a Mozambican foundation of public interest.

What does it cover now?

The Manhiça HDSS initially started producing baseline socio-demographic observational studies describing the patterns and trends of fertility, migration and mortality in the area, together with basic descriptive studies on the epidemiology and burden of the most prevalent infectious diseases. It has now widened its scope to include more in-depth molecular and immunological studies, entomological studies, clinical trials and other intervention studies covering the major health problems of the country, including malaria, diarrhoeal disease, tuberculosis, HIV/AIDS, pneumonia and other invasive bacterial diseases.[1] Figure 1 summarizes the research matrix in which all research activities conducted at Manhiça's HDSS can be found framed within five disease-specific programmes (vertical columns) and five common health areas (horizontal rows). Thus, research activities can cut transversely throughout such health areas and transcend disease specificity. Such a matrix reflects the multi- and trans-disciplinary nature of the research currently conducted in Manhiça HDSS.

As preliminary verbal autopsy studies conducted in the community showed that malaria was the principal cause of death among children, a major focus has historically been placed on the study of this disease. The initial projects included a study on the incidence of malaria in children in the Manhica District[2] and malariometric indicator surveys in this same area.[3]

In Manhiça, diarrhoea accounts for approximately 20% of paediatric hospital admissions and it is the fourth most common cause of death among children aged from 12 to 59 months. The main activities in this area included description of aetiological agents of diarrhoea (bacteria, viruses and parasites) and the molecular characterization of the pathogens.

Similarly, the centre has conducted epidemiological surveillance on the aetiology of pneumonias, bacteraemia and meningitis in the area, focusing on characterizing the burden of disease, antibiotic resistance, improvement of diagnosis and the evaluation of control strategies.

Within the field of HIV/AIDS, the centre has investigated mother-to-child transmission of HIV and the response to anti-retroviral treatment (ART) in adults, as well as describing the prevalence and burden of infection at the community level and promoting a thorough understanding of HIV primo-infection. The centre is now planning to introduce prospective HIV surveillance based on community testing as a mechanism to measure accurately HIV incidence and prevalence in the whole population.

Work in tuberculosis (TB) has focused on the improvement of the laboratory facilities to allow adequate isolation of mycobacteria, and antimicrobial sensitivity testing. The centre built a safety level III laboratory (BSL3) and can now automatically process biological samples using MGIT and GeneXpert. This has allowed work to start on determining the real

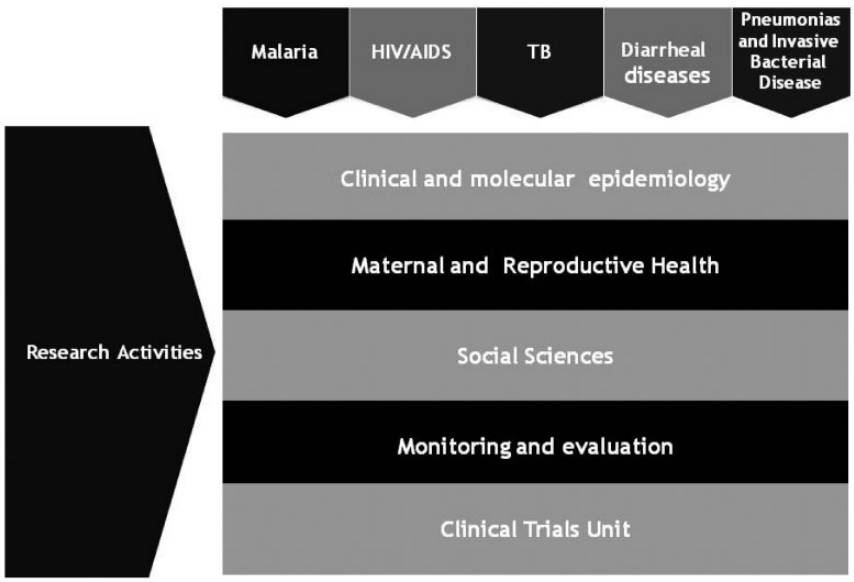

Figure 1 Manhiça Health Research centre's research matrix

TB incidence among children and the evaluation of drugs (fixed multidrug combination) and new vaccines for this disease.

