Mobilising Community-Based Research on Zoonotic Infections

A case study of longitudinal cohorts in Vietnam

Co-authors: Karen Saylors[1,2], Tue Ngo Tri[1,3], Toan Tran Khanh[6], Kiet Bach Tuan[4], Heiman FL Wertheim[3,7], Stephen Baker[3,7,8], Hoa Ngo Thi[3], Juliet E Bryant[3,7]

Implementing collaborators: Corina Monagin[1,2], Ha Luu Thi Thu[5], Juan Carrique-Mas[3], James Campbell[3], Hien Vo Be[4], An Nguyen Ngoc[5], Chuc Nguyen Thi Kim[6], Maia Rabaa[3,9], Cuong Nguyen Van[3], Laura Merson[3], Chi Nguyen Thi Yen[3], Huong Vu Thi Lan[3], Nathan Wolfe[1,2], Mark Woolhouse[9], Guy Thwaites[3], Hien Tran Tinh[3]

1 Global Viral, USA; 2 Metabiota, USA; 3 Oxford University Clinical Research Unit, Wellcome Trust Major Overseas Programme, Vietnam; 4 Subdepartment of Animal Health, Dong Thap Province, Vietnam; 5 Preventive Medicine Center, Dong Thap Province, Vietnam; 6 Hanoi Medical University, Hanoi, Vietnam; 7 Nuffield Department of Medicine, Oxford University, UK; 8 The London School of Hygiene and Tropical Medicine, London, United Kingdom; 9 The University of Edinburgh, Edinburgh, UK

Gateways: International Journal of Community Research and Engagement
Vol 8/No 1 (2015): 23–42

ISSN 1836-3393

List of abbreviations used
APEIR: Asia Partnership on Emerging Infectious Diseases Research
DSS(s): Demographic Surveillance Site(s)
DT: Dong Thap province
DVS(s): District Veterinary Station(s)
HMU: Hanoi Medical University
MBDS: Mekong Basin Disease Surveillance Network
NTS: Non-traditional species (bats, rodents, porcupines, civets, ostrich, wild boar, dog)
OUCRU: Oxford University Clinical Research Unit
PMC(s): Preventive Medicine Center(s)
SDAH: Sub-Department of Animal Health
VIZIONS: Vietnam Initiative on Zoonotic Infections

Emerging infectious disease surveillance in human and animal populations is a global health imperative and represents an enormous challenge to government authorities, particularly in resource-limited settings (Keusch 2009; King et al. 2006). In response to complex threats posed by emerging zoonotic infectious diseases (diseases transmitted from animals to humans), a new paradigm for health research has developed: the One Health approach. The One Health concept is based on core principles of systems thinking, transdisciplinarity, multi-stakeholder participation, equity, sustainability and 'knowledge-to-action' (Charron 2011) and attempts to address the interdependencies of human and animal health by promoting research that considers socioeconomic, cultural and environmental factors. Despite widespread agreement on the need for coordinated surveillance activities that unite public health and animal health objectives (AVMA 2008), there remains little consensus on what comprises the One Health research agenda and relatively few examples of ongoing surveillance that utilise expertise from both human and animal health sectors.

Public agencies dedicated to human and animal health must be responsive to markedly different stakeholders as disease control objectives for protecting human health and animal producers' livelihoods have often been in conflict, resulting in competition rather than cooperation (Coker et al. 2011; Jones et al. 2008). In recognition of these challenges, a variety of interagency partnerships have been established to address these institutional/ sectorial barriers to integrated management of infectious diseases. For instance, the Mekong Basin Disease Surveillance Network (MBDS) was established in 2001 to enhance cooperation in detecting and controlling infectious diseases in southeast Asia (Thailand, Vietnam, Laos, Cambodia, Myanmar). Supported by the Rockefeller Foundation and other donors, the MBDS has focused on strengthening programs that address animal, human and environmental health through establishing capacity and infrastructure improvements and transdisciplinary leadership (MacPherson et al. 2013). The Asia Partnership on Emerging Infectious Diseases Research (APEIR), initiated in 2006, represents a similar effort to promote regional collaboration on avian influenza, with an emphasis on developing collaborative Ecohealth/ One Health research proposals and policy advocacy for cross-disciplinary work (Silkavute, Dinh Xuan & Jongudomsuk 2013).

Vietnam has been one of the epicentres of zoonotic disease emergence over the last decade and has some of the highest densities of human and animal populations in southeast Asia (Horby, Pfeiffer & Oshitani 2013). Approximately 80 percent of the Vietnamese population lives in rural areas and participates in small-scale (backyard) poultry and pig production (Thorson et al. 2006). Many aspects of animal production systems and food consumption habits in Vietnam may promote zoonotic disease transmission, including a predominance of production systems with mixed species and little/no biosecurity; the presence of abattoirs and wet markets operating with very basic hygiene; poor cold chain for distribution and limited meat inspection; widespread consumption of raw/undercooked blood, meat, fish, organ tissues, raw leaf vegetables and wild animal products; and use of untreated waste water for agriculture. In the last two decades, Vietnam has experienced extraordinary economic development and urbanisation and the livestock production and food retailing sectors are undergoing rapid modernisation. These changes will undoubtedly have major impacts on human exposure to animal pathogens, and hence the risk of zoonotic disease transmission.

The One Health research agenda within Vietnam – as elsewhere – has focused almost entirely on zoonotic agents (WHO 2014) and has been dominated by studies that attempt to quantify human exposures and risks associated with avian influenza (Dung et al. 2014; Schultsz et al. 2009; Uyeki et al. 2012). In addition, several studies targeting bacterial food-borne zoonoses have involved linked human–animal sampling (Carrique-Mas & Bryant 2013). For studies of rare or poorly documented viral zoonoses, tools to assess cross-species transmission have relied mostly on comparative seroprevalence investigations (Truong et al. 2009). Due to the challenges of conducting 'animal–human interface' studies, most research has employed cross-sectional sampling of human and in-contact animals at a single time point, or case-control designs that use data from the livestock sector but do not involve concurrent animal and human sampling. Several interface studies have included extensive qualitative interviews to assess attitudes, perceptions of risk and behavioural risk factors (Huong et al. 2014; Liao et al. 2014; Manabe et al. 2012; Paul et al. 2013), but the focus has consistently been on implications for human health rather than on animal impact.

