Chapter 5
Mixed Research Methods for Buruli Ulcer Prevention in Southern Benin Using Geographic Health Surveys

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5.1 Introduction

Emerging diseases linked to environmental contamination are a major public health problem. One such disease is *Mycobacterium ulcerans* infection, or Buruli ulcer (BU), which has become the third most frequent mycobacterial infection after tuberculosis and leprosy (Dhungel et al., 2021). The rural zones of West and Central Africa, with their poor access to water treatment infrastructures and clean drinking water, are the regions most affected by this disease today (Simpson et al., 2021). This infection, caused by an environmental mycobacterium (*M. ulcerans*), causes vast skin ulcers and may lead to severe functional incapacity if the wounds are not treated in time (incidence of disability: 25%). This disease may, in rare cases, be fatal and has a major impact in terms of the stigmatisation, exclusion and poverty of those affected. It affects all age groups, but children under the age of 15 years account for almost half the cases declared worldwide (WHO, 2019). In Benin, women are more frequently affected than men in the adult population, but the sex ratio varies between regions (Vincent et al., 2014).

No interhuman transmission has ever been recorded. Instead, contamination occurs exclusively via an environmental reservoir (Garchitorena et al., 2014; Marsollier et al., 2002, 2007), linked to one or several aquatic ecosystems. Ecological

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studies have shown that an aquatic environment with a low oxygen content and temperatures of 29–33 °C (Merritt et al., 2010) is the ideal environment for *M. ulcerans* development. Other studies (Marion et al., 2011a; Marsollier et al., 2007; Wallace et al., 2017) have shown that the inoculation of skin tissues with the bacillus is required for disease development. In West and Central Africa, aquatic biting insects, including water bugs in particular (Portaels et al., 1999), which tend to develop and reproduce close to slow-moving watercourses or still bodies of water, are strongly suspected to be involved in transmission. The *M. ulcerans* bacterium has been detected in the salivary glands of these insects, and experimental transmission to mice has been demonstrated in the laboratory (Marion et al., 2010, 2014; Marsollier et al., 2007; Robbe-Saule et al., 2017). Studies performed in Australia suggest a different ecology of *M. ulcerans*, in which the bacterium is capable of colonising terrestrial mammals (Betts et al., 2020; O'Brien et al., 2019). The lesions are often localised on the lower limbs (60% of cases), and on the legs in particular, probably due to the mode of penetration of the bacillus into the body (Zingue et al., 2018). In this context, the principal risk factor for exposure to *M. ulcerans* identified to date in Benin is direct contact, of variable duration, with a slow-flowing or stagnant water source harbouring various aquatic organisms, probably leading to human contamination via bites, although this scenario does not exclude other possible modes of transmission (Boccarossa et al., 2020; Dhungel et al., 2021; Muleta et al., 2021).

Between the 1980s and 2006, the number of new cases of BU (between 5000 and 10,000 cases per year according to the WHO) and the number of humid tropical regions affected increased continually (Zingue et al., 2018; Degnonvi et al., 2019). This led to this disease being included in the list of 17 neglected tropical diseases targeted by the WHO. In Benin, the annual number of cases peaked in 2007, at a mean of 1200 reported cases for this year. Following a trend towards an increase in case numbers, 2217 cases were declared around the world in 2019, providing evidence of an unexplained progressive decrease in incidence in Africa (WHO, 2019). Conversely, a close examination of the principal epidemic foci in Africa identified major spatial disparities in the indicator of detection rates over the last 15 years (Fig. 5.2a). Taking the endemic Ouémé/Plateau region of Southeast Benin as an example, we find highly restricted zones in which detection rates remain high (between five and ten cases/year/borough) only a few kilometres away from zones presenting a marked decrease in incidence or even zones of non-endemicity (fewer than ten cases in ten years). Such exceptions can also be found at the scale of a village or quarter (Fig. 5.2b). Our team decided to use mixed methods of research to try to identify the anthropic and environmental factors accounting for this variation of incidence. This global research strategy is based on the principle that the dissemination of knowledge contributes to the adoption of prevention tools and health promotion in village communities.

This chapter aims to retrace the development of our research strategy, since 2016, up to the current research project, COPTER-UB (2022–2025). In the first year, we experimented with a new method: geographic health surveys. These surveys combine a classic case-control study with tools for data collection developed in the social sciences, associated with geolocalised and environmental analyses. Before presenting these surveys based on cross-comparisons of observations and our intermediate conclusions concerning the initial findings, we will explain the reasons for which a precise region of Southeast Benin was chosen as the study zone and the new methodologies and preliminary data available to us for the construction of this new project.

5.2 The Ouémé/Plateau Region: An "Experimental Space" for Investigating Variations in the Incidence of the Disease

Benin is one of the countries that has pioneered the fight against Buruli ulcer. Since 2005, almost all patients have been able to benefit from antibiotic treatment, either as outpatients or during hospitalisation, thanks to the establishment of four specialist centres in this country, in the towns of Pobé, Allada, Lalo and Zagnanado. Today, with early diagnosis, antibiotic treatment (Phillips et al., 2020) based on rifampicin and clarithromycin and appropriate lesion management, it is possible to control the infection and to prevent permanent sequelae, such as amputation and the disabling retraction of one or several limbs. However, this early management of lesions is often difficult in regions of endemicity in which the disease is rife, due to the inability of health structures to cover the rural zones they serve effectively and due to a preference of the local population for the traditional practices of their communities (such as self-care at home or consultations with practitioners of traditional medicine).

Our decision to perform our research in the Ouémé/Plateau region of Benin was based, first and foremost, on the high level of endemicity of Buruli ulcer in this geographic zone. This region is covered by the Centre for the Detection and Treatment of Leprosy and Buruli Ulcer (the CDTLUB) of Pobé, which still receives more than 50% of all cases detected in Benin. This hospital aims to strengthen early screening for skin ulcers in the most remote villages while improving the clinical diagnosis and therapeutic management of patients, with or without surgery. Since 2004, when the missions of the CDTLUB were launched, a research partnership has been established between this centre and the ATOMyCA team based in Angers, for work on the ecology of the bacterium and its mechanisms of transmission. A collaboration with the CNRS UMR 6590 team has also been established more recently, for the identification of territorial practices linked to the incidence of Buruli ulcer. This sharing of experiences and knowledge enables us to base our studies on a large cohort of Buruli ulcer patients. More than 2500 cases have been diagnosed, with biological confirmation by PCR, since 2006. The availability of key indicators, such as the age and sex of the patients, or the number of cases per year in more than 210 villages in the 5 municipalities of the study zone (Pobé, Adja-Ouéré, Bonou, Adjohoun and Dangbo), was also a major factor in our decision to perform investigations in this region (Fig. 5.1).