Where is the HDSS area?

Manhiça HDSS is situated in the district of Manhiça in the southern part of the country, 80 km north of Maputo City, Mozambique's capital, at latitude 25°24′ south and longitude 32°48′ east (Figure 2). Manhiça district is located in a plain, surrounded by the Incomati River, covering an area of 2.373 km^2, with nearly 160 000 inhabitants.[4,5] The area has two distinct seasons. The warm season (November to April) coincides with the majority of the annual rainfall (average of 900–1100 mm) and is followed by a cool, dry season, lasting for the rest of the year.[6] Within the HDSS study area there are five health centres and one referral district hospital, whereby morbidity surveillance is routinely conducted. The District Hospital of Manhiça runs laboratory, X-ray, inpatient, maternity, paediatric, surgery and nutritional services and others. Two critical communication networks cross the town of Manhiça, namely National Road number 1 (connecting the south and north of the country as well as with other southern African countries) and the railway from Maputo to Zimbabwe.

Who is covered by the HDSS and how often have they been followed up?

Demographic surveillance started with a baseline census carried out in late 1996, covering at that time an area of about 100 km^2. In 2002, a first extension increased the study area to 450 km^2, and in January 2005 it was further expanded to 500 km^2. The majority of the study population are rural and most of them are engaged in subsistence farming, some as labourers in sugar cane plantations and sugar refining companies and others in small agriculture companies. The residents are mainly Xichangana and Xironga. The two predominant faiths are Christianity and Islam. The current study area population includes 92 000 individuals. Each person living within the HDSS study area is issued a unique permanent identification number to enable adequate follow-up. A resident is defined as any person who lives in the study area and expects to stay for at least the following 3 months.

Within the study area there are about 20 000 inhabited households that have been enumerated and