The community cohort project described here is part of the Vietnam Initiative on Zoonotic Infections (VIZIONS) program, which encompasses both hospital-based syndromic surveillance and community-based research on zoonotic pathogens. This article describes the establishment of the community-based aspects of the VIZIONS program. The objectives of this ongoing community cohort project are to investigate pathogen ecology and evolution at the human–animal interface and to enhance understanding of viral cross-species transmission events. A core feature of the program is the linkage between syndromic surveillance in hospitals and enrolment of community members within the same 'catchment area' of selected study hospitals. The community cohort involves coordinated sampling of healthy humans and domestic animals, with the goal of establishing a sample bioarchive for future studies of pathogen ecology and population immunity and the capacity-building goal of promoting cross-sectoral cooperation from human and animal health providers, as part of pandemic preparedness. The cohorts comprise people with high levels of occupational and residential exposure to diverse animal species. The concept was to establish sample collections of healthy people and animals that are linked in space and time to clinical hospital-based sampling (for which extensive diagnostics are being done). If new pathogens are detected within hospitalised clinical cases, a mechanism will be in place to readily access community samples – both human and animal – to estimate population-level differences in prevalence. Here we describe the process by which the community cohorts were initiated in Dong Thap (DT) province and BaVi district of Hanoi province.

The purpose of this article is multifold: 1) to describe the structure of the cohort; 2) to document the protocol, methods and implementation approach; 3) to identify differences between the two sites, Dong Thap and BaVi; 4) to galvanise critical self-reflection among the partners about challenges, strengths and weaknesses, in order to inform extension of the cohort to additional provincial study sites.

METHODOLOGY

The Cohort Structure and Collaborative Partnerships

The lead international organisation on this project is Oxford University Clinical Research Unit (OUCRU). OUCRU was established in Ho Chi Minh City within the Hospital for Tropical Diseases in 1991, with a mandate to conduct clinical biomedical research on tropical infectious diseases. Until recently, the scope of OUCRU activities was largely limited to hospital-based research; thus, implementation of community-based research within healthy populations and work within the agricultural sector of Vietnam required modifications to the organisational statutes that provide permissions for a UK-based entity to conduct research in Vietnam.

An additional international partner directly involved in field implementation of VIZIONS is Global Viral, a US-based non-government organisation with extensive experience implementing field research among high-risk populations. Global Viral was responsible for developing the behavioural and risk analysis components of VIZIONS and assisting with recruitment guidelines for the cohort.

The key Vietnamese partners in the first two provinces targeted for implementation, Dong Thap and BaVi, differed in terms of approach to and history of involvement in managing research cohorts. The selection of these provinces as study sites was driven by the long history of the OUCRU partnership with the provincial hospital in Dong Thap and by the existence of an ongoing demographic surveillance site in BaVi. The partners in DT province were the Sub-Department of Animal Health (SDAH-DT) and the Preventive Medicine Center (PMC-DT). These entities submitted a combined permission request to the provincial People's Committee, as the project was to be jointly administered by the human and animal health sectors. The time from submitting project requests to obtaining approvals was approximately three months.

Dong Thap partnerships

The SDAH-DT had the primary role of identifying potential cohort households and study sites (i.e. farms, markets, slaughter points). SDAH-DT also provided general oversight of project implementation, based on their knowledge of local farming communities and their role in overseeing the District Veterinary Station (DVS) for animal sampling. Following the selection of potential cohort households, both SDAH-DT and PMC-DT jointly hosted community meetings to explain project objectives and initiate the recruitment process.

BaVi partnerships

For BaVi coordination, a decision was made to collaborate with Hanoi Medical University (HMU). HMU was selected as the lead agency because of its long history in maintaining the Fila BaVi Demographic Surveillance Site (Chuc & Diwan 2003), a cohort of approximately 11 000 households located within a western rural district of Hanoi province. Ethical clearance was obtained through the university Institutional Review Board. The project was envisioned as a nested cohort within the existing structure of Fila BaVi cohort, and thus recruitment was restricted exclusively to the BaVi district of Hanoi province. Provincial-level authorities (such as SDAH-Hanoi or PMC-Hanoi) were not directly involved in the planning phase of the project; rather, HMU liaised directly with the corresponding district offices in BaVi (District Veterinary Station and District Preventive Medicine Center) to recruit part-time project staff for human and animal sampling. Experienced interviewers from the Fila BaVi cohort conducted the enrolment behavioural questionnaires.

Study Design: Protocol, Methods and Implementation Approach

The study was designed as a descriptive longitudinal cohort of individuals with significant occupational or residential exposure to domestic livestock or wildlife. The intention was to prioritise recruitment of individuals with exposure to exotic non-traditional species (NTS) (e.g. rodents, porcupines, civets, ostrich, wild boar, bats), as well as people with typical livestock exposure (pigs, chickens, ducks). The sampling frame designated four different types of study sites (farms, markets, slaughter points, and restaurants serving NTS). Sampling of humans and representative in-contact warm-blooded animals was conducted at enrolment and yearly intervals; additional 'responsive' sampling was conducted in the event of any reported clinical episodes among the cohort members.

Of note, the possibility of sampling diseased animals ('normal' causes of mortality/morbidity as well as epizootic outbreaks) was discussed at length during the planning phase of the project. While awaiting ethical approvals for human enrolment, we initiated a six-month pilot project in DT which attempted to monitor animal disease episodes on sentinel farms. Unfortunately, the pilot encountered difficulty and resulted in unreliable data regarding animal illness. In addition, we encountered resistance from animal health authorities who perceived the study protocol as conflicting with internal regulatory policies for reporting notifiable animal diseases. Thus, although sampling of animal diseases (and concurrent sampling of humans during animal disease outbreaks) was originally of interest to the overall project objectives, these activities were *not* written into the final approved study protocol for either site.

