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Cohort Profile

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Cohort Profile: Moramanga health survey in urban and rural areas in Madagascar (MHURAM project)

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Why was the cohort set up?

Despite public health policy on communicable and non-communicable diseases in Madagascar, the resources for obtaining reliable data at a national level are lacking. Although existing death notification data make it possible to monitor cause-specific mortality trends in the main cities, including the capital city Antananarivo,[1] national demographic and health statistics mostly result from epidemiological models such as those developed by the WHO or the Global Burden of Disease Study.[2,3] These estimates suggest that cardiovascular diseases are the leading cause of death in Madagascar, but evidence remains scarce on the burden of cardiovascular diseases and other non-communicable diseases in rural areas and in urban areas outside the capital.

The Moramanga Health survey in Urban and Rural Areas in Madagascar (MHURAM project) was set up to fill the gap in health surveillance for communicable and non-communicable diseases in urban and rural areas. By systematically collecting information on causes of death through verbal autopsies, the project helps assess the population's burden of disease and can potentially measure the impact of epidemics. It also collects detailed data on socio-demographic characteristics of individuals and households, and specific data such as blood pressure (BP) measurements or specimens for infectious diseases in order to shed light on varying epidemiological patterns in different population sub-groups.

Moramanga is a district spanning over 9336 km^2 and is included in the Alaotra Mangoro region, which comprises 21 communes divided into 175 '*fokontany*'. The '*fokontany*' represents the smallest administrative entity in Madagascar and is equivalent to a neighbourhood. Moramanga district is located 112 km from Antananarivo (latitude 18°57′ S; longitude 48°13′ E; mean altitude 900

m), and lies at the boundary between the east coastal area and the highlands (Figure 1). The climate is characterized by a 5 month rainy season in which temperature and precipitation peak from November to April. The winter is fairly cold for a tropical setting.

The Institut Pasteur of Madagascar (IPM) has implemented several research projects in this district, which is close to the capital city and easily reachable. In 1995, the district of Moramanga was initially considered to be a typical example of a fringe transmission pattern, according to the criteria of malaria endemicity defined by the Ministry of Public Health (MoH), and therefore it was selected by IPM as a field site for malaria control studies.[4]

In 2007, following the outbreak of chikungunya in the Indian Ocean, the MoH, with the support of IPM, set up a fever sentinel surveillance (FSS) network based on daily data collection. The main primary health care centre (HCC) and the district hospital based in the urban commune of Moramanga (UCM) were pioneer institutions within the new FSS network.[5]

In 2008, IPM conducted a large study in 14 districts of Madagascar, including Moramanga, in order to determine the prevalence and pathogenicity of bacterial, viral and protozoal enteropathogens in a case-control study of diarrhoeal and non-diarrhoeal stools of children <5 years of age. In 2009, a large animal study focusing on a small-mammal population to detect *Leptospira sp*. revealed that rates of infection based on positive PCR results were higher in Moramanga ($P < 0.001$) than in other districts in Madagascar (Toliara, Mahajanga, Antsiranana, Toamasina).[6] In 2010, IPM decided to establish a community-based longitudinal survey in Moramanga, and a hospital-based case-control study focused on diarrhoeal diseases in children <5 years of age in two rural villages.[7] In 2011, for the first time in Madagascar, a cross-sectional survey was conducted in the urban of Moramanga to estimate the prevalence of leptospirosis in humans.[8]

In 2012, the MHURAM project was established when the community longitudinal survey of children <5 years of age was extended to the entire population. The reasons for setting it up were varied. First, the location and socio-demographic profile of the population suggested that the site could be representative of the island. Furthermore, the local authorities were willing to collaborate and the MHURAM project had acquired expertise while implementing and conducting previous research projects. The project was carried out as a platform for conducting a variety of community- and/or hospital-based research studies on communicable and non-communicable diseases. In a subset of the population, biological samples or additional information were collected for specific studies, such as history of diarrhoea and intestinal parasite infection,[9] weight and height of children aged <5 years[10] and BP in adults aged ≥15 years.[11] In addition, knowing that at least four malaria-parasite vectors (*Anopheles funestus, Anopheles mascarensis, Anopheles gambiae* and *Anopheles arabiensis*) were circulating in the area, experimental huts were set up by IPM to test the effectiveness and safety of insecticidal solutions as well as to study mosquito behaviours in order to control malaria.[12]