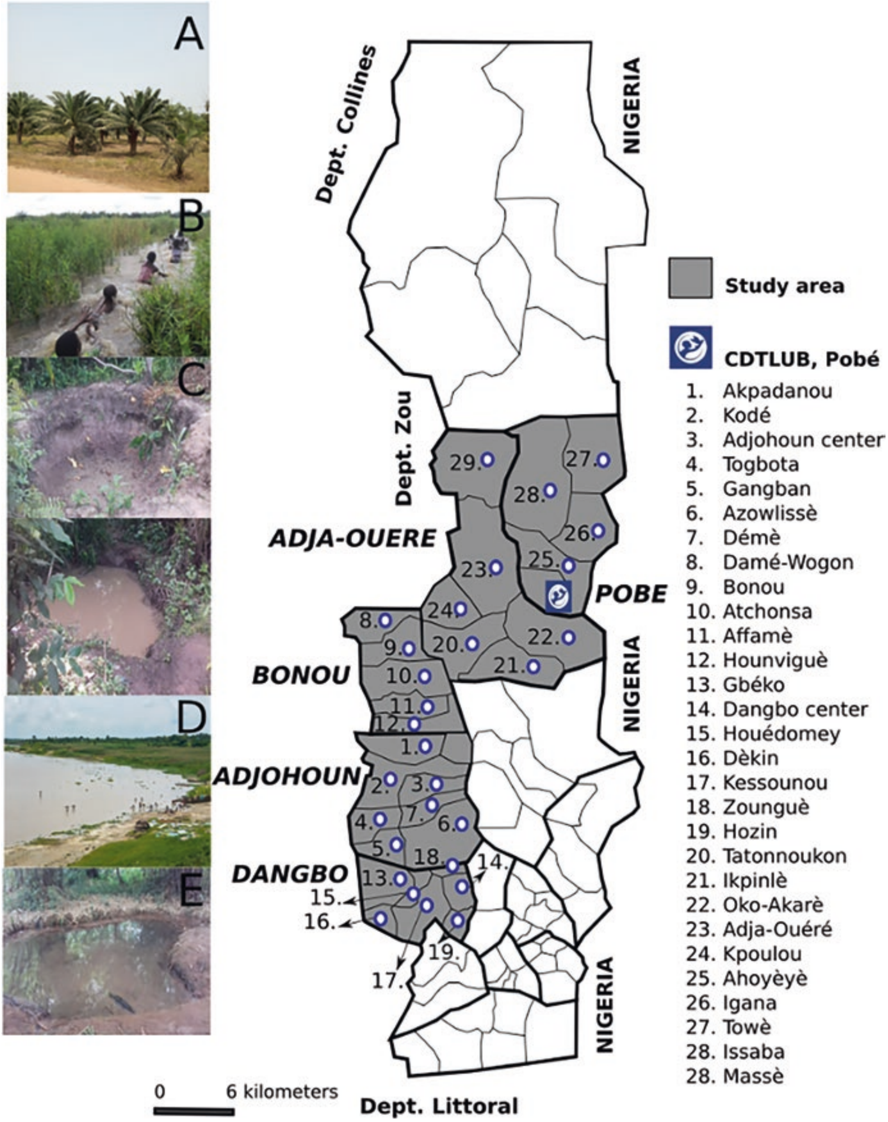

Fig. 5.1 Geographic location of the study zone: the Ouémé/Plateau region of Southeast Benin. (**a**) Oil palm plantations in the Plateau zone, (**b**) a seasonal body of water used by children for bathing, (**c**) seasonal water holes dug by humans, (**d**) the Ouémé River and (**e**) a managed spring in the Ouémé valley. (Source: *Cahier des villages et quartiers de ville du Département de l'Ouémé et du Plateau*, RGPH-4, 2016; Personal photographs taken by Boccarossa A. 2019–2022)

The study area can be split into two distinct zones: the Plateau and Ouémé zones. Oil palm plantations divide up the countryside in the two municipalities of Plateau (Pobé and Adja-Ouété) (Fig. 5.1a). Percolation levels are low in the soils of the villages of these municipalities, which are located far from the river and its principal tributaries. Many areas, including agricultural areas in particular, are flooded with rainwater runoff for several months of the year. When the level of flooding is sufficient to form a basin of water, children play (the school holidays coincide with this period), look for fish and bathe in these temporary bodies of water (Fig. 5.1b). Villagers in the Plateau zone generally get their water from bore holes or wells during the dry season. However, it is not unusual for them to shift these activities to natural seasonal water sources, ponds or water holes during the rainy season (Fig. 5.1c). These water sources were dug out by humans for the construction of dwellings or infrastructures for the village communities. They are of very different sizes, and the water they provide often originates from multiple closely spaced rain episodes. This context explains the rates of drilling work (for bore holes and wells) in the villages of Plateau being the highest in the study zone, with endemicity levels for Buruli ulcer that have remained stable for a decade (lower number of incident cases than the Ouémé zone). Buruli ulcer is endemic to 2 of the 44 villages of the Pobé municipality. These 2 villages, Eguelou and Onigbolo, recorded 18 and 23 cases of Buruli ulcer, respectively, between 2006 and 2020.

Unlike Plateau, the Ouémé zone is characterised by a large floodplain with a complex hydrographic system. The Ouémé river (Fig 5.1d) is used by the villagers, who have settled along its banks (village of Agonlin, Fig. 5.2b). This zone also contains tributaries and streams that join the river via various branches and springs located at the top of many of the drainage basins (Fig. 5.1e) that criss-cross the extremely shallow gradient of the fertile wetlands on which food crops predominate. The villages located close to this flooded and irrigated environment still have the largest numbers of Buruli ulcer cases. In the north of the Ouémé zone, two boroughs—Bonou and Damè Wogon—report between five and ten cases per year (Fig. 5.2a).

In this chapter, we associate the Plateau/Ouémé region with an "experimental space" for investigating these variations of incidence. If we focus on the endemic zone, it is frequently possible to find one or several endemic villages located close to non-endemic villages (Fig. 5.2b). For example, in the boroughs of Gangban and Togbota (Adjohoun municipality), the village of Gbada had 60 cases between 2006 and 2020, and Yokon had more than 25 cases over the same period. Each of these sites is located 4–6 kilometres away from villages with low detection rates over this period (Fingninkanme had only 5 recorded cases in 15 years) and non-endemic villages, such as Agonlin, along the banks of the river (Fig. 5.2b). The observation of isolated sites with discontinuous epidemic episodes is not unusual (Gbekandji, with 21 recorded cases). Our methodology is based on these spatial variations and exceptions.