Study sites

Four types of study sites were identified in the study protocol: 1) farms; 2) live bird markets; 3) slaughter points/abattoirs for larger livestock (predominantly pigs, cows, dogs); and 4) restaurants serving NTS. Study sites comprised epidemiological units to be used for classifying types of human–animal contact behaviours during subsequent analysis. The sampling frame (frequency, numbers of samples, specimen types) was different for each type of study site. Farm sites were intended to represent typical residential exposures to diverse domestic livestock species within rural settings, and were of particular interest due to the possibility of enrolling children from the households. Markets and slaughter points were intended to represent more intense occupational exposures (particularly to blood), and were of interest due to the feasibility of sampling post-mortem tissues of representative animals. The restaurant study sites were solicited to target the most unusual exposures to exotic species (NTS) because issues surrounding 'wildlife farming' and the wildlife trade had previously been identified as a concern for the emergence of novel infectious agents (Daszak, Cunningham & Hyatt 2000; Karesh et al. 2005; WCS 2008; Wolfe et al. 2000).

Participant inclusion and exclusion criteria

Individuals were considered eligible if they were involved in raising animals for at least three years, had the intention of long-term animal husbandry, and agreed to sign an informed consent form that specified their willingness to be sampled and to have their animals sampled, both during the enrolment phase and periodically thereafter. It was also specified that households must be located within 40 km of the designated hospital site for clinical presentation in the event of illness. This constraint was introduced for logistical reasons, and also because it ensured linkage between clinical episodes occurring in communities and those detected at the hospital (through the hospital-based syndromic surveillance project). In this way, the community cohort could be linked in time and space to the hospital clinical data, lending the project a more rigorous epidemiological framework.

Human sampling and questionnaires

We identified two types of participants: *fully enrolled cohort members*, for whom baseline enrolment and yearly sampling was conducted, plus completion of a behavioural survey; and *contact members*, who were identified through follow-up investigation of an illness episode in a cohort member as being symptomatic at the same time as the cohort member, and who consented to provide specimens at a single point in time. A distinction was also made between cohort members enrolled as part of a household unit (i.e. farm study sites), where only the individual who was most in contact with animals (defined as 'lead' family member) was interviewed, and cohort members enrolled as individuals (associated with an occupational study site, i.e. a market/slaughter point/restaurant). All occupational and lead household cohort members were interviewed using a questionnaire that provided information on personal disease history, animal exposures, and disease history for animals maintained at the study site (for farm sites only). The questionnaire was designed to investigate knowledge of zoonotic disease transmission and health risks associated with animal exposures and food consumption. It was tailored to reflect the anticipated diversity of cohort members' occupational exposures, with separate sections to be answered by farmers, market/slaughter workers, and restaurant workers/animal traders. The human specimen collections at enrolment, yearly follow-ups and in the event of clinical episodes were identical, and comprised a 5 ml blood specimen (from adults), 3 ml blood collection (for children <5), nose/throat swabs and rectal swabs.

Animal sampling

Animal sampling on farms was designed to be random and proportionally representative of the typical warm-blooded domestic livestock species present on the farms. Fifteen individual animals were sampled at each farm per visit (regardless of farm size, and regardless of whether the visit comprised enrolment or responsive sampling following notification of a human clinical illness episode). A worksheet was designed to assist study staff in calculating the number of animals to sample from each species, based on a weighted scoring system and estimations of the total herd or flock size and numbers of NTS. Staff were instructed to preferentially sample any animals with symptoms of illness. The weighted scoring system was essential to provide clear and simple guidance to animal sampling teams, and was piloted during the first phase of DT enrolments to ensure that rarer species present on the farm (e.g. ostrich, porcupines) would also be sampled. The specimen types collected varied by species, but were intended to complement the human collections by representing the three major compartments: systemic blood, gastrointestinal, respiratory. For the cohort members associated with markets/ slaughterhouses and restaurants, a separate program of periodic cross-sectional sampling was implemented to collect blood and post-mortem tissues from representative species at each slaughter point.

Clinical episodes

During enrolment, participants were given oral and written instructions for procedures to follow should they develop an illness. Each cohort member was given a laminated study card showing their study site and unique participant ID, as well as contact phone numbers for the Project Coordinator (to contact in case of clinical illness) and the Community Veterinarian (to contact in case of animal disease). Participants were encouraged to notify the Project Coordinator of any illness within 24 hours of symptom onset. An initial telephone consultation between the Project Coordinator and the cohort member would determine if the illness was of probable infectious origin, in which case the cohort member would be encouraged to present directly to the provincial or district study hospital (with compensation provided to cover the cost of transport). If the cohort member did not wish to go to hospital, then a project team would be despatched to the household to sample the cohort member at home and to identify any symptomatic household contacts. The follow-up procedures were identical regardless of whether the follow-up occurred at home or at the hospital. These comprised completion of an Incident Report Form and human sampling identical to that of enrolment (whole blood; rectal swab; nasal/throat swab). Immediately upon notification of a clinical episode of a farmer, the Project Coordinator was also required to mobilise the veterinary teams to visit the farm study site for 'responsive' animal sampling. The responsive animal sampling protocol was identical to the enrolment protocol, comprising sampling of 15 animals and 3 specimen types per animal for a total of 45 animal samples.

METHODOLOGY AND IMPLEMENTATION

Implementation Differences between Dong Thap and BaVi Sites

To establish good working relationships with the Sub-Department of Animal Health in DT (SDAH-DT), a baseline survey of enteric pathogens in domestic farm animals was conducted. This survey was not part of the official roll-out of the cohort and did not include any human sampling; rather, it was performed prior to setting up the cohort and focused on a rigorous, systematic and randomised study design for cross-sectional sampling of animal faeces on duck, chicken and pig farms. Farms were selected based on census data and randomised from three different scales of production (small, medium, large). The rationale for the animal enterics survey was to review animal census data for the province; to learn about the structure of the livestock sector; to visit field sites and train SDAH-DT personnel in animal sampling and research methodology; to set up standard operating procedures related to sample storage, labelling and transport; and to generate baseline data on animal pathogen diversity within the predominant livestock species (i.e. the most relevant 'human–animal interface') (Anh et al. 2014; Carrique-Mas et al. 2013). These activities proved critically important for increasing the overall research capacity of the SDAH-DT, which had not previously engaged in partnerships with foreign collaborators. A number of important logistical details were addressed during this preparatory phase and key project staff from SDAH were identified. In addition, it became clear that some District Veterinary Stations had better capacity for sampling than others, and this information helped guide site recruitment for the human cohort study. Following the initial success of the baseline animal enteric surveys, OUCRU and SDAH study teams approached the PMC-DT together to introduce the concept of establishing a longitudinal human cohort.

