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Strengthening the surveillance of and response to HIV in the Western Pacific

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Countries in the Western Pacific Region have low-level epidemics – HIV may have been present for many years but never spread to substantial levels in any subpopulation; i.e. prevalence has not been consistently >5% in any subpopulation - or concentrated HIV epidemics – the spread of HIV has occurred in a defined subpopulation; i.e. prevalence is consistently >5% in a defined subpopulation but is <1% in pregnant women in urban areas.¹ Predominantly affected subpopulations, usually referred to as key populations, in the Region are sex workers (SW), people who inject drugs (PWID), men who have sex with men (MSM) and transgender people (TG).² These populations also show high rates of sexually transmitted infections (STI), which play an important role in enhancing the HIV transmission.³ Understanding levels of STI (other than HIV) could help to identify populations for which HIV prevention interventions are needed, especially in areas where HIV prevalence is currently low.² Over the past decades, tremendous efforts and resources have been invested to establish functional HIV surveillance systems in many countries in the Region.^{4,5} However, the same cannot be reported for strengthening STI surveillance.²

In this issue, we publish a collection of papers on the surveillance of and response to HIV in the region including assessment of HIV surveillance systems, innovative tools for use in outreach to key populations, interventions for preventing mother-to-child HIV transmission and human resource difficulties for HIV programmes. These papers illustrate the current status and discuss the gaps and challenges for HIV surveillance and programme monitoring in many countries in the Region.

Loo *et al.*⁶ provides an analysis of HIV surveillance systems of 20 countries in the Asia Pacific region and demonstrates that countries have broadened the number

and types of HIV surveillance components over time. This has included introducing population size estimation and integrating behavioural surveys into routine HIV sentinel surveys. Moreover, routine programme monitoring data and case reporting were recently included into some HIV surveillance systems. However, analysis and utilization of surveillance data for programme improvement still lags behind, especially at the subnational level. In a supplemental survey of World Health Organization (WHO) Member States, Yu *et al.*⁷ report on the coverage and frequencies of HIV serosurveillance surveys among key populations. Female SW are routinely captured by HIV serosurveillance surveys in all seven reported Asian countries; PWID and MSM less so. HIV and STI data among TG are hardly available and often included (if at all) in MSM populations. It is noteworthy that current surveillance systems in most of the Pacific island countries and areas do not include key populations.

Reddy *et al.*⁸ discuss the development of a data hub for HIV to promote evidence-informed advocacy and action. It includes a regional HIV database of subnational indicators, a data analysis team and web site with data products and serves as a regional tool to support national and international partners with updated HIV data for policy advocacy and tracking of progress. This large repository contains data from 26 countries in the Asia Pacific region.

The results from these three studies on the improvements of HIV surveillance in the Region are not surprising given the attention and investment from the countries themselves and from the international community over the past two decades. Despite these gains, there are still some areas for strengthening, including the analysis and utilization of surveillance data for programme strengthening, especially at the subnational level.

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One major challenge addressed in this issue is keeping track of outreach efforts to key populations such as PWID, SW and MSM. This has been difficult due to privacy and confidentiality concerns and because these groups can be highly marginalized. Nga *et al.*⁹ report on an innovative data suite for managing outreach data among key populations in Viet Nam, which includes a unique identifier code, field data collection notebook (the “databook”) and a computer data entry system. The databook was found to be inexpensive and can document 40 individual clients, commodity distribution, group contacts and needles/syringe collection. The suite is progressively being used by outbreak workers in more than 40 of the 63 provinces in Viet Nam.

Another important area of HIV prevention is the uptake of interventions for the prevention of mother-to-child transmission (PMTCT) of HIV. Sovannarith *et al.*¹⁰ examines the coverage of six key interventions of the PMTCT cascade in 11 operational districts of Cambodia: maternal antiretroviral (ARV) treatment or prophylaxis, delivery in a health facility, infant ARV prophylaxis at birth, infant cotrimoxazole prophylaxis at six weeks, first infant deoxyribonucleic acid-polymerase chain reaction (DNA-PCR) test at six weeks and second infant DNA-PCR test at 30 weeks. Programme data from April 2008 to December 2011 revealed critical gaps in monitoring the PMTCT service delivery under the routine programme conditions in Cambodia.

Another article by Rule *et al.*¹¹ highlights that one of the main challenges for the response to HIV in Papua New Guinea is training and maintaining adequate human resources. They identify several workforce issues that need to be addressed.