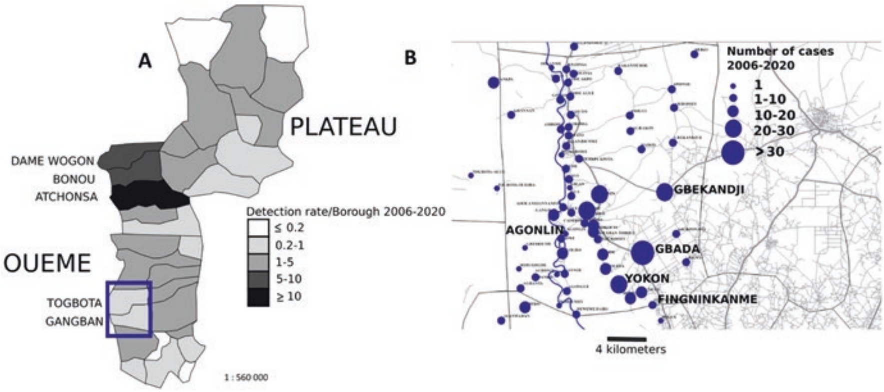

Fig. 5.2 Spatial disparities of incidence (by borough) and exceptions (villages) at the scale of the Ouémé/Plateau region. (Source: Surveillance data from the CTDLUB de Pobé; A. Boccarossa, 2022)

5.3 Preliminary Data and Methodological Advances

Over the last 15 years, many case-control studies have demonstrated that visiting natural and unprotected water sources for domestic activities (e.g. fetching water, washing oneself and doing the laundry) is reported more frequently by cases (Buruli ulcer, BU) than by controls (Aiga et al., 2004; Debacker et al., 2006; Kenu et al., 2014; Maman et al., 2018). Permanent surface water bodies located close to dwellings have, thus, become the reference spaces for studying risk factors for exposure to the disease. In parallel with these prospective studies, Benin launched a national anti-BU programme in 1997 (Johnson et al., 2008). One of the priority axes of this programme was the establishment of an epidemiological surveillance system. Since 2010, the surveillance data obtained have shown a progressive decrease in the number of new cases (Boccarossa et al., 2022; Degnonvi et al., 2019). However, inequalities in exposure to the disease are continuing to increase and translate spatially into marked differences in incidence between villages and, sometimes, even between quarters of villages within the same geographic area. The Ouémé/Plateau region in Southeast Benin is particularly strongly affected by these health inequalities. Our team therefore started from the initial hypothesis that these within-village fluctuations might be linked to the some water sources being more exposed than others to the bacterium, due to different organisations or different natural elements likely to influence the contamination of individuals either directly or indirectly. Differences in the modes of use of these resources were also suspected. Since 2016, we have performed coupled analyses of socioenvironmental data, shedding new light on these risk factors.

5.3.1 First Experimental Study (2016–2017): Relationship to the Establishment of Artificial Protected Water Sources

From 2005 onwards, studies (Wagner et al., 2008) showed that sites with daily access to hydraulic facilities (wells, bore holes or hand pumps), in both the dry and rainy seasons, had few, if any, cases of Buruli ulcer. This was the case in conurbations, which were better equipped with bore holes than remote rural areas, and in villages with no access to natural water sources in their immediate environment. In 2016–2017, a first experimental study (Degnonvi et al., 2019) aimed to investigate the possible correlation between this decrease in incidence and the progressive installation of hydraulic equipment in the villages along the banks of the river Ouémé close to semipermanent water courses or water sources (ponds and naturally formed water basins). This study was based on cross-comparisons of data from the CDTLUB of Pobé (epidemiological surveillance data) and the Ministry of Energy, Water and Mines of Benin (data on hydraulic installations in the area), followed by a case-control study (106 cases and 212 controls) in the community of Bonou (Ouémé).

This study showed that the progressive installation of hydraulic equipment in the villages had contributed to a decrease in the frequency of contact with natural water sources associated with a risk of exposure to BU (Degnonvi et al., 2019). By contrast, these protective actions alone were insufficient to account for the variations in BU incidence, because many domestic activities continued to be performed at natural unprotected water sources. In-depth interviews with the village communities and field observations provided us with an explanation for this situation (Boccarossa et al., 2020). Price was the first factor identified. Drinking water is often pumped or taken from a well, which is more expensive than using natural water sources, because of the higher quality of subterranean water, but many domestic activities are maintained in free surface waters. The decision to use a natural water source rather than water obtained with hydraulic equipment may also be correlated with site of residence according to the principle "you go to what is nearest". The large amounts of water available at natural water sources also facilitate washing activities, particularly for laundry (Fig. 5.3a). In addition to the distance between dwellings and the hydraulic equipment, and the price of water, which may limit the use of water from certain sources for certain purposes, we also observed a diversity of local microconfigurations contributing to the maintenance of domestic activities at unprotected water sources. Firstly, water supplies were sometimes cut off following disputes within the village or with public authorities. Insufficient maintenance of many wells and bore holes also led to many breakdowns and the abandonment of certain wells and bore holes by the population concerned (Fig. 5.3b). Finally, when the depth of the water is sufficient for bathing activities, these natural water sources become the site of leisure activities for children (Fig. 5.3c) and a space for relaxation for adults. These bodies of water are also key sites for gatherings that are particularly appreciated by the local population (Fig. 5.3d).

Fig. 5.3 Local microconfigurations contributing to the maintenance of domestic and recreational activities in and around bodies of free surface water. (**a**) The large amount of water available facilitates washing activities, (**b**) definitive abandonment of a bore hole, (**c**) children bathing in the surface waters and (**d**) a site for social activities and meetings. (Source: Personal photographs taken by A. Boccarossa 2019–2021)

Using a bore hole or well was found to be associated with protection against BU in this study (Degnonvi et al., 2019), but the results also showed that the presence of hydraulic equipment in a village or quarter did not always guarantee the complete cessation of activities associated with free surface waters. The villagers continued to adopt mixed practices, using different water sources for different purposes (e.g. bore holes for drinking water and bodies of surface water for washing activities), thereby maintaining activities at risk of exposure to *M. ulcerans*. Our work then naturally focused on the precise identification and comparison of these water sources and the practices and behaviour of the local population with respect to water. This work was part of the GéANT programme, which obtained funding from the Pays de la Loire region (regional scientific issues) and the Raoul Follereau Foundation in 2017.