The objectives of the MHURAM cohort are as follows.

i. To establish baseline data on the demographic, socio-economic, environmental and health characteristics.
ii. To document all births, deaths, in-migrations, out-migrations, socio-economic status, pregnancy outcomes and causes of death at regular intervals.
iii. To study changes in infectious diseases, chronic diseases and reproductive health.
iv. To provide a platform for interventional studies and health programme evaluation.
v. To provide facilities for training and multidisciplinary research for researchers, health professionals and graduate students.

What makes the cohort unique in Madagascar is that it exhaustively covers well-defined rural and urban areas. Another cohort exists in Madagascar, but it is located in a rural area only.[13] In the future, we plan to enhance the utility of the cohort by collaborating with the district authorities to link our database with those of the maternity, paediatric and adult wards in the hospital. Record linkage with health facility data will further improve health surveillance in the area.[14]

Who is in the cohort?

The entire population of 30 *fokontany* in 3 of the district's 21 communes was included in the MHURAM cohort: the urban commune of Moramanga (UCM, 13 *fokontany*); the rural commune of Ambohibary (AMB, 12 *fokontany*); and the rural commune of Ampasimpotsy (AMP, 5 *fokontany*). From October 2012 to May 2014, an initial census of the population in the 3 communes was conducted after mapping all the dwellings. Each dwelling in a *fokontany* was encoded in a geographic information system (GIS) and, in the case of households, fieldworkers asked for the number of household members before beginning to collect data on individuals.

The fieldworkers were recruited among young residents of Moramanga who had at least a bachelor's degree and were familiar with the study area.

During this initial census, data were collected from 71 587 inhabitants, representing 24% of the district population. A first round of follow-up was conducted from July 2016 to December 2017 and new arrivals were added