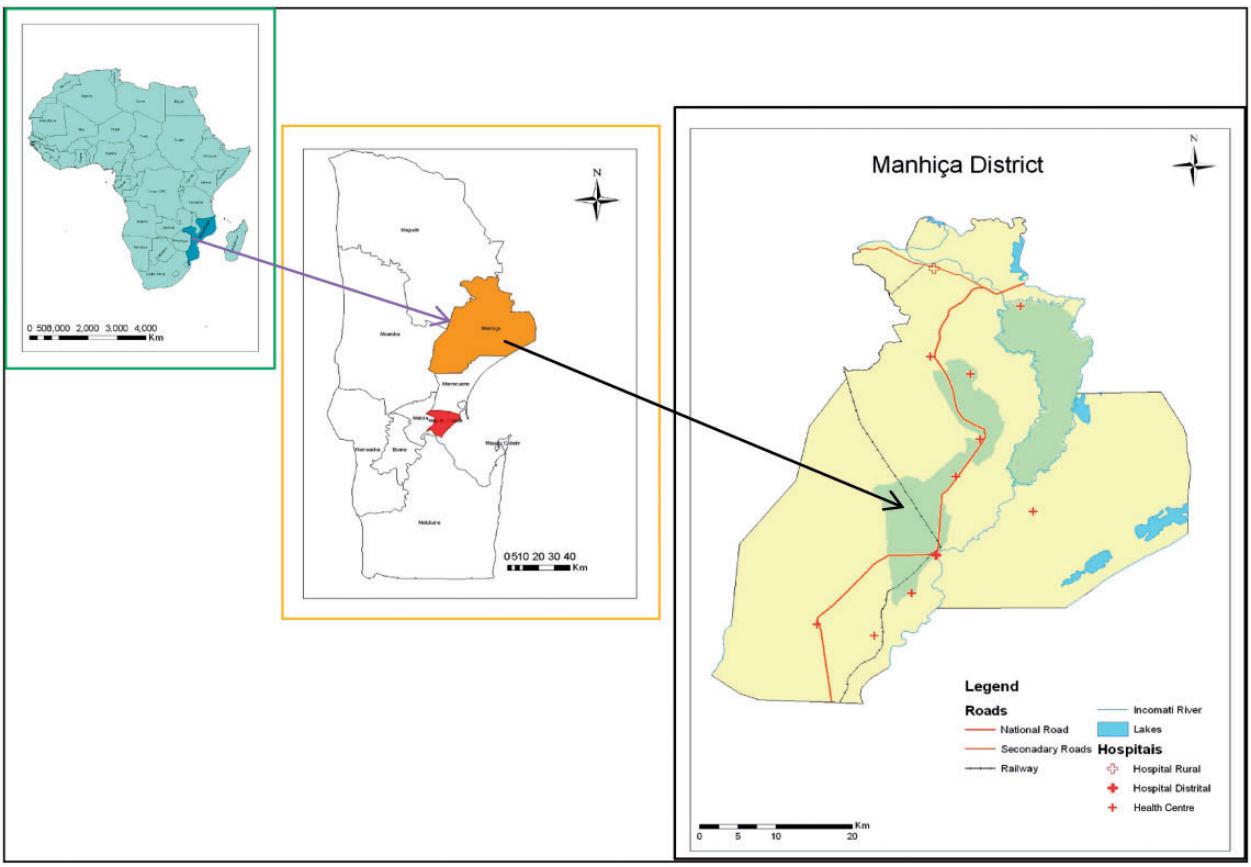

Figure 2 Location of the Manhiça HDSS study area

geo-positioned. Settlements are generally characterized by a loose conglomeration of compounds separated by garden plots and grazing land.[7]

Table 1 summarizes mid-year population and household numbers for the study area at four different time points during Manhiça's HDSS history, including the most recent available data. The 1997 data represent only the first study area (Posto Administrativo da Manhiça-Sede), the 2003 data represent data from Posto Administrativo da Manhiça-Sede, Mantchiana, Palmeira and Ilha Josina after the first expansion of the study area, and the 2006 data represent the mid-year data after including Taninga in 2005. Finally, the 2011 column shows the significant increase of the study population in recent times.

The age and sex structure of the HDSS population (Figure 3) is similar to the Mozambican population structure and to that of many other sub-Saharan countries, with predominance of young people and a dearth of older age groups. A particular feature of Manhiça includes the sharp reduction of males from ages 20 years and above, whose numbers decrease to almost half of those for females. This feature is also seen in other districts of southern Mozambique and may be explained by migration to Maputo City, South Africa and Swaziland and also by mortality, which is higher among males than among females[8]: the sex ratio is 79 and the age-dependency ratio is 110. Female-headed households account for 34.8% of households. The general adult literacy rate is 73.3% (males 88.1%; females 64.2%).

To update the demographic information, we adopted three different types of visits (Figure 4), with the rounds carried out on a 6-monthly basis being the regular update and most important visit. During the visit, vital events such as deaths, births and maternity, migrations, pregnancies, basic individual social characteristics and household characteristics and assets are recorded. The semestral visits are complemented by weekly updates from the key informants in the community and daily hospital visits, to avoid possible omission of events.[7,8] Additionally, verbal autopsies of all deaths occurring in children under 15 years old are routinely conducted to determine the underlying causes of death. For the period between 2002 and 2006, verbal autopsies were also conducted among adults.

Table 1 Population by year in Manhiça HDSS in four different years

Population characteristics		1997	2003	2006	2011
Mid-year population	Male	14 314	30 990	34 931	39 484
	Female	18 157	39 852	45 188	50 133
	Total	32 471	70 842	80 119	89 617
Mid-year households		11 784	19 871	20 702	20 354
Female-headed households		36.6%	35.7%	35.9%	34.8%

What has been measured and how have the databases been constructed?