Cohort implementation in BaVi district of Hanoi province occurred only after DT activities had been well established. The process of study initiation was markedly different in BaVi due to the structure of partner relations; Hanoi Medical University had the lead role and provincial offices of the SDAH and PMC were not involved, since the intent was to focus enrolment of cohort members within a single district (i.e. a much smaller administrative unit). The envisioned project was 'nested' within an existing large-scale Demographic Surveillance Site (DSS), the Fila BaVi cohort, comprising approximately 51 000 people who had been continuously monitored for over 10 years (Nguyen & Vinod 2003). Because there was no perceived need to involve provincial-level animal-health authorities, we were unable to obtain animal census data or information on prior animal disease outbreaks, and no baseline animal enteric surveys were conducted.

To identify potential cohort members from within the larger Fila BaVi DSS, a 'pre-screening' questionnaire was developed to determine the occupational animal exposures to the Fila BaVi heads of households, to identify the predominant animals present at the household sites and to obtain specific information regarding patterns of raw blood consumption. Approximately 9000 people completed the 'prescreening' questionnaire, and the output was incorporated into an ongoing PhD student project on food consumption behaviours and risk perceptions relating to *Streptococcus suis*, a pig bacterium that can cause bacterial meningitis in humans (Huong et al. 2014; Wertheim et al. 2009). The results indicated the presence of large numbers of unusual species (in particular, porcupines, civets, ostrich), which were considered of significant interest to the project as these species presented a contrast to the predominant pig/poultry farms of DT. In addition, although the survey indicated that large numbers of people were routinely involved in slaughtering livestock, these activities took place largely within households, as there were no abattoirs within the district.

Training and informational meetings

The VIZIONS team organised several trainings for personnel from SDAH-DT and PMC-DT to refine the study protocol and familiarise the team with details of various standard operating procedures for human and animal sampling, laboratory workflow, and sampling transport and storage, and to plan coordinated human and animal sampling. All project staff of PMC-DT were trained in Good Clinical Practice; this was held in conjunction with training for project staff at the provincial hospital. Key SDAH-DT staff were also invited to attend Good Clinical Practice training and this provided the first opportunity for the human and animal health field staff to meet.

Cohort recruitment in DT was facilitated through three informational meetings in three target communes: 1) at SDAH headquarters, targeting farmers in Cao Lanh district and Cao Lanh city; 2) at SDAH headquarters, targeting people involved in slaughtering and meat processing (of poultry, pigs, rodents); 3) in Chau Thanh district veterinary offices, targeting farmers. At the informational meetings, participants were requested to sign a list indicating whether they were interested in enrolling, and these lists were subsequently used by the SDAH-DT and PMC-DT to organise home visits.

At the first recruitment meeting in Cao Lanh, the study team had not yet developed sufficient skills to clearly communicate project objectives and engage community members. At that time, the study team at district and commune levels did not have a thorough understanding of the project and local farmers did not have a good rapport with commune animal health staff. These factors contributed to poor recruitment levels at the first informational meeting. In the subsequent meeting at the Chau Thanh veterinary station, the local study team had improved their presentation skills and was more experienced in explaining the study protocol and responding to questions. The second meeting also proceeded more smoothly due to the positive reputation of local veterinary staff.

Prior to launching activities in BaVi, two training exchanges between staff from BaVi and DT were organised in order to learn from the DT experience. These exchanges were also intended to promote coherence of protocol implementation across the northern and southern sites. Initially, the newly recruited coordinators from BaVi travelled south to visit OUCRU headquarters in Ho Chi Minh City and field sites in DT. They met with counterparts, reviewed procedures for human enrolment and behavioural questionnaires, discussed animal sampling, and received hands-on training for sampling and laboratory processing techniques. Subsequently, staff from Dong Thap visited BaVi in May 2013. DT staff provided guidance to the BaVi field team on animal sampling as the lack of veterinary expertise within both OUCRU and HMU project teams was identified as a key concern. The BaVi DVS had never been involved in projects requiring animal bleeding, invasive sampling or oral fluids collection, nor did they have experience with basic laboratory procedures for aliquoting, labelling, or storing and maintaining sample inventories. The DVS office had only very rudimentary facilities; hence, equipment purchases were required, including a centrifuge and air-conditioner. Training study teams on biosecurity procedures (disinfections) was also necessary for visiting multiple farms on the same day.

Site selection and engagement

In DT, recruitment of farming household members and market/slaughter workers was handled entirely by SDAH-DT. Based on experiences gained from the baseline survey, the SDAH was also able to identify districts with strong, supportive local DVS offices. Three districts were identified as focal points for enrolment: Chau Thanh district, Cao Lanh district and Cao Lanh City. Staff from each of the three respective DVSs sent lists of potential farms to the SDAH provincial office. SDAH staff visited these farms and verified the numbers and types of animals present, as well as the number of household members, to prepare a roster of candidate heads of households to be invited to community informational meetings. The SDAH identified three daily wet markets within the study districts and discussed the study with poultry market workers at these sites. They also met with the owner/manager of the largest abattoir responsible for slaughtering the majority of swine/cattle to identify potential cohort members. A specific effort was made to identify individuals involved in the rat trade, which required scoping visits to markets in other districts.