5.3.2 The GéANT Project (2017–2021): A Cross-Sectional Approach Focusing on Water Sources

In this project, we sought to acquire knowledge of the bodies of water most favourable to *M. ulcerans* and the activities associated with the highest risk of contracting the disease (detailed in Sect. 5.4.1). We also eliminated from our considerations all sites and behaviours considered "protective" (detailed in Sect. 5.4.3). For these reasons, the project was based on a three-principle transverse approach: observation of the principal water sources visited by village communities and the various activities practised at these sources, follow-up of cases and controls coming into contact with the water sources and a comparison of different attitudes with respect to environmental sampling, and a spatial analysis to characterise these spaces (Fig. 5.4).

Our preliminary data were obtained in a pilot study in health geography (Boccarossa et al., 2020) focusing on the hydrogeographic characteristics of the water sources frequented in village environments and the activities and attitudes of the inhabitants, at the scale of 37 villages in which BU was either endemic or non-endemic (non-endemic defined as fewer than ten cases over a period of ten years). Direct observation was at the heart of the research methodology. It involved walking around the perimeter of the village and identifying and characterising the principal water resources visited by the local population (Fig. 5.5). These field surveys, coordinated by the ESO team, provided us with quantitative and qualitative data for 198 water sources (167 water courses and 31 bodies of water) visited daily by

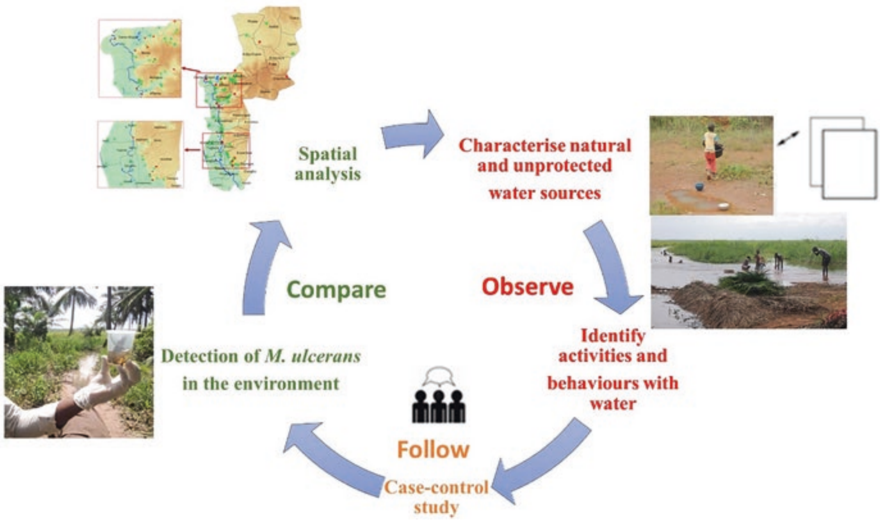

Fig. 5.4 Construction of the GéANT project around three principles: observation, follow-up and comparison. (Source: A. Boccarossa, 2022)

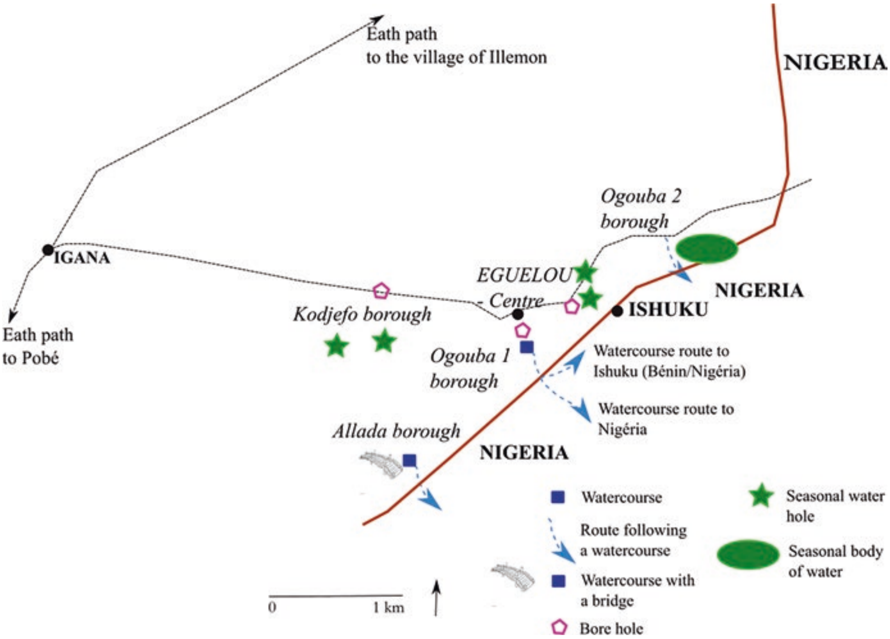

Fig. 5.5 Diagram summarising the natural water sources and hydraulic structures at Eguelou, an atypical village on the border with Nigeria. (Source: A. Boccarossa, 2022)

villagers. Not only did these prospective surveys make it possible to distinguish, at each site studied, traditional (river, tributary, water hole, etc.) and modern (bore holes, drinking fountains, cemented wells) water sources, but they also made it possible to identify clearly sites at which material had already been collected on the practices and behaviours of villages with respect to water. Observations were initially itinerant or "diffuse" (Gumuchian et al., 2000), with "fixed" or "posted" observations (Chapoulie, 2000) for nine natural water sources eventually completing the research strategy. These surveys took place in several steps: one or several periods of interaction with the population, observations of all the activities performed at different moments of the day and, finally, the recording of data with the assistance of printed and numbered observation grids. Finally, ten different activities involving contact with water were analysed. Collecting water (for drinking, cooking, washing-up or washing at home) and walking through watercourses on foot to reach cultivated fields or a neighbouring village were the two most frequently observed practices. In a sample of 1411 individuals observed, women aged 20–50 years (45%) and children of both sexes (27%) were the groups most frequently represented in these spaces.