Demographic histories of individuals including details of births, deaths, maternity, migrations, pregnancies, household characteristics and assets were collected from 1996 to 2011 on paper-based forms and stored on a relational database based on the Household Registration System (HRS) version 1[9] implemented in Microsoft Fox Pro™ version 5. In 2011, a new paper-free system was deployed, allowing the collection of more socio-demographic variables

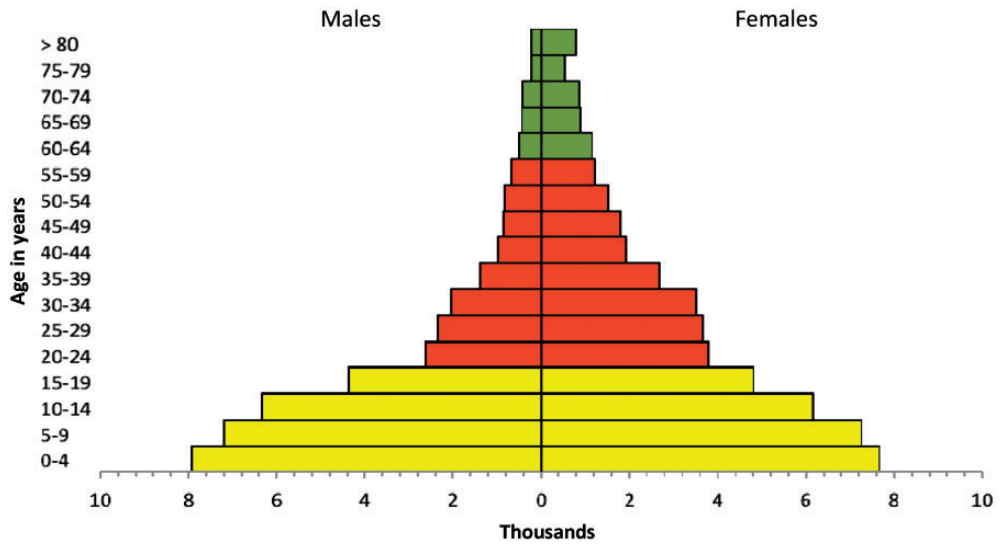

Figure 3 Manhiça HDSS population pyramid, 2011

(Table 2). The new data capture is implemented on advanced PDAs (Cogent Mobile Ident 3) using Microsoft Net Visual Basic™ forms and a SQLite database,[10] and feeding a central data warehouse based in MySQL™ version 5.1. Verbal autopsies of all deaths occurring in children under 15 years old continue to be performed.

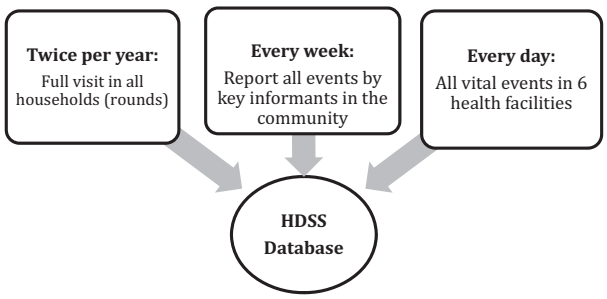

Figure 4 Diagram showing the three mechanisms for updating demographic data

Morbidity surveillance is routinely conducted among all children less than 15 years old visiting the outpatient consultation and inpatient clinics in the study area. Clinical data, including medical history, physical examination, routine laboratory basic investigations, ICD-10 based diagnosis, outcome and medication prescribed (Table 3) are collected daily on paper-based forms and reviewed daily by senior medical staff before being sent to the Data Centre for entry and archiving. To guarantee identification of HDSS children, the Permanent Identification Number is copied from a special HDSS card carried by all children. Data archiving relies on an application built in Microsoft FoxPro™ version 5, covering a range of specific forms with validation rules, alerts and error reporting lists.