Although much has been achieved in HIV surveillance and response in the Region, challenges remain. Countries need to make continuous efforts to win the battle against HIV by increasing domestic funding, strengthening surveillance systems and scaling up the coverage of prevention, treatment and care services.

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How are countries in the Western Pacific Region tracking the HIV epidemic? Results from a 2011 survey of ministries of health

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In 2011, as part of the World Health Organization global reporting tool to collect data on the progress of improving the health sector response to HIV/AIDS towards universal access, a questionnaire was sent to ministries of health of Western Pacific Region Member States on the scope and functioning of their HIV surveillance systems. Of the 17 countries that responded, 13 were low- to middle-income countries and four were high-income countries. Regular serosurveillance surveys are conducted with female sex workers in all lower- and middle-income countries that responded to the survey but less so with people who inject drugs and men who have sex with men. Furthermore, there are no surveillance activities of the key populations in most of the Pacific island countries. It is recommended that estimations of high-risk populations be conducted in priority Pacific island countries and tailored surveillance systems be designed. Efforts should also be made to gather and accumulate data from sufficient geographic coverage to allow the HIV epidemic to continue to be monitored.

An appropriate and effective national HIV surveillance system is necessary for countries to be able to understand and monitor the HIV epidemic and evaluate the national response. Such surveillance systems facilitate countries in estimating the magnitude of the epidemic, monitoring the trend of the epidemic, evaluating the effectiveness and outcome of health promotion efforts and advocating for commitment and resources. Countries in the Western Pacific Region have made significant progress in developing their HIV surveillance systems over the past years, but there are still important gaps. This includes surveillance data on high-risk groups such as men who have sex with men (MSM).^{1,2}

Periodic assessment and review of countries' HIV surveillance systems are important to identify gaps and improve their performance, integration and long-term sustainability.³ There have been several reviews and assessments of HIV surveillance systems at global and regional levels, focusing on the different dimensions of surveillance such as flexibility and simplicity, usefulness, timeliness, data completeness and quality.^{4,5} Since 2007, the World Health Organization (WHO), together with United Nations Children's Fund (UNICEF) and Joint United Nations Programme on

HIV/AIDS (UNAIDS), has been collecting national-level data from ministries of health to report on the progress of the health sector response to HIV/AIDS. In the 2011 country reporting, a set of programmatic questions related to the functioning of routine serosurveillance systems in countries were included, providing a snapshot of the scope and operation of HIV surveillance systems. This included the major populations, periodicity and geographic location covered by the surveillance systems, the most recent sexual and injecting drug behaviour surveys and any surveillance of HIV drug resistance.

In this paper, we report on the data from the 2011 survey for the Western Pacific Region. This assessment does not intend to be a comprehensive evaluation of HIV surveillance systems or a detailed account of sampling and reports, but it provides the most recent updates of the scope and functions of countries' surveillance systems as reported by the countries themselves.

METHODS

In 2011, a questionnaire was sent to ministries of health of Western Pacific Region Member States on the scope and functioning of their HIV surveillance systems. It

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included questions on the coverage of population groups by routine serosurveillance surveys, determining whether sexual and drug use behaviour surveys or demographic health surveys with HIV testing had been conducted and whether of any surveillance of HIV drug resistance had been implemented.

A total of 17 countries from the Western Pacific Region submitted their data. Thirteen were from lower- and middle-income countries: Cambodia, China, Fiji, Kiribati, the Lao People's Democratic Republic, Malaysia, Mongolia, Papua New Guinea, the Philippines, Samoa, Solomon Islands, Tonga and Viet Nam; four were from high-income countries: Australia, Brunei Darussalam, New Zealand and Singapore. Epidemiologic and programmatic data on antiretroviral therapy (ART), prevention of mother-to-child transmission, prevention with key populations and other indicators have been published previously.⁶

The survey results were reported for lower- and middle-income countries, separately for Asian and Pacific island countries, and for high-income countries.

RESULTS

(1) Routine serosurveillance surveys

Sex workers

All the Asian lower- and middle-income countries reported that routine serosurveillance surveys have been in place for female sex workers (FSW). Most countries conduct these surveys every two to three years, except for China and Viet Nam where they are conducted on a yearly basis.

Among the Pacific island countries, only Kiribati and Papua New Guinea report routine serosurveillance for FSW every two to three years. For other Pacific island countries, including Fiji, Samoa, Solomon Islands and Tonga, no serosurveillance was conducted for FSW.

Among the high-income countries, Australia and Singapore reported routine serosurveillance for FSW, while Brunei Darussalam and New Zealand do not conduct surveys for this population ([Table 1](#)).