The village of Eguelou, located in the borough of Igana, to the northeast of Pobé, on the border with Nigeria, had an incidence of BU of 5.2 for the 2006–2022 period. This incidence is relatively high for the zone. At this site, 19 cases of Buruli ulcer were reported, whereas most of the other villages in this borough are little affected or have never been affected by this disease. The village of Eguelou was, therefore, studied as an exception. During itinerant observations, we noted the installation of two functional bore holes in 2011 and a hydraulic structure that was not working. In the borough of Kodjefo, bore hole water was used by the entire population, for all domestic activities. By contrast, in the other three boroughs (Ogouba 1, Ogouba 2 and Allada), bore holes were used more occasionally and seasonally (when the natural water sources dried up). A first watercourse in Ogouba 1 constitutes the principal source of water in the village. The water flows slowly along a route regularly used by the population to get to the fields or to other villages on the Nigerian border. This water source dries up during a very short period, while the water table that feeds it is refilled. During this short period, the villages make use of bore holes or another watercourse located in Allada. At this water source, a wooden bridge has been built to enable villagers to cross from one bank to the other without having to enter the water. We also observed several water holes that had been dug in Ogouba 2 and Kodjefo. During periods of heavy rain, the water is stored and used for domestic activities and for the preparation of palm oil, but only rarely for drinking. These water sources may be considered a "back-up" in that they are only used for a few days or weeks of the year. Finally, a basin of water was subsequently discovered that is essentially visited by children for bathing and fishing activities. Repeated episodes of rain in the months of June and July create these new masses of water, the precise location of which may change over the course of seasons and years.

In the GéANT programme, an initial prospective (case-control) study provided us with data on the individual and social trajectories of 111 patients with BU confirmed by the CDTLUB of Pobé, who were then compared with a group of 222 controls. The dimensions covered by a questionnaire and an interview guide used from January 2018 to December 2020 broadly concerned personal characteristics, everyday habits and the modes and reasons for the use or non-use of free surface waters. A PhD student from Benin (thesis defended on December 3, 2021) visited the subjects at home for questioning. These epidemiological data were collected not only for statistical purposes but also as part of a territorialised environmental approach. More than 500 sets of GPS coordinates were recorded at the three types of site visited by the study subjects: (1) home, (2) work or school and (3) protected artificial water sources (wells and bore holes) and unprotected natural water sources (courses and bodies of water). These results enabled us to map the spatial and social practices of the patients, cases and controls in a geographic information system

(GIS) developed by the OIEs (Indian Ocean Spaces and Societies) laboratory of the University of Reunion Island. At the natural water sources identified by the patients, more than 1300 samples of aquatic plants, invertebrates and vertebrates and organic matter were collected from the environment, at more than 65 sites, and tested for *M. ulcerans*. The environmental samples were collected by a Beninese research assistant training at the HECOTES (Hygiene, Sanitation, Ecotoxicology, Environment and Health) laboratory at CIFRED (the Interfaculty Centre for Environmental Training and Research for Sustainable Development), at Abomey-Calavi University. Finally, the search for molecular signatures of *M. ulcerans* by quantitative PCR on tissue homogenates was performed by the ATOmycA team at the Nantes-Angers Centre for Cancerology and Immunology Research. This team had already developed the methodological know-how for this microbiological analysis in a previous ANR project (the EXTRA MU project), during which almost 30,000 PCR tests were performed on environmental samples over a period of 2 years (Marion et al., 2010, 2011b).

The results of this mixed-method research were recently published in *PLOS Glob Public Health* (Boccarossa et al., 2022). We showed that the frequentation of water sources is more risky if these resources are located in regularly flooded or irrigated wetlands, which can be grouped together under the umbrella term "low-lying" areas. The distribution of BU patients in the south of the country is delimited by the perimeter of two types of wetland (Fig. 5.6). On one side, there are lands with a shallow slope situated along or close to a large plain regularly flooded by the Ouémé in spate (type 1). On the other side, there are low-lying lands that are more circumscribed in space and characterised by shorter periods of flooding due to the accumulation of runoff water or the backing up of a downstream river or stream (type 2). The analysis of environmental data also demonstrated a greater abundance of *M. ulcerans* in the aquatic organisms collected in this low-lying area. Furthermore, our field observations revealed that the water sources present in these spaces were associated with a greater cumulative number of risk factors for transmission (slow flow rate, flow obstructed by an accumulation of sediment and plant material, greater number of biting insects in the water), particularly when the water levels of the river subside (in October–November). Finally, these observational data revealed that the behaviours and territorial practices taking place in these low-lying areas are far from limited to domestic activities. As a means of diversifying their income and supplying the markets of the towns and their surrounding areas with fresh produce, the villagers have developed rice and maize production and market gardening activities (Hounsou et al., 2020; Iwikotan et al., 2016). Since the 1980s, runoff and irrigation networks have been traced out, to improve the use of the damp and fertile low-lying areas (Abou et al., 2018). These localised practices in the low-lying areas, which have increasingly been shown to be associated with risk factors for exposure in recent case-control studies (Dhungel et al., 2021; Muleta et al., 2021), remain little known and have not yet been systematically analysed. In future projects, we will therefore need to broaden our view, expanding from studies of water source use (GéANT project) to studies of all spaces favourable to vectors of the disease. The DAILYRISK-MU project, funded by *Fondation de France*, aimed to explore a new

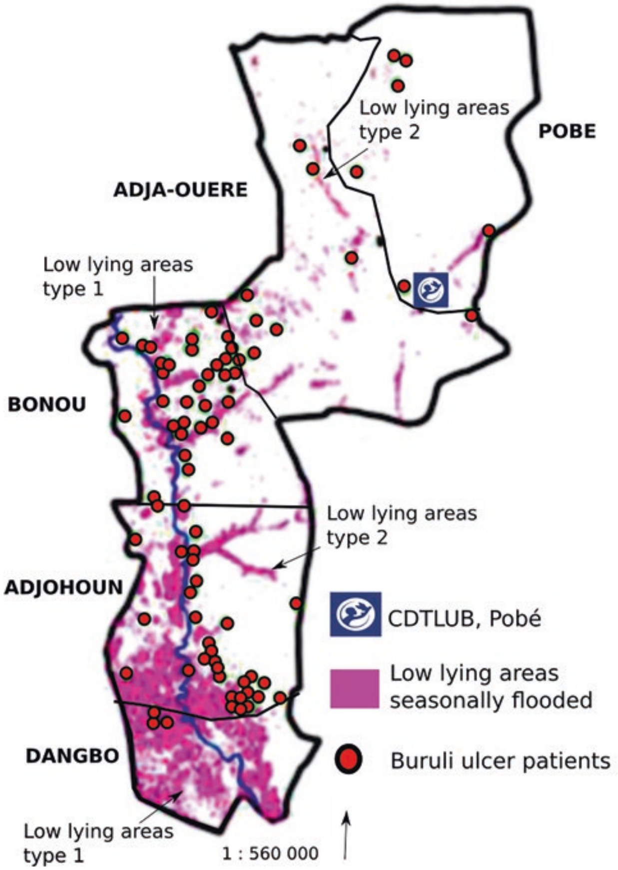

Fig. 5.6 Distribution of BU cases in the zones of Plateau and Ouémé in South Benin in the 2018–2020 period (Source: GéANT project data, 2022)

research protocol following this rationale—geographic health surveys—over the course of a year.