Samples collected in the health facilities from specific studies are managed and archived using a laboratory information system (LIS) based on SERVOLAB Medizin Software Gmbh version 4. Every sample collected and sent to the CISM laboratory is identified with a labelled sticker, which includes a barcode-based

Table 2 Socio-demographic variables

Subject	Information collected since 1996	Information incorporated in 2012	Update visit
Demographic surveillance			
Household	Latitude, longitude		Round
	Type of construction, material of construction		Round
	Sanitation, number of places for sleeping		Round
	Water source, electricity, main fuel for cooking		Round
	Household assets		Round (once per year)
	Tools to prevent malaria		Round (once per year)
	Head of household characteristics (residency, HDSS ID)	Education, occupation, religion, place of birth	Round
Individuals	HDSS identification, names, sex, date of birth, education	Fingerprint, marital status, religion, occupation, place of birth	Round
	Relationship to the head of household		Round
Females of reproductive age	Pregnancy status		Round and hospital visits
Child less than 5 years of age		Retrospective immunization status (last 5 years)	Round
Pregnant women (maternal data)	Pregnancy outcomes, parity, IPT, tetanus vaccine,		Round, hospital and key informant visits
Newborn	Type of delivery, place of delivery, weight,		Round, hospital and key informant visits
	Length and gestational age		Round, hospital and key informant visits
Migration	Date, type of migration, origins and destinations	Causes of migration	Round and key informant visits
Death	Date	Place of death and raw cause of death	Round, hospital and key informant visits

Table 3 Clinical variables

Paediatric Morbidity surveillance	Information collected since 1996	Update visit
Outpatient and inpatient	Names, sex, date of birth, education, residency location	Every day
	Father's name, mother's name, head of household's name	
	HDSS identification	
	Anthropometric measures (brachial perimeter, height and weight)	
	Temperature	
	Samples for diagnosis	
	ICD-10 diagnosis	
	Treatment and outcome	

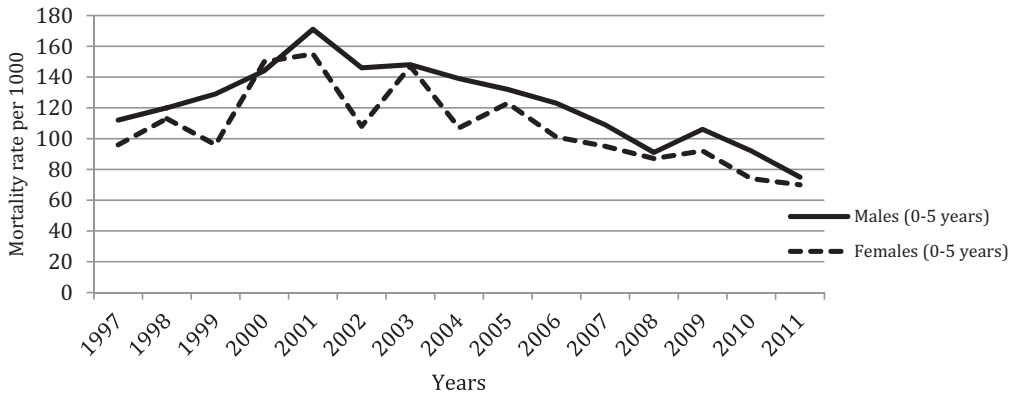

Figure 5 Manhiça HDSS under five rates between 1997–2011

unique identifier called NIDA (Sample Identification number). Thus parasitological or microbiological surveillance data routinely obtained from all children admitted to the hospital are stored in the centralized databases, with other study-specific laboratory data (molecular biology, immunology, etc.) similarly.