In DT, human sampling and enrolment was conducted at participants' homes, at their request. After discussion with potential participants during the informational meetings, enrolments were most frequently conducted on weekends when family members (including school-age children) were available. The PMC-DT team was responsible for assessing inclusion/exclusion criteria for each

Figure 1: Enrolment of children during home visits in Dong Thap province

participant, obtaining consent, providing a unique ID number for each participant and responding to any questions about human sampling. During enrolment, a medically qualified PMC-DT staff member provided a free medical consultation to family elders. This service helped to establish trust and build a relationship with the family members. Children were often scared of the blood collection and the PMC-DT study team members worked to dispel their fear (Figure 1). A total of 282 study participants were recruited from a total of 64 sites in 5 districts of DT. The cohorts comprised 214 persons from 60 farming households; 30 commune animal health workers; and 38 workers from 1 abattoir and 3 wet markets. The farming households included enrolments of 35 children <15 years old (12 percent).

For BaVi, HMU led the household recruitment and enrolment process. Households with NTS that had been previously identified in the pre-screening were not approached for enrolment as the majority were considered too far away from the district hospital or had gone out of business since the time of the pre-screening questionnaire. HMU proceeded to identify other potential households based on previous involvement in the Fila BaVi DSS, the numbers of animals and mix of species present at the household sites, and proximity to the district hospital. To recruit households, experienced project staff from Fila BaVi DSS visited households with a representative from the district PMC office to introduce and explain the project. Despite a high refusal rate during the first months of recruitment, a total of 109 people from 29 households were successfully enrolled in July–August 2013. In August 2013, enrolment was temporarily suspended due to the suggestion that more effort should be made to identify and engage households with NTS and 'wildlife' restaurant staff, since the presence of these unusual sites was an important rationale for working in BaVi. Following the model of DT, an additional staff member was hired as Community Veterinarian. The role of the community vet was to assist in identifying potential households with NTS for enrolment, to build rapport and improve communication with cohort members through periodic (monthly) visits to the households, and to enhance the ability to respond to cohort members' concerns about animal health. At this time, it was also agreed that recruitment of additional cohort members (to meet the target of 270 individuals) would be facilitated by holding a community information meeting to explain the project.

Attempts to identify farms with NTS and restaurants involved in the 'wildlife' trade in BaVi were successful; however, these farms tended to be located in the more isolated parts of the district and poor access roads rendered them impractical as study sites due to anticipated difficulties for managing response to clinical episodes. In addition, participants from these sites had very high refusal rates. The project teams were reluctant to invest more time in recruiting individuals from these sites, in part due to a lack of experience with animal sampling. DVSs were overwhelmed by the amount of work entailed in the enrolment sampling, and enrolments in late 2013 were generally delayed through lack of human resources, as DVSs were busy with routine annual vaccination campaigns.

BaVi enrolment targets were completed by the end of December 2013 and comprised a total of 270 people, classified as either members of farming households, commune animal health workers, restaurant workers, and three types of traders (those who raise/slaughter/sell animals from their home; those who slaughter at home and sell fresh meat at the market; and those who sell fresh meat at market but are not directly involved in slaughtering). The cohort households and study sites were located in 20 of the 32 communes of the district. In order to promote reporting of clinical episodes, an SMS phone-based text messaging system was implemented, sending weekly reminders to cohort members asking them to contact project staff in the event of mild or severe illness.

DISCUSSION

Strengths and Challenges

Herein we have described the project launch of two longitudinal community cohorts in southern and northern Vietnam that are linked to a complementary hospital-based syndromic surveillance project conducted in the same areas. The two community cohorts originated under a single study framework with the same objectives and study design, and yet the process of study initiation differed greatly between the two sites and offers an opportunity to reflect on different approaches.

Clearly the success of community-based projects depends on engagement and buy-in from key community leaders. In DT, where human health (PMC) and animal health (SDAH) teams led project implementation, the two departments had prior history of being involved in joint training programs related to avian influenza education campaigns, but they did not have a history of active collaboration. The VIZIONS project required intensive time commitments and provided increased opportunities for interaction among key staff. Roads to villages were often in poor condition and impassable by four-wheel drive vehicles, so team members shared motorcycles to visit the cohort households together. Overcoming the challenges of flooded roads and flat tyres on such excursions helped to build camaraderie among the field teams, resulting in bonds and friendships that strengthened communication and collaboration between SDAH and PMC. The project also provided numerous opportunities to interact with local community members, and the commune information meetings, recruitment contacts and subsequent follow-up visits have provided a forum for the local government staff to demonstrate leadership and develop rapport with a wide circle of community households.

For DT, local empowerment and establishing leadership capacity within SDAH-DT in the early phases of the project launch was a key to later success. The initial animal enteric survey was also essential for building local capacity for basic research management. OUCRU leaders recognised the need for multi-sectoral bridging of animal/human health as a key objective of the project, and helped provide resources for coordination between SDAH and PMC at all levels (provincial, district, commune) during the training and preparation phases.

In BaVi, the PMC and DVS district offices were not involved in identifying potential participants; however, they were responsible for sampling at enrolment. The project coordinator (HMU staff) and local assistants (PMC and DVS staff) visited eligible sites to inform potential participants about the project and obtain consent on an individual household basis; this proceeded before holding initial commune-level meetings to introduce the project. Human and animal health concerns were regularly discussed with district PMC and DVS staff during sampling, and resulting information on human and animal diseases detected during sampling was shared between PMCs and DVSs.

Establishing and regularly strengthening relationships with cohort members and grassroots partners is essential to assuring the sustainability of the cohort. In DT, the key means for engaging directly with cohort members is through the Community Veterinarian, who often provides complementary animal feed supplements or advice on animal husbandry. The project coordinator from PMC-DT often visits cohort households and sometimes provides vitamin supplements for participants, conducts on-site medical exams and provides referral advice for additional diagnostics. In BaVi, a similar regime of frequent household visits by staff from local commune health centres helps to ensure the regular reporting of human clinical episodes. The relationship between the study team and cohort members has been strengthened through this individualised attention; thus, the cohort members know and trust key study team members.

A community cohort often foresees recruitment challenges, especially when the subject matter is sensitive and deemed potentially harmful to business. The objective of collecting behavioural and risk-factor data, however, necessitated posing questions about animal husbandry and food consumption that were potentially sensitive, in particular questions about handling of diseased animals, carcass disposal, notification/reporting of animal disease, and consumption of raw blood and other animal products. Participants were reluctant to share details that were perceived as jeopardising the value of their livestock or livestock products. As observed in many similar projects, we found that farmers were mistrustful and reluctant to participate if the project focused on documenting biosecurity risks, so successful engagement depended upon building trust among stakeholders (Hernandez-Jover et al. 2012). It was thus important that the study team has a good relationship with cohort members and field-site communities and that there be clear, regular communication about confidentiality and the neutrality of the research study.