People who inject drugs

Among the Asian countries, China and Viet Nam conduct routine, annual serosurveillance of people who inject drugs (PWID), while Cambodia, Malaysia and the Philippines use a two-to-three-year cycle. The Lao People's Democratic Republic conducts sporadic serosurveillance among PWID in cities other than the capital. Mongolia does not conduct serosurveillance of PWID.

For the Pacific island countries, only Kiribati reported conducting routine serosurveillance of PWID in cities other than the capital on a three-year basis.

For the high-income countries, Australia and New Zealand reported routine serosurveillance of PWID – annually at the national level in Australia and in cities other than the capital in three-to-four-year intervals in New Zealand ([Table 1](#)).

Men who have sex with men

Among the Asian countries, Cambodia, China, the Lao People's Democratic Republic, Malaysia, Mongolia and the Philippines reported routine serosurveillance surveys of MSM. Viet Nam notably reported no routine surveys for this population group.

For Pacific island countries, only Kiribati reported conducting routine serosurveillance among MSM. It is notable that Papua New Guinea does not conduct these surveys among MSM.

For the high-income countries, Australia, New Zealand and Singapore reported conducting routine serosurveillance of MSM on an annual or biennial basis ([Table 1](#)).

Antenatal care attendees

Among the Asian countries, only the Lao People's Democratic Republic and the Philippines reported not conducting routine serosurveillance for antenatal care (ANC) attendees. China and Viet Nam both reported annual serosurveillance of ANC patients, while the other Asian countries conduct ANC serosurveillance every two to five years.

Table 1. Coverage of routine serosurveillance surveys for HIV of major populations grouped into lower- and middle-income and high-income countries in the Western Pacific Region, 2011

Lower- and middle-income countries—Asia	Cambodia	China	Lao Peoples' Democratic Republic	Malaysia	Mongolia	Philippines	Viet Nam
Sex workers							
Surveillance	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Periodicity	Every 3 years	Annual	2 years	Every 2 years	Every 2 years	Every 2 years	Annual
Location	National	National	National	National	National	-	National
People who inject drugs							
Surveillance	Yes	Yes	No, but with surveys	Yes	No	Yes	Yes
Periodicity	Every 3 years	Annual	-	Every 2 years	-	Every 2 years	Annual
Location	National	National	Other cities	National	-	-	National
Men who have sex with men							
Surveillance	Yes	Yes	Yes	Yes	Yes	Yes	No
Periodicity	Every 3 years	Annual	Every 2 years	Every 2 years	Every 2 years	Every 2 years	-
Location	National	National	Other cities	National	Capital city	-	-
Antenatal care attendees							
Surveillance	Yes	Yes	No	Yes	Yes	No	Yes
Periodicity	Every 3 years	Annual	-	Annual	Every 2–5 years	-	Annual
Location	National	National	-	National	National	-	National
Others	Moto-taxi drivers	Migrants, STI patients, youth students, long-distance truck drivers	-	-	Male STI client, pregnant women, blood donor, mobile men, youth (aged 15–24)	-	Military recruits, Mobile population (fishermen)
Lower- and middle-income countries—Pacific							
	Papua New Guinea			Samoa	Solomon Island		Tonga
Sex workers							
Surveillance	Yes			No	No		No
Periodicity	Every 2–3 years			-	-		-
Location	Other cities			-	-		-
People who inject drugs							
Surveillance	No			No	No		No
Periodicity	-			-	-		-
Location	-			-	-		-
Men who have sex with men							
Surveillance	No			No	No		No
Periodicity	-			-	-		-
Location	-			-	-		-
Antenatal care attendees							
Surveillance	Yes			Yes	Yes		Yes
Periodicity	Annual			Annual	Annual		Every 3 years
Location	National			National	National		Capital city
Others	Long-distance truck drivers, petroleum workers, plantation workers (sugar, coffee and oil palm), high-risk youth in border areas			-	Youths		Youth (aged 15–24)
High-income countries							
	Australia		Brunei Darussalam		New Zealand		Singapore
Sex workers							
Surveillance	Yes		No		No		Yes
Periodicity	Annual		-		-		Annual
Location	National		-		-		National
People who inject drugs							
Surveillance	Yes		No		Yes		No
Periodicity	Annual		-		Aprox 3–4 years		-
Location	National		-		Other cities		-
Men who have sex with men							
Surveillance	Yes		No		Yes		Yes
Periodicity	Annual		-		Every 2 years		Annual
Location	National		-		Other cities		National
Antenatal care attendees							
Surveillance	No		Yes		No		Yes
Periodicity	-		Annual		-		Annual
Location	-		National		-		National
Others	-		-		-		STI patients, TB patients

All the Pacific island countries reported conducting annual serosurveillance of ANC attendees, either at the national level or in capital cities.