To accommodate specific needs from the studies (for example data related to a specific clinical trial or to a community-based specific survey), other systems for data collection coexist with the abovementioned systems. These systems, originally fed by paper, are now progressively being substituted by paper-free methodologies involving mobile phones and scanned documents for archiving. Three software packages are currently used: (i) Openclinica®,[11] (ii) Data Management for Field Trials Software (DMFTT2), an in-house application based on Microsoft Fox Pro™; and (iii) OpenDataKit (ODK)[12] mobile applications. All of them allow the introduction of study-specific validation rules to leverage the different required study checks.

Key findings and publications

During the past 16 years we have noted important changes in the mortality patterns in this community where child mortality rates have dropped by about 50% (Figure 5). In terms of causes of death, according to verbal autopsy data, among children less than 5 years of age the top five causes of death include malaria (21.8%), pneumonia (9.8%), HIV/AIDS (8.3%), diarrhoeal diseases (8.0%) and malnutrition (6.4%).[13] Conversely, adult mortality seems to be increasing particularly among men where the rates are double those of women (Figure 6). The HIV/AIDS pandemic and its high, associated TB co-morbidity seem to have played a major role in these trends. Causes of adult mortality have not yet been published for our HDSS. However, HIV/AIDS and TB seem to make a significant contribution due to the higher prevalence of these two diseases among adults in this area.[14]

Data for morbidity surveillance from the past 6 years (Figure 7) reveal an increase in the total number of outpatient visits, ranging from about 60 000 patients annually in 2006 to 80 000 in 2011. In contrast, there is an overall reduction in hospital admissions, despite some fluctuations observed over the years. The highest peak in hospital admission was observed in 2006 with about 3500 cases, and the nadir was in 2010 (about 2250 cases), mainly driven by decreasing malaria incidence rates in the area. Indeed, an upscale of malaria control tools in the past decade has probably contributed to the observed decrease in malaria transmission, which reduced the number of overall malaria cases and