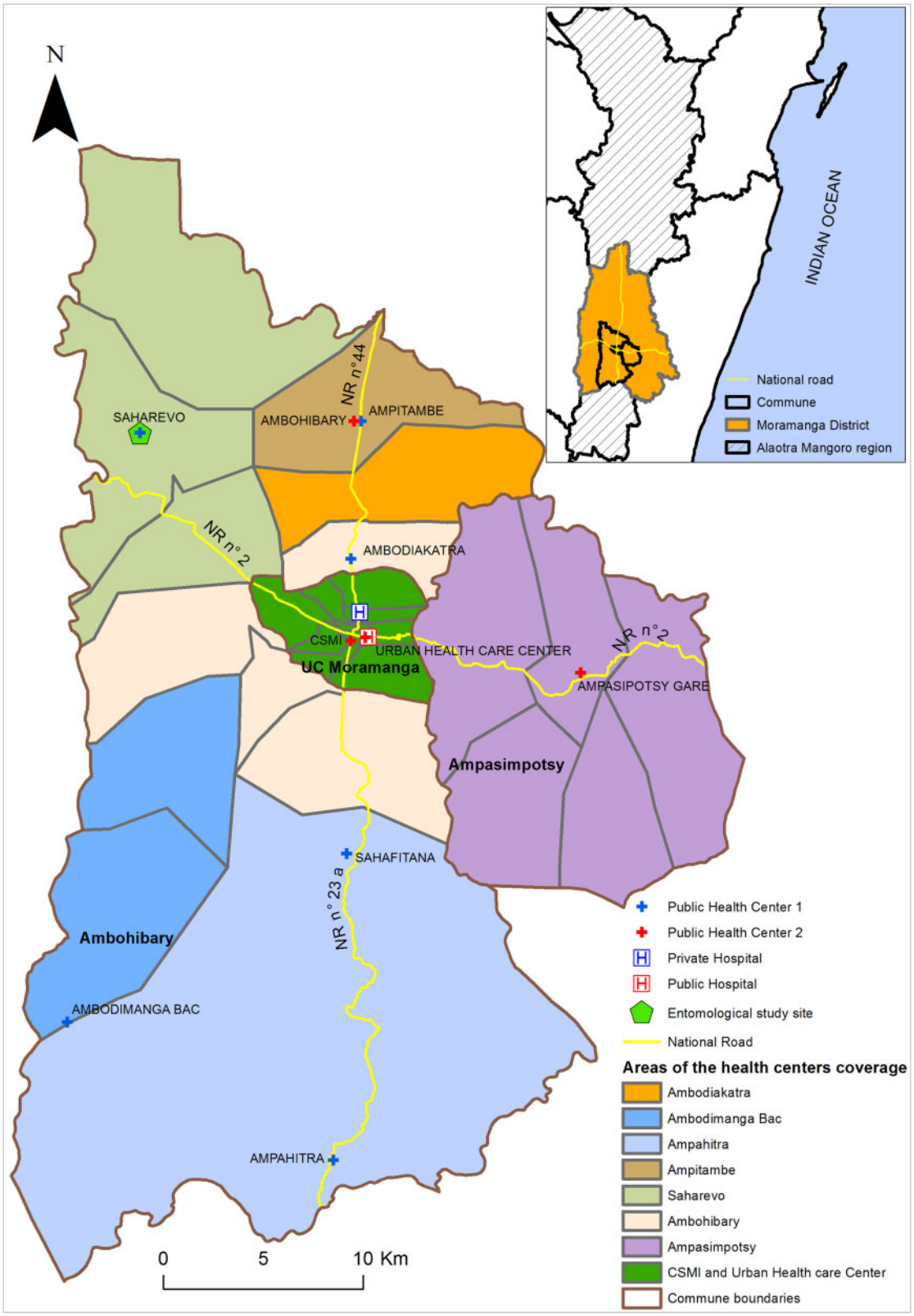

Figure 1. Localization and catchment areas of the Moramanga Health Survey in Urban and Rural Areas in Madagascar project and health care access centres, district of Moramanga.

(6814 inhabitants), thus giving a total of 78 401 individuals in the database after this wave.

As shown in Figure 1, the study site includes: 9 public primary HCCs and 6 private HCCs; one referral district hospital (with 13 paediatric and 63 adult beds, the district anti-rabies centre, a clinical laboratory and radiology facilities); and one private hospital (28 beds).

How often were they followed up?

After the initial census (October 2012–May 2014), a first round of follow-up was performed from July 2016 to December 2017. Because the paramedical staff that provided primary care to the inhabitants accompanied fieldworkers in each *fokontany*, very few refusals were encountered during the initial census and the following round (<5% in the majority of the *fokontany*).

The second round of follow-up is planned for 2019–2020. In 2018, Madagascar conducted a national housing and population census (Recensement Général de la Population et de l'Habitat, RGPH III), 25 years after the preceding census (in 1993), which was conducted by the National Institute for Statistics (INSTAT).[15] In order to augment the data already available for the cohort, we plan to collaborate with INSTAT and use the data from this RGPH III referring to the area under study.

What was measured?

The household is the basic survey unit made up of members who usually live in the same residence, share resources (such as food) and recognize one person as the head of the household. A resident is defined as an individual who usually lives in the household, slept in the household the night before the survey and/or intends to stay in the household for at least 6 months. The information collected during the initial census is shown in Table 1: the household's head (name, ethnic group and religion), composition of the household, and access to healthcare (in case of illness, need for family planning, pregnancy or accident) were recorded using electronic questionnaires on tablets. Trained fieldworkers who visited each household recorded as well their assets and property values to determine their socio-economic characteristics. Specific information was also collected according to the age of the participants: nutrition data for women of childbearing age and children aged <5 years in the households, pregnancy characteristics for pregnant women and vaccination and breastfeeding status for all children aged <5 years. The initial census collected information on basic socio-demographic characteristics, reports on deaths that occurred in the household over the last 5 years, and a complete birth history of all women of reproductive age. We obtained fertility rates by dividing the reported number of births (by 5-year age groups of mothers at the time of birth) and person-years lived by women aged 15–49 in the period 2003–2014.