In BaVi, recruitment challenges revolved around a lack of perceived direct benefit to cohort members from participation in the study, as well as lack of interest and reluctance to have animals sampled. Although the HMU team already had established relationships with the community due to the long-running Fila BaVi DSS, cohort members still feared blood draws and worried that giving a blood sample would negatively impact their own health, and that animal sampling would similarly impair productivity of their livestock. Some people in BaVi expected test results would be provided to them immediately after enrolment, and when it was explained that this was not part of the protocol, some declined to participate. Of 84 eligible farm sites, only 62 signed consent forms and 59 agreed to give human and animal samples. Fifteen restaurants were approached and only three agreed to participate; the others did not admit that they sold wild animal meat or were afraid of negative impact on their business due to participation in the project.

The informed consent form stipulated that participation in the project would involve periodic sampling of farm animals. Many farmer participants in DT expressed reluctance at having their pigs sampled as they were concerned about production losses due to stress. During the first week of animal sampling in DT, one baby pig died following the enrolment sampling because he was restrained too tightly, and the animal health team were worried about the cohort participants' possible reaction. The situation was handled through compensation to the farmer for the value of the pig. Subsequently, the animal handling teams gained experience and to date there have not been any additional accidents. Reluctance to allow animal sampling also proved a challenge during the BaVi farm enrolments. Particular difficulties were experienced with wild boars and porcupines. For the porcupine farms, sampling has been restricted to faecal collections due to the difficulty of restraining porcupines. In principle, porcupine farmers have agreed to assist the project staff in obtaining other sample types (respiratory swabs and blood) whenever porcupines are restrained for transport/sale/slaughter; however, to date, the logistics and timing of obtaining these samples has been difficult. For the one farm that rears ostrich, the farmer has accepted the collection of rectal swabs and blood; however, collection of respiratory swabs was considered too problematic and dangerous.

For both DT and BaVi sites, the logistics and planning for hospital involvement in follow-up of clinical episodes posed some particular challenges. This was largely due to the fact that the syndromic surveillance component of the project (known as '04VIZIONS') was concurrently running at the same hospitals. The study protocols for the two projects (the community-based and hospital-based arms of VIZIONS) required completion of different Case Reporting Forms and collection of different specimen types. Concerns were raised about whether parallel implementation of the two projects would cause confusion among the hospital staff. To avoid these difficulties in DT, it was agreed that the project coordinator (based at the provincial PMC office) would be responsible for sampling of cohort members regardless of whether the cohort member was sampled at the hospital or at home, and they would also be responsible for completion of the Incident Report Form and transfer of samples back to the PMC laboratory for aliquoting and storage. A similar solution was proposed for BaVi, whereby the district PMC project staff report to the hospital to assist hospital staff with sampling and completion of paperwork whenever a cohort member falls ill.

In discussions with field teams of the district offices in BaVi, project staff have expressed frustration with the lack of adequate compensation for their time on the VIZIONS project and have not developed a sense of ownership of the project. This is particularly true of the DVS staff responsible for animal sampling, as they are often overstretched due to competing responsibilities and, additionally, the ad-hoc farm visits for responsive animal sampling to clinical episodes is very time consuming and logistically hard to manage. There is also a sentiment that the animal health staff (at DVS) and human health staff (at PMC) should be differentially compensated because the animal sampling is more labour intensive and involves additional risks. HMU manages compensation for the field staff in the district government offices, and currently it is not considered feasible to augment payments. Consequently, the field teams in BaVi are relatively disengaged from the project and have not yet built rapport with cohort households through proactive visits or outreach activities. Discussions are ongoing to ameliorate community involvement and clinical episode reporting.

These challenges point to one of the major difficulties of working exclusively with district level offices, where human resources are far more limited than in provincial headquarters (for example, SDAH-DT has approximately 40 staff, while BaVi DVS has only 5 full-time employees).

Lessons Learned

One lesson learned from project management experiences in DT is the value of repeated face-to-face visits with cohort members at their homes and workplaces. In DT, the Community Veterinarian and lead coordinator from PMC fulfil this role. They are both based in Cao Lanh city, the provincial capital, and they are the staff who visit households when there are ill household members. In addition to assuring follow-up procedures of sampling and documentation, these visits provide a social/cultural function. In BaVi, the Community Veterinarian visits households once per month (regardless of the occurrence of clinical events) and a group of commune health workers have been recruited to visit each household once per week.

In response to cohort members' specific requests for more education/training, workshops on animal health have been held in both DT and BaVi. The DT workshop in October 2013, led by lecturers from Nong Lam University, provided basic training on animal nutrition and vaccination issues. Topics also included information on antibiotic use in feed and for therapeutics. For the animal health workshop in BaVi, the program was led by experts from Hanoi University of Agriculture and chaired by a TV celebrity who hosts a program on animal husbandry for local television. The workshop provided cohort members with basic information on the most high-profile animal diseases (Avian Influenza, Foot and Mouth Disease, and Porcine Reproductive & Respiratory Syndrome) and a chance to voice concerns relating to animal vaccination programs.

Another project implemented in DT, 'Health in the Backyard' (www.oucru.org/health-in-the-backyard/), has also enhanced community engagement on topics relating to zoonoses and human–animal interactions. This program involved producing photo-documentaries and storytelling by cohort members, who recounted their own experiences of husbandry practices and perceptions of health risks in their daily lives. The films were then viewed in group settings, with the purpose of stimulating dialogue and debate within the community and between scientists and stakeholders regarding public health concerns and research priorities. The participatory format of 'Health in the Backyard' greatly contributed to cohort members' appreciation of the project, and the intent is to use a similar approach in the north.