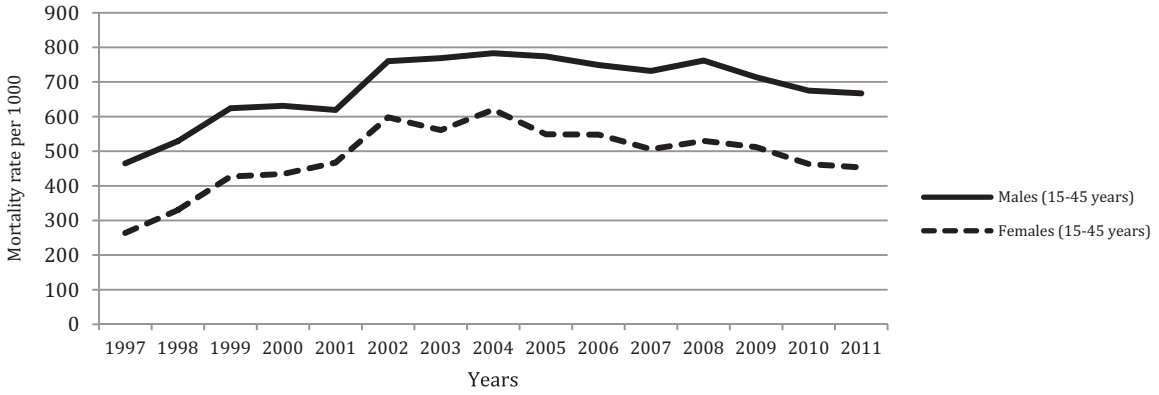

Figure 6 Manhiça HDSS adult mortality rates between 1997–2011

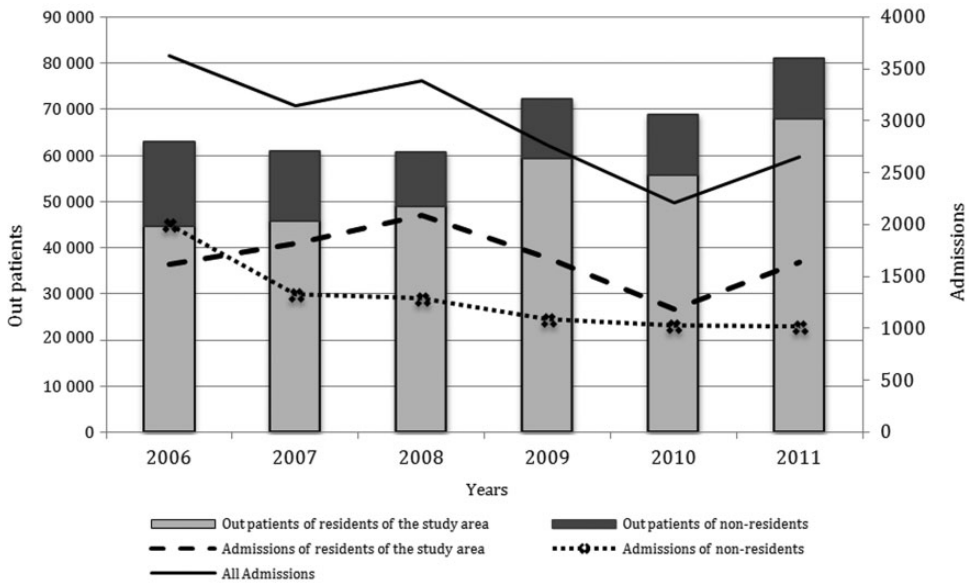

Figure 7 Manhiça HDSS: numbers of paediatric in- and out-patient cases, 2006–11

has contributed to emptying some of the hitherto very busy wards at Manhiça District Hospital MDH. Other major causes of paediatric morbidity in Manhiça, including pneumonia, diarrhoea, HIV/AIDS and neonatal conditions, have remained relatively constant.

Regarding the research studies conducted in Manhiça, major findings include the first clinical trials of the RTS,S/AS02A malaria vaccine that generated evidence on the vaccine's safety, tolerability, immunogenicity[15] and efficacy against clinical malaria (35.5%) and severe malaria (48.6%) among children and infants during a period up to 4 years post-vaccination.[16] Similarly, this HDSS also conducted a proof-of-concept trial of the RTS,S/AS02D malaria vaccine in newborns, providing evidence for the first time that it is possible to protect newborns with a malaria vaccine.[17] Other major trials on malaria preventive strategies included the evaluation of sulfadoxine-pyrimethamine as intermittent preventive treatment, both in pregnant women (IPTp) and infants (IPTi), demonstrating the validity and potential impact of such a strategy in malaria-endemic areas.[18,19]

On respiratory diseases, the centre's surveillance generated data on the high incidence (416/100 000 child-years at risk, reaching 779/100 000 in children under 3 months of age) of community-acquired respiratory infections[20] and their associated high case fatality rates (10%), and of bacteraemia per 100 000 child-years which was $1730/10^5$ in children less than 1 year old, 782/105 in those 1–4 years old, and $49/10^5$ in children aged 5 years and older.

Diarrhoeal disease, also frequent in the community, included incidence rates as high as $488/10^5$ child-years at risk for shigellosis among children aged 12–47 months[21] and $240/10^5$ child-years at risk for invasive *Salmonella typhimurium* among infants.[22]

Finally, cross-sectional studies in the community where 722 adults were recruited (50.7% women) described a worryingly high HIV overall prevalence of 39.9% [95% confidence interval (CI) 35.9–43.8], peaking to 44.8% in individuals aged 38–47 years (95% CI 38.4–51.2).[23] Our research findings contributed to guiding the health authorities and decision makers in defining or adjusting the national health policies. Some of these contributions were also used to define international health policies such as, for example, the WHO 2010 Intermittent Preventive Treatment (IPTi) recommendation to control malaria among infants.[24]