In addition, a GIS was incorporated to map all dwellings during data collection. In a subset of the population, additional details were collected:

- In adults aged ≥15 years, height, weight and BP measurements were collected for a study on the prevalence of arterial hypertension. Additional information on risk factors of hypertension were collected through questionnaires (history of blood pressure >130 mmHg for systolic BP or 80 mmHg for diastolic BP, family history of hypertension, recent weight gain, inactivity, consumption of salt in diet, smoking, alcohol consumption).
- The height and weight of children were measured for a study on malnutrition in children aged <5 years. One stool specimen was collected from each child for intestinal parasite identification.
- A case-control study was conducted to study the aetiology of diarrhoeal diseases in children aged <5 years. Cases were recruited at the hospital and the controls were randomized in the population of children during the initial census. Some fieldworkers trained in standardized anthropometry determined the weight and length/height at enrolment. Fresh stools were collected from participants.

During the first round in 2016—2017, data were updated on all pregnancies, deaths, in-migrations and out-migrations that occurred since 2012—2014. For all pregnancies, details regarding the pregnancy outcome (live birth or stillbirth) were recorded, and for live births, information was collected on the date of birth, sex of the child, weight, place of birth, survival status and the duration of breastfeeding. All previously registered and new households in the 30 *fokontany* were visited by the local fieldworkers, who had been trained to use the same procedures as those of the initial census to interview heads of households or adults living in the house. If no inhabitants were present, the fieldworkers asked the neighbours if the household members were still living in the house. If so, they re-visited a maximum of three times within the data collection period, after which the household was listed as a non-responding household until the next update. If the neighbours answered that the household members had moved but were still living in the project area, fieldworkers asked for more information (date and reason for departure), and they searched for the household members in their new residence. They reviewed the composition of the previously identified households and collected any new information since the previous round. All households where

Table 1. Information collected during the initial census and each round of follow-up in the Moramanga Health Survey in Urban and Rural Areas in Madagascar

	Variable	Information	Characteristics
	Dwelling	Latitude and longitude	
		Type of building (administrative building, dwelling, health facility)	
Initial census	Household	Name of the household head, ethnic group and religion	
		Housing characteristics	Type of roof, main materials of the walls and floor, number of rooms used for sleeping, source of drinking water, type of toilet facilities, type of fuel used
		Household assets	Ownership of dwelling, rice field and/or vegetable garden
			Other assets: television, radio, sewing machine, telephone or mobile devices, computers, car, motorcycles, bicycles, refrigerator
			Livestock: cattle, poultry, domestic animals
		Food security: number of months per year when rice had to be purchased for the family, number and quantity of meals per day during the annual lean season	
		Food items taken the day before the survey for mothers and children <5 years old	
		Malaria	Occurrence of fever within last 3 months, need to take malaria drug, bed net, long-lasting insecticidal nets and participation in insecticide spraying campaigns
		Access to healthcare in case of illness, need for family planning, pregnancy, accident	
Initial census	Individuals	Name, date of birth, education level, main occupation, marital status, relationship with household head	
	For women aged between 12 and 49 years old	Fertility	Complete birth history
	For pregnant women	Pregnancy characteristics	Length of pregnancy, antenatal care conducted, use of preventive antimalarial drug
	For children aged <5 years	Vaccination status	Compliance with the schedule in the national program (BCG, diphtheria, tetanus, pertussis, polio, hepatitis B, *Haemophilus influenza* B, rotavirus, measles)
		Breastfeeding	Duration of breastfeeding
		Malnutrition study	Height and weight
			Stool specimen
	In a subset of a population: Individuals ≥15 years old	Hypertension	Two BP measurements after 5 min rest and at least 5 min apart
			Height and weight

(continued)