In summary, the key mechanisms we have developed to facilitate good relations with the cohort communities include: 1) providing free health checks during annual cross-sectional sampling; 2) providing free consultations/medicine when cohort members fall ill; 3) performing on-site rapid diagnostic tests for influenza for all respiratory cases (conducted at the time of consultation at the commune health station); 4) recruiting commune health workers and a Community Veterinarian to regularly visit cohort households; 5) hosting educational workshops on animal health/agriculture issues; 6) hosting engagement activities such as the photo-documentary project, 'Health in the Backyard'; and 7) creating opportunities to socialise with project staff, such as group lunches for staff and key community leaders.

CONCLUSION

The One Health concept has recently gained recognition amongst veterinary, animal health and public health practitioners involved in infectious disease research, and new research and surveillance activities are increasingly including linked sampling of humans and animals (Carrique-Mas et al. 2013; Cuong et al. 2015; Dung et al. 2014). Most research conducted to date, however, has been limited to single-time-point cross-sectional sampling. This is because maintaining a network for longitudinal sampling presents many additional challenges and difficulties in project management. In this article, we have discussed experiences from the first year of a longitudinal cohort study that monitors human illness episodes and conducts coordinated animal sampling in response to reported illnesses. A future extension of the project to enable synchronous monitoring of animal and human disease would represent a truly remarkable 'One Health' achievement, but this is not practical at present. The achievements to date, however, enable responsive sampling of humans and animals within the immediate period following a human illness episode (48 hours). We have also achieved an informal ear-to-the-ground mechanism for learning about ongoing animal disease outbreaks. We suggest that informal (non-official) networks for obtaining information on animal diseases are likely to remain important sources of data for the foreseeable future.

The risks of possible zoonotic pandemics have never been greater, due to exponential increases in mobility of people and goods around the world, rapidly changing agro-ecosystems and other ecological changes associated with urbanisation and climate change. The primary lesson learned to date from the project launch of VIZIONS in northern and southern Vietnam has been a reaffirmation of the critical importance of community engagement activities in promoting cross-sectoral work, specifically bridging activities that require input from both the human and animal health sectors. These engagement activities are central to building trust and supportive relationships among researchers, partner agencies and stakeholders. Thus far, the project has been implemented in two unique sites (in north and south Vietnam) and under two very different management structures (government-led and academic-led). We suggest that programs embedded within existing government-led surveillance structures, with strong presence in local communities, are most likely to succeed and directly contribute to improved awareness and reporting of disease episodes in communities. Strengthening of partnerships with government institutions is preferable to working through temporary, externally funded academic partnerships, as the staffing within government agencies is less transient and thus may promote the sustainability of the research activities by enhancing leadership capacity at the community level and the training of local actors.

As the project continues, we anticipate that the participatory research approach will foster improved coordination and collaboration at provincial, district and commune levels, and will provide new local leadership for research on surveillance systems and zoonotic disease transmission in Vietnam.

REFERENCES

American Veterinary Medical Association (AVMA) 2008, *Contributing to One World, One Health: A strategic framework for reducing risks of infectious diseases at the animal–human– ecosystems interface*, Consultation Document, FAO, OIE, WHO, UNSIC, UNICEF, The World Bank, p. 9.

Anh, P, Carrique-Mas, J, Cuong, N, Hoa, N, Anh, N, Duy, D, Be, H, Rabaa, M, Farrar, J, Baker, S & Bryant J 2014, 'The prevalence and genetic diversity of group A rotaviruses on pig farms in the Mekong Delta region of Vietnam', *Veterinary Microbiology*, vol. 170, nos 3–4, pp. 258–65, http://dx.doi.org/10.1016/j.vetmic.2014.02.030.

Carrique-Mas, J & Bryant, J 2013, 'Bacterial zoonoses in Vietnam', *Ecohealth*, vol. 10, no. 4, pp. 465–89, doi: 10.1007/s10393-013-0884-9.

Carrique-Mas, J, Bryant, J, Nguyen, C, Nguyen, H, Campbell, J, Nguyen, H, Ngoc, D, Tien, D, Ngo, H, Thompson, C, Be, H, Vinh, P, Farrar, J & Baker, S 2013, 'An epidemiological investigation of Campylobacter in pig and poultry farms in the Mekong delta region of Vietnam', *Epidemiology and Infection*, vol. 142, no. 7, pp. 1425–36, doi:10.1017/S0950268813002410.

Charron, D (ed.) 2011, *Ecohealth research in practice: Innovative applications of an ecosystem approach to health*, Springer/IDRC, Ottawa, Canada.

Chuc, N & Diwan, V 2003, 'Filabavi, a demographic surveillance site, an epidemiological field laboratory in Vietnam', *Scandinavian Journal of Public Health*, vol. 30, suppl. 62, pp. 1–5s.

Coker, R, Rushton, J, Mounier-Jack, S, Karimuribo, E, Lutemba, P, Kambarage, D, Pfeiffer, D, Stark, K & Rweyemamu, M 2011, 'Towards a conceptual framework to support One-Health research for policy on emerging zoonoses', *Lancet Infectious Diseases*, vol. 11, no. 4, pp. 326–31.

Cuong, NV, Carrique-Mas, J, Be, HV, An, NN, Tue, NT, Anh, NL, Anh, PH, Phuc, NT, Baker, S, Voutilainen, L, Jaaskelainen, A, Huhtamo, E, Utriainen, M, Sironen, T, Vaheri, A, Henttonen, H, Vapalahti, O, Chaval, Y, Morand, S, and Bryant, JE, 2015, 'Rodents and Risk in the Mekong Delta of Vietnam: Seroprevalence of Selected Zoonotic Viruses in Rodents and Humans', Vector-Borne and Zoonotic Diseases, vol 15, no 1, pp. 65-72.

Daszak, P, Cunningham, A & Hyatt, A 2000, 'Emerging infectious diseases of wildlife: Threats to biodiversity and human health', *Science*, vol. 287, pp. 443–49.

Dung, T, Dinh, P, Nam, V, Tan, L, Hang, N, Thanh, L & Mai, L 2014, 'Seroprevalence survey of avian influenza A (H5N1) among live poultry market workers in northern Viet Nam, 2011', *Western Pacific Surveillance and Response Journal*, vol. 5, no. 4, doi:10.5365/wpsar.2014.5.2.006.