Future analysis plans

In addition to the aforementioned research ongoing at the site, in the short-term future we aim to continue analysing the morbidity and demography databases to evaluate trends and independent risk factors associated with disease patterns and population dynamics. Currently there are ongoing analyses to investigate the impact of parental HIV/AIDS deaths on child survival. In the context of malaria, studies are also ongoing aiming at describing the changing epidemiology of malaria, and its specific transmission dynamics, at both the mosquito (by measuring entomological parameters) and human host (by measuring parasite clonality, gametocytes and transmission hotspots) levels. These projects also include detailed descriptions of the principal vectors involved in malaria transmission and their seasonal and spatial variability, information that will be linked to data collected through the use of geographical information system (GIS) technology. Analysis of socio-demographic determinants for neonatal and infant mortality and analysis of underlying causes of death using verbal autopsies based on the InterVA model will also be conducted using the demographic data.

Strengths and weaknesses

Manhiça HDSS provides ongoing and periodically updated socio-demographic information (including births, deaths, pregnancy, migration and socio-economic status from a large population. Additionally, for those children under the age of 15 years who are part of this catchment area population, routine morbidity data from in- and outpatient visits to the health facilities within the HDSS are also collected. Since the baseline census, the participation rate in this community has been high. Only four households (0.02%) have officially declined to participate in our demographic update visits. Participation rates in studies in which blood samples are collected remain high, ranging from 70% to 80%. The centre includes its own laboratories, which are critical to conducting clinical trials and laboratory-based basic research. The combination of highly equipped laboratory facilities with demographic, morbidity and geographical platforms including GIS positions the centre advantageously with regard to other HDSS in Africa. Moreover, the centre has a clear capacity-building focus, and since its creation over 25 young Mozambican university graduates have benefited from research fellowships including field experience and master's and doctoral training opportunities in different recognized academic institutions around the world. The centre also offers internship possibilities to researchers from non-tropical countries. Although descriptive epidemiological data generated in Manhiça cannot be fully extrapolated to the entire country, nor to neighbouring ones, it is true that other results of research projects conducted in Manhiça are of high value to the developing world. The HDSS does not yet cover the entire Manhiça district area, and people not part of the study area cannot be adequately followed up. Similarly, some of the data derived from the HDSS may not be directly comparable to the official district statistics produced by the National Institute of Statistics of Mozambique because of different denominators. However, despite these limitations, Manhica HDSS provides the best and most accurate demographic and morbidity data for the whole of Mozambique.

Data sharing and collaboration

The Manhiça HDSS data are shared within the INDEPTH Network for different types of multicentre analyses and within the different INDEPTH specific working groups in which Manhiça has been invited to participate. Any collaborative proposal or any wish to use any of Manhiça's demographic, geographical or morbidity data (available from 1998 onwards) are always welcome and should be accompanied by a formal request directed to the scientific coordinator of the Centre, Dr Diana Quelhas (diana.quelhas@manhica.net) and a full protocol that will be analysed by the centre's internal scientific committee (CCI) and internal ethics committee (CIBS).

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Conducting research routinely in the same population entails some risk of population tiredness that can negatively affect compliance and acceptance to participate in new studies. We would like to specifically acknowledge and thank a highly participative and engaged community, with special mention of the

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Conflict of interest: None declared.

KEY MESSAGES

- The inclusion of a morbidity surveillance platform within the Manhiça HDSS has enabled a variety of complex clinical trials and disease-specific surveillance studies, leading to prolific and high quality scientific production, with over 70 publications.
- Manhiça HDSS was selected by the George Institute for International Health in 2007 as one of six mature research sites with technical capacity to conduct licensure malaria product trials and has become a model for other burgeoning research institutions in the continent.
- Manhiça HDSS conducted the first trial of the RTS,S malaria vaccine candidate in children aged 1–4 years (>2000 children) and infants (>200 newborns). In both cases, it showed vaccine efficacy against infection and clinical disease (including most severe cases), providing the first evidence that it is possible to protect newborns and children in a highly endemic malarious area of Sub-Saharan Africa.

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