5.4 Geographic Health Surveys: Shifting Focus to a Search for All Spaces Favourable to Vectors of the Disease

The aim of these surveys is to continue to follow all new patients over the 2022–2024 period, according to the integrative approach developed in the GéANT programme (Fig. 5.4). However, the acquisition of territorial and environmental data has been expanded to all living spaces (home, work, school, water sources, bathing areas, routes taken to get from one place to another, cultivated fields, etc.). As in the GéANT study, the patients recruited for this study are defined as people who have developed one or several “Buruli ulcers” detected by screening and confirmed by PCR. The inclusion of cases contracting the disease in regions other than those covered by the CDTLUB of Pobé is avoided by including only patients residing in the geographic area of the study zone at the time of diagnosis (Fig. 5.1). The study area encompasses the villages belonging to two municipalities in the Plateau zone (Pobé and Adja-Ouéré) and three municipalities in the Ouémé zone (Bonou, Adjohoun and Dangbo). All villagers in these two zones have similar access to care, and the same preventive strategies have been deployed to combat this disease (in terms of sensitisation, active screening, treatment and follow-up campaigns). The basic principle of a case-control study is also conserved in this study, with the selection of two controls from the community for each patient recruited, matched for site of residence, age, sex and profession (for adult cases). Based on our initial study, we estimate that the geographic health surveys should be based on 150 cases and 300 controls (given a mean of 50 new cases/year).

The GéANT programme gave rise to a prospective case-control study and made it possible to determine the attitudes of the villagers and the activities associated with the greatest risk of exposure to *M. ulcerans* through fixed and itinerant observations (Figs. 5.4 and 5.5). We are currently extending this work, by combining these methods to determine which of the patients, cases or controls are most prone to practices exposing them to infection. The methodology of this new project, thus, follows the same process of iterative engagement, involving a long interview with cases and controls at their home (with an interview guide and a questionnaire) and then accompanied field visits combining the taking of GPS coordinates with environmental sampling if risk factors for transmission are found at the site (detailed in Sect. 5.3.2). The novelty of this project also lies in the implementation of surveys specifically adapted for children aged 8–14 years, based on several tools described below.

5.4.1 Long Interviews at Home: Collection of Qualitative and Quantitative Data on Lifestyle and Habits with Respect to Water

We retained the questionnaire and interview guide developed in the GéANT study, to ensure compatibility between our future data and those previously collected. The current study is novel in the addition of questions on factors explaining disease and the local perception of these factors among patients and controls. The objective is to determine whether the perception of the disease, and, thus, the adoption of preventive attitudes on the one hand, or recourse to care on the other, varies according to the site and the life context of the people interviewed. Finally, we are extending the GéANT programme by adding items relating to five types of behaviour specifically associated with a risk of transmission to the interview guide. These types of behaviour have been identified in our results or in published studies but have rarely been analysed with a systemic approach (Fig. 5.7): (a) children’s bathing activities, (b)

Fig. 5.7 Five types of behaviour specifically at risk identified in Southeast Benin. (**a**) Children bathing, (**b**) washing activities at "seasonal sites" and at water sources submerged by local flooding, (**c**) hydroagricultural work in the low-lying areas, (**d**) walking through watercourses to get to a field or neighbouring village and (**e**) the collection of aquatic forage plants to feed domestic animals. (Source: personal photographs taken by A. Boccarossa 2019–2022)

washing activities at "seasonal sites" and water sources submerged by local flooding, (c) hydroagricultural practices in the low-lying lands, (d) walking through watercourse to get to cultivated fields or to a neighbouring village and (e) the collection of aquatic forage plants to feed domestic animals.

5.4.2 Guided Tours: Collection of Geolocalised and Environmental Data

With a view to characterising the activities and spaces at risk of exposure to *M. ulcerans* as well as possible, the long interview at home was followed by a guided tour. This tour was scheduled to take place either directly after the interview or at another

In the preparatory phase of the project, the fifth of these elements—"collecting aquatic forage plants to feed domestic animals"—was not specifically targeted. In 2011, a case-control study in the region endemic for BU of Bankim in Cameroon revealed an association between the presence of domestic animals, such as pigs, goats and chickens, in domestic living spaces and an environmental risk of infection (Landier et al., 2011). In our study zone, domestic animals also live in close contact with the local population, in enclosures or freely roaming, but interventions between humans and animals were not previously suspected to play a role in BU. Nevertheless, our investigations in the municipality of Adjohoun (Ouémé) in November 2021 enabled us, for the first time, to identify a type of risky behaviour linked to animal husbandry: daily searches for herbaceous plants in the low-lying lands for use as animal feed, a form of feed particularly appreciated by sheep. *Ipomoea aquatica Forssk*, also known as kangkong or water spinach, is a semiaquatic plant that grows specifically in marshes and wetlands. The plants of this species are collected by hand, without the use of protective clothing (e.g. boots or long clothes). Based on this observation, the bacillus could be transmitted during this specific practice, if the aquatic plants that proliferate in the Ouémé valley are considered to be a possible reservoir of *M. ulcerans* (Marsollier et al., 2007). DNA from *M. ulcerans* has already been detected in insects and molluscs sampled from the roots of aquatic plants in Southeast Benin (Portaels et al., 1999) but also in the stems and leaves of these plants. We have added a section to the questionnaire dealing specifically with this behaviour, to explore the role of this practice in transmission mechanisms.

time in the week. This method is inspired by work performed by the Cresson team at the University of Grenoble (Lenel, 2014) and the mobile research method developed in the (Extra)Ordinary Lives project (Ross et al., 2009). It involves planning a tour of the everyday living spaces of the people interviewed, on foot, in the spirit of a guided tour, with the person guiding the tour providing comments, during the walk and on site, of their practices and attitudes with respect to the sites evoked in the interview guide. In this study, the patients/controls receive some advice at the start. They are asked to plan a route including all the sites at which direct contact with water occurs together with permanent or seasonal wetlands. As in GéANT, GPS coordinates are recorded for all the sites visited, with a Garmin Etrex 10 device, and environmental samples are collected. Aquatic invertebrates and vertebrates (insects, spiders, molluscs, shrimps, etc.) are collected at all the "points of contact with the aquatic environment" visited by the cases and controls studied (in years 1 and 2 of the project). Samples are collected with a net with a mesh size of less than 1 mm (Fig. 5.8a). Water bugs are separated from the other invertebrates (Fig. 5.8b) and samples of aquatic plants (Fig. 5.8c) to complete the sampling procedure.