Table 1. Continued

	Variable	Information	Characteristics
		Risk factors of hypertension	History of BP >130 mmHg for systolic BP or 80 mmHg for diastolic BP, family history of hypertension, recent weight gain, inactivity, salt content of the diet, smoking, alcohol consumption
	Children identified as controls in the diarrhoeal study	Anthropometric measurements	Weight and length/height
			Stool specimen
For each round of follow-up	Births	Date and place of birth,	
		birth weight,	
		survival status of newborn,	
		medical attendance at birth,	
		mode of delivery,	
		child relationship with household head	
	Deaths	Date and place of death,	
		cause of death determined through verbal autopsy	
	Migrations	Date of immigration or emigration, type of migration (internal or not), place of migration,	
		reasons for migration	
	Pregnancy	Length of pregnancy,	
		antenatal care conducted,	
		use of preventive antimalarial drug	
	Pregnancy outcome	Information on pregnancy outcome,	Live birth, stillbirth, miscarriage, abortion
		date of delivery,	
		type of delivery (simple, multiple births),	
		antenatal care	
	For children aged <5 years	Vaccination status	Compliance with the schedule in the national program (BCG, diphtheria, tetanus, pertussis, polio, hepatitis B, *Haemophilus influenza* B, rotavirus, measles)
		breastfeeding	
	For the study on neonatal hepatitis B vaccination:	In case of pregnancy last year before the survey:	
	Women aged between 12 and 54 years old	If antenatal care not performed	Reasons why not performed
		Information on Hepatitis B screening, management and care	Reasons why not available
		If the delivery was not in health facility	Reasons why not
		Post-natal care	Reason why not performed

a death was reported to have taken place between the initial census and the first round were revisited for verbal autopsies to determine the causes of death. At the household level, relationships between the head of household and all residents were updated if there was a change in headship. The system also evaluates access to care by monitoring the distribution of health care facilities in the area.

During the first round in 2016–2017, women aged between 12 and 54 years were also invited to participate in a study to assess the feasibility of neonatal hepatitis B vaccination implementation in Madagascar. Specific questionnaires on behaviours during antenatal consultations, childbirth or pregnancy outcomes 12 months before the survey were asked in case of pregnancy at the time of data collection (Table 1).

Finally, after allowing for a grieving period of ~2 months, verbal autopsy (VA) interviews were conducted by trained fieldworkers in all households where a death had occurred. The interviews were conducted using the WHO's 2012 standardized verbal autopsy questionnaire during the initial census, and the WHO's 2014 questionnaire during the first-round follow-up.[16] The completed questionnaires were reviewed by

two physicians to determine the probable cause of death. Codes of the 10th revision of the International Classification of Diseases were used to classify all causes of death.[16]

The protocol for implementing and amending the first round of follow-up of the MHURAM project was approved by the National Ethics Committee of the MoH (approval N°52-CE/MINSAN 02/11/2009 and amendment N°60/MSANP/CE 26/05/2016).

What was found?

Key findings and publications

The initial census registered 16 789 households with 71 587 inhabitants living in the three communes during the period 2012–2014. The study site was 56.3% urban and 43.7% rural. The population was 50.3% female. Most heads of households were Christian (Catholics 44%, Protestants 37% and other Christian religions 17%); the remaining 2% were split into Muslim or without religion.

During the first round of follow-up, the information on 11 207 households was updated for 58 425 residents. The date of last information was recorded for the remaining individuals (either departure, still living in the household or death). Among households for which information was not updated, 3799 were reported by the neighbour or the head of the *fokontany* to have left their homes after the initial census but were not found in the study area (Table 2), and 1783 were not recognized by the neighbour or the head of the *fokontany*. These households were not considered as refusals, and their information will be updated in the next round if they are found in the study area. Fieldworkers added 6814 new arrivals who resided either in the former households surveyed or in new households (Table 2). The characteristics of households in urban and rural areas show differences in access to improved drinking water, the availability of and connection to the electricity grid and ownership of an indoor or outdoor shower (Table 2). People who never went to school were more frequently found in rural areas, whereas people who had been to high school or a trade school were scarce: 7% of all individuals interviewed in either 2014 or 2016 in urban areas and 0.8% in rural areas (Table 2).