Hernandez-Jover, M, Gilmour, J, Schembri, N, Sysak, T, Holyoake, P, Beilin, R & Toribio, J 2012, 'Use of stakeholder analysis to inform risk communication and extension strategies for improved biosecurity amongst small-scale pig producers', *Preventative Veterinary Medicine*, vol. 104, nos 3–4, pp. 258–70.

Horby, P, Pfeiffer, D, Oshitani, H 2013, 'Prospects for emerging infections in East and Southeast Asia 10 years after severe acute respiratory syndrome', *EID Perspective*, vol. 19, no. 6.

Huong, V, Hoa, N, Horby, P, Bryant, J, Toan, T, Wertheim, H 2014, 'Raw pig blood consumption and potential risk for *Streptococcus suis* infection, Vietnam', *Emerging Infectious Diseases*, vol. 20, no. 11, http://dx.doi.org/10.3201/eid2011.140915.

Jones, K, Patel, N, Levy, M, Storeygard, A, Balk, D, Gittleman, J & Daszak, P 2008, 'Global trends in emerging infectious diseases', *Nature*, vol. 451, no. 7181, pp. 990–93.

Karesh, W, Cook, R, Bennett, E & Newcomb, J 2005, 'Wildlife trade and global disease emergence', *Emerging Infectious Diseases*, vol. 11, no. 7, 1000–02.

Keusch, G 2009, *Sustaining global surveillance and response to emerging zoonotic diseases*, IOM and NRC, Washington.

King, D, Peckham, C, Waage, J, Brownlie, J & Woolhouse, M 2006, 'Epidemiology. Infectious diseases: Preparing for the future', *Science*, vol. 313, no. 5792, pp. 1392–93.

Liao, Q, Lam, W, Bich, T, Dang, V & Fielding, R 2014, 'Comparison of behaviors regarding live poultry exposure among rural residents in Vietnam and Thailand, *Journal of Infection in Developing Countries*, vol. 8, no. 4, pp. 526–34, doi:10.3855/jidc.3545.

MacPherson, N, Kimball, A, Burke, C, Abernethy, N, Tempongko, S & Zinsstag, J 2013, 'Key findings and lessons from an evaluation of the Rockefeller Foundation's Disease Surveillance Networks Initiative', *Emerging Health Threats Journal*, pp. 62–66.

Manabe, T, Tran, T, Doan, M, Do, T, Pham, T, Dinh, T, Tran, T, Dang, H, Takasaki, J, Ngo, Q, Ly, Q & Kudo, K 2012, 'Knowledge, attitudes, practices and emotional reactions among residents of avian influenza (H5N1) hit communities in Vietnam', *PloS One*, vol. 7, no. 10, doi:10.1371/journal.pone.0047560.

Nguyen, T & Vinod, D 2003, 'FilaBavi, a demographic surveillance site, an epidemiological field laboratory in Vietnam', *Scandinavian Journal of Public Health*, vol. 31, pp. 3–7.

Paul, M, Baritaux, V, Wongnarkpet, S, Poolkhet, C, Thanapongtharm, W, Roger, F, Bonnet, P & Ducrot, C 2013, 'Practices associated with Highly Pathogenic Avian Influenza spread in traditional poultry marketing chains: Social and economic perspectives', *Acta Tropica*, vol. 126, no. 1, pp. 43–53, doi:10.1016/j.actatropica.2013.01.008.

Schultsz, C, Nguyen, V, Hai, L, Do, Q, Malik Peiris, J, Lim, W, Garcia, J-M, Nguyen, D, Nguyen, T, Huynh, H, Phan, X, van Doorn, H, Nguyen, V, Farrer, J, de Jong, M 2009, 'Prevalence of antibodies against avian influenza A (H5N1) virus among cullers and poultry workers in Ho Chi Minh City, 2005', *PloS One*, vol. 4, no. 11, doi:10.1371/journal.pone.0007948.

Silkavute, P, Dinh Xuan, T & Jongudomsuk, P 2013, 'Sustaining a Regional Emerging Infectious Disease Research Network: A trust-based approach', *Emerging Health Threats Journal*, pp. 48–53.

Thorson, A, Petzold, M, Nguyen C & Ekdahl, K 2006, 'Is exposure to sick or dead poultry associated with flulike illness? A population-based study from a rural area in Vietnam with outbreaks of Highly Pathogenic Avian Influenza', *Archives of Internal Medicine*, vol. 166, no. 1, pp. 119–23.

Truong, T, Yoshimatsu, K, Araki, K, Lee, B, Nakamura, I, Endo, R, Shimizu K, Yasuda, S, Koma, T, Taruishi, M, Okumura, M, Truong, U & Arikawa, J 2009, 'Molecular epidemiological and serological studies of hantavirus infection in northern Vietnam', *The Journal of Veterinary Medical Science*/ Japanese Society of Veterinary Science, vol. 71, no. 10, pp. 1357–63.

Uyeki, T, Nguyen, D, Rowe, T, Lu, X, Hu-Primmer, J, Huynh, L, Hang, N & Katz, J 2012, 'Seroprevalence of antibodies to avian influenza A(H5) and A(H9) viruses among market poultry workers, Hanoi, Viet Nam, 2001', *PLoS One*, vol. 7, no. 8, doi:10.1371/journal.pone.0043948.

Wildlife Conservation Society (WCS) 2008, *Commercial wildlife farms in Vietnam: A problem or solution for conservation?* Hanoi, Vietnam.

Wertheim, F, Nghia, H, Taylor, W & Schulsz, C 2009, '*Streptococcus suis*: An emerging human pathogen, *Clinical Infectious Disease*, vol. 48, issue 5, pp. 617–25.

Wolfe, N, Eitel, M, Gockowski, J, Muchaal, P, Nolte, C, Prosser, A, Torimiro, J, Weise, S & Burke, D 2000, 'Deforestation, hunting and the ecology of microbial emergence', *Global Change and Human Health*, vol. 1, no. 1, pp. 10–25.

World Health Organization (WHO), Vietnam Zoonoses Fact Sheet, 2014.