Fig. 5.8 Collection of environmental samples from the aquatic sites visited by the study subjects. (**a**) Equipment required for the collection of insects and plants, (**b**) water bugs sampled in the field, (**c**) aquatic plants sampled in the field and (**d**) environmental sampling session at a village endemic for BU. (Personal photographs taken by A. Boccarossa, 2019)

For each sample collected, a form is completed, providing information about the topographic and hydraulic characteristics of each point of contact with the aquatic environment. The individuals present during sampling (Fig. 5.8d) are also asked about water management and associated behaviours with respect to water. Rainfall patterns in this zone are marked by a four-month period of flooding (from July to November) that modifies the interactions of villagers with aquatic resources and the ways in which they can use water. For example, children can bathe and washing activities can take place in temporarily flooded zones that are dry during the rest of the year. Seasonal dynamics have been integrated into our analyses, with scheduled sampling at points of contact with the aquatic environment at this precise time in the year or during two periods of the year (once in the dry season and once in the rainy season). Based on our experience in the field and the method used, we estimate that we will need to analyse about 300 sites during the study period (a mean of 100 sites sampled per year).

5.4.3 Survey Tools Adapted for Use with Children Aged 8–14 Years

Over the 2018–2020 period, almost 52% of the patients diagnosed and treated at the CDTLUB of Pobé were schoolchildren, high-school students or adolescents not attending school (Degnonvi et al., 2019). Based on this information, we considered it essential, in this new study, to identify more precisely the behaviours, representations and opinions of this group of young people. The difficulties experienced in the questioning of children and adolescents with classical survey methods (questionnaires and interviews) constitute a subject increasingly frequently dealt with in articles and seminar reports in the domains of sociology (Camus et al., 2020), anthropology and social sciences (Danic et al., 2006; Potin, 2012; Robin et al., 2017) and education science (Euillet, 2017). The research objectives and terrains dealt with in these previous studies were all different, but all studies on childhood cultures and the world of adolescence agree on one point: the need to adapt the data collection methods to these young individuals or to "create" an appropriate method. On reading the articles corresponding to the principal case-control studies performed to date on our subject in Africa (Aiga et al., 2004, Debacker et al., 2006, Kenu et al., 2014, Landier et al., 2011, Maman et al., 2018), we noted that exactly the same data collection methods had been used for the children as for adults. This approach has two limitations: a methodological limitation relating to the risk of the child or adolescent not understanding or misunderstanding the questions and an ethical limitation linked to the well-being of these youngsters, who, in a classic interview based on questions and responses, may have the feeling that they are seen and considered to be different from the other youngsters living in their district (Potin, 2012). Our field experience also suggested that some children are very prudent and circumspect when asked about the disease at the start of the interview and that they have difficulty expressing themselves about their activities and the sites they visit if interviewed in the presence of their parents. For this reason, we felt that the implementation of survey methods specifically adapted for children and adolescents was particularly important in this project.

For this purpose, we decided to use fun supports for the collection of data. After carefully studying published articles on the subject, we chose supports that evoked the spaces of everyday life, and the different types of behaviour with water were presented as drawings on cards (Fig. 5.9). This new approach was based on the WASH programme, which had already been tested in schools, notably in Benin, and which made use of drawings to raise the awareness of children concerning hygiene and sanitation (Peal et al., 2011). For our study, 24 cards were developed. The regular or seasonal activities depicted on these cards are based largely on the results of the GéANT case-control study and our observational data (see Sect. 5.3). The card collection has an amusing and stimulating graphical environment designed in partnership with a Beninese designer (Fabel Art Pobé).

In addition to being more agreeable for the children, this new survey system aims to improve the quality of the results obtained. The children are questioned directly,

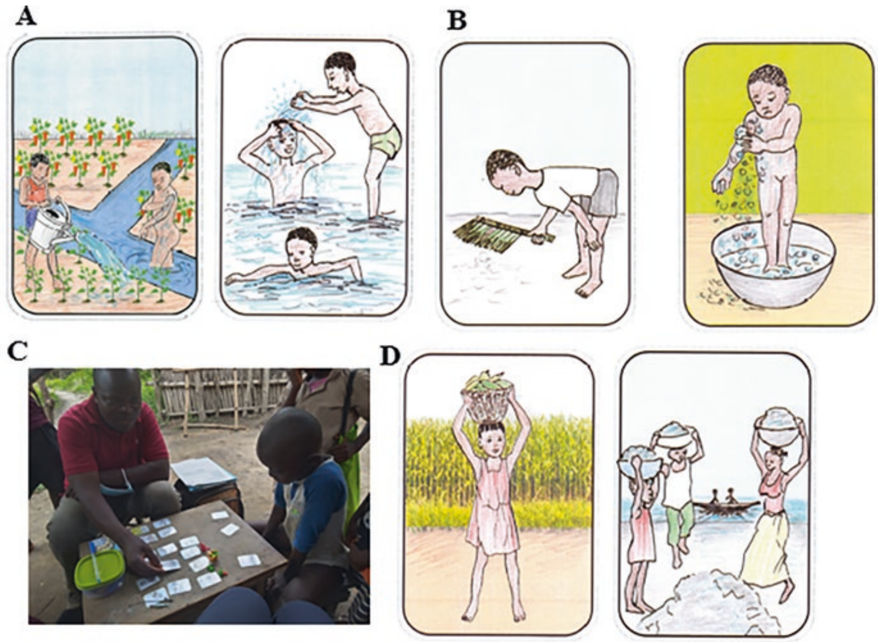

Fig. 5.9 Several examples of the drawings on cards used in surveys with children. (**a**) Activities associated with a risk of transmission, (**b**) "protective" activities, (**c**) testing of the protocol with a child with BU diagnosed in 2020 and (**d**) weekend and holiday activities. (Source: COPTER UB, 2022)

in the first person, without interference from their parents. The children are asked to choose, from among the cards presented to them, those best corresponding to their living spaces and the activities they perform during a typical weekday: when they get up in the morning, at school, what they do when they come home from school and before going to bed (Fig. 5.9c). Some of these cards (Fig. 5.9a) represent specific risky practices (e.g. playing in the water or washing in irrigation channels), whereas others (Fig. 5.9b) show practices that are considered to be "protective" (playing with a ball, washing clothes or oneself in the courtyard of the house). Each set of drawings selected by a child case is photographed by the investigator and then compared with equivalent photographs for the corresponding two cases. The children are also asked to select two other series of cards corresponding to a typical day during the weekend and during the school holidays (Fig. 5.9d). During these two periods, many children help their parents with work in the fields, have jobs in the sand quarries, amuse themselves in the water and go fishing. The preferred times for interviewing children are the school holidays and the hours of the day during which the children are free (after school). As for adults, the exchanges are recorded and retranscribed at the end of the fieldwork. Finally, the children are also given the possibility of extending the interview with a guided tour. They can be replaced by their parents or guardians for this tour if they do not wish to be seen at the sites they regularly visit.