For the high-income countries, Brunei Darussalam and Singapore implement routine serosurveillance to ANC attendees while Australia and New Zealand do not (Table 1).

Other populations

Routine serosurveillance of other populations was reported according to the epidemic situation in each country. For example, China, Fiji, Mongolia and Singapore include sexually transmitted infection (STI) clinic attendees in their routine serosurveillance. Long-distance truck drivers and taxi drivers are under regular serosurveillance in Cambodia, China and Papua New Guinea. Military recruits and police are monitored in Fiji and Viet Nam. Migrant populations are targeted for serosurveillance in several countries, including China, Fiji (seafarers), Mongolia, Papua New Guinea and Viet Nam. Youth are also under periodic serosurveillance in China, Fiji, Mongolia, Papua New Guinea, Solomon Islands and Tonga. It is noteworthy that Singapore conducts periodic HIV serosurveillance among tuberculosis patients (Table 1).

(2) Recent sexual and drug use behaviour surveys

In addition to the routine serosurveillance of the high-risk groups reported above, several countries also conduct sexual and drug use behaviour surveys for these population groups. Among the lower- and middle-income countries, China conducts annual surveys on sexual and drug use behaviours for the different at-risk populations; the most recent surveys in other countries were conducted in 2008 through 2010.

Among the Pacific island countries, Kiribati and Papua New Guinea reported surveys on sexual and drug use behaviours of key populations at the same time as serosurveillance.

For the high-income countries, Australia conducts a sexual and drug use behaviour survey of PWID on an annual basis. The most recent behaviour survey data for Singapore were collected in 2007 among university students, the general population and STI clinic attendees.

(3) Demographic and health surveys with HIV testing

Four low HIV prevalence countries – Kiribati, Mongolia, the Philippines and Samoa – reported that demographic and health surveys (DHS) with HIV testing have been carried out among the general population. The DHS reports are publicly available for the Philippines⁷ and Samoa,⁸ although the HIV testing results were not reported.

(4) Surveillance of HIV drug resistance

The four Asian countries with the highest number of people on ART – Cambodia, China, Papua New Guinea and Viet Nam – have implemented one or more elements of HIV drug resistance (HIVDR) strategies: development of HIVDR prevention and assessment strategies, HIVDR early warning indicators, data collection, monitoring survey of patients on ART, HIVDR transmission survey among recently infected individuals and preparation of annual HIVDR report and recommendations. In other countries, there are no major HIVDR surveillance activities.

DISCUSSION

Countries in the Western Pacific Region all have concentrated or low-level HIV epidemics, where the high-risk behaviour of key populations, particularly FSW, PWID and MSM, drive the epidemics. HIV surveillance for low-level and concentrated epidemics should include estimates of the population size of these key populations and routine HIV serosurveillance and behavioural surveys among them. These should be regularly assessed and evaluated so they can be adapted to any changes in the HIV epidemic situation and response from countries.⁹

This study shows that in 2011, most Asian countries were adequately tracking their HIV epidemics, although there are gaps in tracking the key populations in most Pacific island countries. Serosurveillance had been established for FSW in most Asian countries, although there were gaps for surveillance among PWID and MSM. For example, Viet Nam does not conduct routine surveillance for MSM, despite this being a high-risk group for HIV. Despite these surveillance efforts it can be difficult to determine the

HIV trends among different population groups in some countries due to the insufficiency of data and limited geographic coverage of these surveys. For example, the Lao People's Democratic Republic conducted some surveys of PWID but not in a consistent and continuous manner. Asian countries are encouraged to continuously and consistently conduct surveillance among these populations and expand the geographic coverage.

In the Pacific island countries, surveillance activities in most countries focus on ANC attendees, although Kiribati and Papua New Guinea did report surveillance of FSW, with Kiribati also reporting surveillance of PWID and MSM. Fiji also reported surveillance of other high-risk groups. Using ANC attendees is not recommended for low-level HIV epidemic countries and is done as ANC data are easy and convenient to collect. There is a lack of capacity of the surveillance systems to track other at-risk populations in these countries. Therefore it is recommended that mapping of high-risk populations should be conducted in priority Pacific island countries, and if these high-risk behaviour groups are indeed existing and active, tailored surveillance systems should be designed to track the HIV epidemic and risk behaviours. As STIs are especially high in many of the Pacific island countries,¹⁰ active surveillance of STIs and HIV among groups with risk behaviours is warranted. Furthermore, greater efforts should be made to strengthen HIV testing and counselling and HIV and STI case reporting in the Pacific island countries.