At the initial census, the total fertility rate was estimated at 4.1 children per woman (3.1 in urban areas and 5.1 in rural areas), compared with an estimated 4.8 for all of Madagascar—according to the Demographic and Health Survey 2008–2009.[17] The collection of mortality data in the MHURAM project between the initial census and the first round of follow-up allowed us to compute mortality rates (which corresponded to a crude death rate of 8.3 per thousand per year) and life expectancy (which averaged 63.5 years for women and 59 years for men). The population pyramid for the initial census (Figure 2) shows an enlarged base, which reflects the youth of the population in Madagascar. As in the initial census, the first round of follow-up found more young people living in urban than in rural areas, which could be due to migration for employment and education. However, as a result of attrition (households who were reported as gone by the neighbours between the two waves of data collection), the population in 2016–2017 is slightly older than in the initial census (Figure 2).

In addition, several studies have been conducted in the area since 2012.

- Prevalence of arterial hypertension in people aged ≥15 years:[11] the results of this study showed a prevalence of 27% [95% confidence interval (CI) 25.6–28.5%] in rural areas and 29% (95% CI 28.3–31.1%) in the urban areas of Moramanga. Among hypertensive subjects, only 1.7% in rural areas and 5.3% in urban areas were on antihypertensive treatment for at least 1 month before the survey.
- Malnutrition in children aged <5 years:[10] ~42.1% (95% CI 39.0–45.4) had a poorly diversified diet, consisting mainly of foods rich in carbohydrates and poor in meat products. Poor maternal education was associated with a high likelihood of having a non-varied diet [OR (odds ratio) = 2.2 (95% CI 1.3–3.8)].
- Aetiology of diarrhoeal diseases in children aged <5 years:[9] rotavirus infection was the most frequently detected cause of diarrhoea. The presence of garbage around the house constituted the risk factor for severe diarrhoea (OR = 3.2; 95% CI 1.9–5.4) and nutritional wasting at enrolment (OR = 9; 95% CI 4.5–17.9).

Other studies had been conducted on the MHURAM cohort but the data was not collected between the initial census and the first round of follow-up. They relate to the aetiology of respiratory diseases,[8] antibiotic resistance in newborns,[19] family planning and access to care[20] and the burden of rabies.[21]

Finally, Moramanga is pre-identified as a potential study site for future vaccine and drug trials [two European & Developing Countries Clinical Trials Partnership (EDCTP) projects]. However, conducting clinical trials will imply some capacity building, adaptation of the facilities and staff training.

Major strengths and weaknesses

A major strength of Moramanga is its location and size. It provides a large population surveillance sample that comprises urban and rural populations. In terms of land size, it covers a large area for observation and is composed of easily accessible as well as very landlocked areas. It provides a robust sampling frame and physical infrastructure for

Table 2. Demographic and health characteristics in the Moramanga Health Survey in Urban and Rural Areas in Madagascar, overall and by round