5.5 The Lessons Learned Mid-study

Health geographic surveys were tested with 40 patients and 80 controls (between November 2021 and July 2022), in the framework of the DAILYRISK-MU project (2021–2023). Midway through the study, we have learned several lessons through the use of this new research strategy based on the cross-comparison of observations.

Firstly, this new research protocol provided data complementary to the classical data on new spaces that had never before been studied as sites of possible contamination or that had been little documented (bathing areas, paths through water, fields cultivated in flooded areas, etc.). The information about the identity and lifestyles of the cases and controls has been enriched in this study, together with information about activities outside domestic spaces. An analysis of the new data provides more detailed knowledge of the habits of the subject, which should make it possible (in year 3 of the project) to establish typical behaviour profiles related to the risk of contamination (and, subsequently, the targeting of prevention measures for these profiles). The guided tour method also proved useful in this first phase of the project. The field visits progressively led those questioned to mention sites or activities that they would not spontaneously have thought of during interviews at home. This method also made it possible to place the initial description of territorial practices and behaviours with respect to water within an environmental context. Finally, new activities associated with a risk of transmission were discovered through these field visits (collection of forage plants from the low-lying areas for use as animal feed, washing activities (washing the feet or the clothes worn in the field) in irrigation channels, etc.) and were progressively integrated into the definitive version of the questionnaire. The collection of these territorial and environmental data will be continued in the COPTER-UB (2022–2025) project funded by the ANR (the National Research Agency), to reach our objective of 150 cases and 300 controls investigated. As a means of determining the extent to which this global research method can be transposed to other endemic areas, we will also test geographic health surveys on patients diagnosed and treated at the hospital in Lalo (15 cases per year, on average, since 2019), in October 2022. This centre is located in Southeast Benin, about 140 kilometres from Pobé.

The collection of numerous series of environmental samples since the GéANT project has enabled us to identify visually the aquatic sites at which we expect to find *M. ulcerans* and those that are probably safe. Rather than searching for the presence of the bacillus in the environment, by collecting very large numbers of samples, as in the past, we can now work on bioindicators of exposure. This profoundly changes the way in which we approach fieldwork and the manner in which we transmit knowledge to the local population. The sites not considered at risk include, for example, (1) springs and streams for which plant cover had been conscientiously removed from the contours, (2) water sources that have a good flow rate and are never contaminated with salt water from the low-lying areas and (3) protected springs, with a horizontal trench dug by the villagers over several metres to identify the source of the spring, which has been concreted over. Our experience of

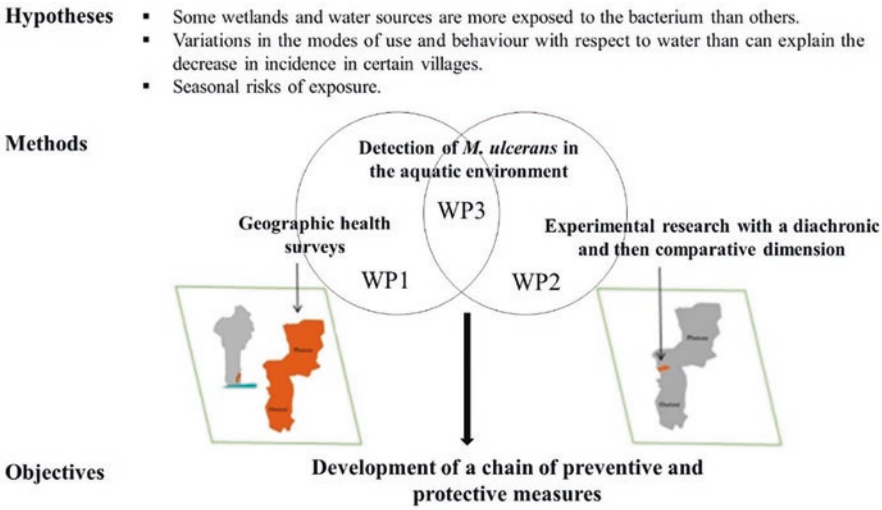

Fig. 5.10 Structure of the COPTER-UB project, indicating the links between WP1, WP2 and WP3. (Source: A. Boccarossa, 2021)

environmental follow-up in the field has also shown that the collection of invertebrates and vertebrates in the environment often triggers a reaction among local actors, with discussion or even participation (Fig. 5.8d). To date, control measures based on the collection of environmental samples have been designed to determine whether or not *M. ulcerans* is present in the areas of contact with the aquatic environment frequented by patients. From now onwards, we also aim for environmental monitoring to become an instrument of prevention capable of sending local actors signals concerning the best way to act. For this, various types of knowledge, including environmental data, have been integrated into a new research action programme (Fig. 5.10) that will be implemented in parallel with the geographic health surveys.

We plan to decrease the risks of exposure to *M. ulcerans* by adopting the principle that preventive and protective actions must be based on the experiences of local communities, their traditional organisation of spaces and their local knowledge. For this reason, the methodology has evolved in the COPTER-UB project, through experimental research with a diachronic and then a comparative dimension. This second research axis aims to demonstrate differences in the dynamics of exposure to *M. ulcerans* (based on a detailed territorial diagnosis) and to reflect on protective solutions based on the participatory learning tools of the ComMod approach (Etienne, 2010; Fauvelle et al., 2012). For this purpose, we will organise discussion groups (in four test villages), to disseminate our results and to develop with local communities (at the end of the project) what we refer to as "adaptation scenarios". Today, we imagine that these solutions will operate at the levels of individual behaviour, health education targeting both typical profiles (e.g. fishermen/farmers) and specific spaces, with the community surveillance of cases (through active screening) and the organisation of community health actions (treatment accessibility) and, finally, through changes in the layout and organisation of the territory (e.g. access to clean water). This perspective also meets the UN Sustainable Development Goal 3.d, whose aim is to strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks.

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