Variable	Total households enrolled in either 2014 or 2016		Households retained in both 2014 and 2016		Households present in 2014 but not participating in 2016		Household newly enrolled	
Household (HH) characteristics								
Total HH	17 300		11 207		5582[a]		511	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
Total number of HH	9665	7635	5161	6046	4284	1298	220	291
Mean HH size	3.9	4.4	4.3	4.6	3.5	3.6	3.1	3.4
% of HH with access to improved sanitation facilities	29.8	27.7	35.1	28.3	23.8	27	20.9	19.2
% of HH with access to improved drinking water (bottled water, private or public tap)	49.4	0.7	48.1	0.7	51.6	0.5	37.3	1.4
% of HH with an indoor or outdoor shower	58.8	10.8	58.9	9.8	59.4	15.7	48.2	8.6
% of households with electricity	62.9	6.8	64.5	6.2	61.1	9.9	59.5	6.5
Individual characteristics								
Total individuals	78 401		51 611		19 976		6814	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
Total individuals	40 767	37 634	22 738	28 873	15 235	4741	2791	4019
Male sex %	49.1	50.2	48.9	50.2	49.7	50.4	48.1	49.8
Age group (in years) %								
0–4	15.4	20.1	11.9	15.5	15.1	17.5	46.1	56.2
5–14	23.8	27.5	25.8	29.9	22.7	25.3	13.9	13.1
15–49	50.9	43.8	49.6	44.9	55.7	49.4	36.2	28.7
50–64	7.5	6.4	9.7	7.3	5.2	5.7	2.7	1.5
65–79	2.0	1.7	2.6	2.0	1.1	1.4	0.9	0.3
≥80	0.4	0.4	0.5	0.4	0.2	0.7	0.2	0.2
Maximum education (for people aged ≥6 years old) %								
Never in school	2.4	11	2.1	10.8	3.0	13.4	9.8	1.9
Primary school	31.6	60.5	33.2	69.3	30.5	53.5	29.0	54.6
Middle school	59.0	27.7	60.6	29.6	58.3	31.6	59.9	34.6
High school or professional school	7.0	0.8	6.1	0.7	8.2	1.5	9.2	1.0
Marital status (for people aged ≥12 years old) %								
Single	38.2	35.5	38.7	36.6	36.3	28.8	47	7.1
Partnered	52.1	55.1	50.6	54	55.4	60.8	43.9	55.7
Separated, widowed	9.7	9.4	10.6	9.4	8.3	10.4	9.1	37.2
Exclusive breastfeeding duration (for children aged <5 years old) %								
<6 months	36.4	39.7	35.4	37.2	38.2	35.3	35.3	46.1
6 months	56.5	49.6	58.7	53	54.8	54.4	54.8	41.2
>6 months	4.4	5.4	4.9	6.8	5.5	8	1.2	1.8

[a]Including: households visited in 2016 that were recognized and reported as having left, according to neighbours or the *fokontany* administrator, although their final destination was not reported ($n = 3799$); and households visited only once, which means during the initial census ($n = 1783$).

supporting different study designs, including clinical trials. Moreover, a GIS of all constructions has been set up since the census, which allows for easy geo-localization of the residents and the mapping of other desirable parameters. Located 112 km from Moramanga, the IPM and all its laboratory and clinical research facilities are relatively nearby.

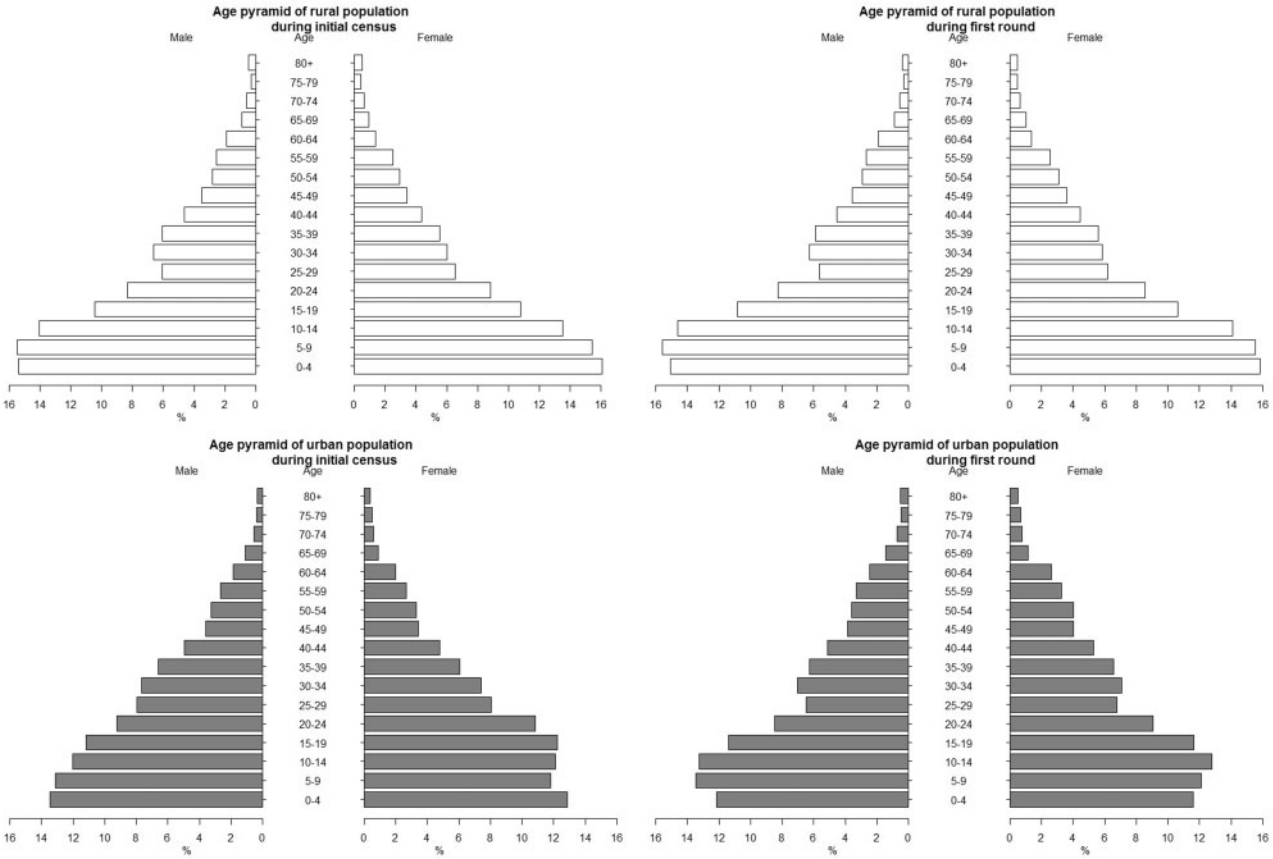

Figure 2. Age pyramid of rural and urban population during the initial census (2012–2014) and the first round (2016–2017) in Moramanga.

The MHURAM project provides a platform where researchers and students can conduct their scientific, clinical and socio-anthropological research. It may support research on both infectious and chronic diseases in all age groups.

Another strength is the close working relationships with the district health facilities. Moramanga is a district with one hospital that includes a paediatric ward and clinical laboratory equipment, with whom strong collaboration has been encouraged through several research projects.

The main weakness is the high cost of running the surveillance of a large population and the constant need to seek external funding. The project is not yet well known and has not forged strong collaborations with members of the International Network for the Demographic Evaluation of Populations and Their Health (INDEPTH) network.[22]

There is also a risk of community fatigue. To balance this, some projects taking place in Moramanga compensated their participants by distributing gifts (cereals, oil, soap, etc.) or disbursing cash payments for time spent during the investigation. Efforts are being made to reduce this practice by recruiting a paramedical staff to accompany fieldworkers and provide primary care to sick people at the household level.

Collaboration with the National Statistics Institute has been planned, and this will allow us to use data from RGPH III to triangulate and augment data from the demographic follow-up in Moramanga.

Can I get hold of the data? Where can I find out more?

We encourage scientific and medical research collaboration, and this includes sharing data for specific research questions, providing that formal agreements can be made. A standardized template for a data-sharing agreement is available at IPM (French and English versions). Enquiries and queries can be submitted to the first (rila@pasteur.mg) and last (lbaril@pasteur.mg) authors of this paper.

Profile in a nutshell

- The Moramanga Health Survey in Urban and Rural Areas in Madagascar (MHURAM) project is unique in Madagascar, as it includes urban and rural Malagasy populations. Its exhaustiveness also reinforces the importance of this project.

- The MHURAM project is a decision-making tool for health authorities, supported by research projects that can ensure sustainability and funding that also benefit the population of Moramanga.
- The Epidemiology and Clinical Research Unit team has the capacity to perform all the steps needed for clinical research, from protocol development after feasibility assessment to operational work, Standard Operating Procedures (SOPs), data collection and analyses; and this includes scientific validation. Maintaining high quality in research and developing innovative methods constitute key drivers for this team, which is accustomed to collaborating with international teams.
- Moramanga is a site where the laboratories based at IPM (entomology, virology, biology, mycobacteria, immunology, etc.) can work closely with the local facilities. The IPM hosts 11 national reference laboratory centres in Madagascar.

Funding

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