DHS with HIV testing has been reported as implemented in several low prevalence countries, but data are not available in the public domain. As for surveillance of ANC attendees, this may not be a suitable method for these low epidemic countries as it requires HIV testing of very large samples. As most HIV cases are found within the key populations, a more targeted approach might be better.

HIV drug resistance surveillance was reported from the four countries with the highest number of people on ART, and this is essential to optimize ART delivery. The implementation, however, needs to be strengthened in this Region, as has been extensively discussed by a recent systematic review.¹¹

There are several limitations to this report. Not all countries responded to the survey; therefore, the

representativeness of the results might be affected. Moreover, it is based on self-reported results, which might be affected by the understanding of the questions, leading to possible misreporting. There are several other issues that this current survey could not cover but that are important for countries' surveillance systems. In some countries, surveillance surveys are conducted in facilities such as detention centres and STI clinics using convenient sampling. The representativeness could be improved with better sampling methods, such as respondent-driven sampling or time–location cluster sampling. There is also the need for better mapping and size estimation of the key populations in some countries, especially in the Pacific island countries. Improvement in the consistency of methods, data quality and data use for the surveillance activities is also needed.

Conflicts of interest

None declared.

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HIV surveillance systems in the Asia Pacific region

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In 2011, the United Nations Joint Programme on HIV/AIDS (UNAIDS) Regional Support Team for Asia-Pacific conducted a stock-taking process of available strategic information in the Asia Pacific region. This paper summarizes the progress of HIV surveillance for 20 countries in the region, covering population size estimates of key populations at higher risk, HIV case reporting, HIV sentinel surveillance and probability surveys of behavioural and biological markers. Information on surveillance activities was obtained from publically available surveillance reports and protocols, supplemented by personal communication with the UNAIDS monitoring and evaluation advisers and surveillance experts in country. Key findings include substantial efforts in broadening the number and types of HIV surveillance components included in national HIV surveillance systems and adopting approaches to make surveillance more cost-efficient, such as integrating routine programme monitoring data and passive surveillance case reporting systems. More investment in regularly analysing and applying surveillance data to programme strengthening at the subnational level is needed but will require additional capacity-building and resources. The ability to triangulate multiple sources of surveillance data into a more comprehensive view of the HIV epidemic will be enhanced if more investment is made in better documentation and dissemination of surveillance activities and findings.

During the decade following the introduction of second generation surveillance for HIV and AIDS in 2000,¹ there was a proliferation of surveillance data collection activities throughout the Asia Pacific region. HIV and AIDS surveillance systems evolved differently in different countries depending on a host of factors including type and stage of the epidemic, level of government and donor commitment and support and local capacity. Over the last decade, two global HIV surveillance conferences and several reviews of HIV surveillance systems have documented some of this progress.²⁻⁴ In 2011, the Joint United Nations Programme on HIV/AIDS (UNAIDS) Regional Support Team for Asia-Pacific reviewed available strategic information in the Asia Pacific region as part of a stock-taking process.⁵ The intention was to describe how surveillance and monitoring and evaluation systems had evolved in the countries in the region and to identify strengths and opportunities for better use of data to understand and respond to the epidemic. This paper focuses on the surveillance components of the project.

METHOD

The project included 20 countries within the UNAIDS Asia Pacific region, including Afghanistan, Bangladesh, Bhutan, Cambodia, China, Fiji, India, Indonesia, the Lao People's Democratic Republic, Malaysia, Maldives, Mongolia, Myanmar, Nepal, Pakistan, Papua New Guinea, the Philippines, Sri Lanka, Thailand, and Viet Nam. Four types of surveillance activities were included: estimation of the size of key populations at higher risk; HIV case reporting; HIV sentinel surveillance (HSS) and probability surveys of risk behaviours, including those integrated with biological markers. It also covered the use of surveillance data for epidemic modelling, programme design and monitoring and evaluation.

Information on surveillance activities collected for this review came from publically available surveillance reports and protocols supplemented by unstructured interviews with the UNAIDS monitoring and evaluation (M&E) advisers and surveillance experts in country.

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Table 1. Surveillance terminology used in this assessment

Term	Definition used	Variations in terminology and methods from different countries
Second generation surveillance (SGS)	A multi-component system of surveillance activities intended to collect and analyze data to understand the trajectory of the HIV epidemic. SGS goes beyond biological measures of HIV to include surveillance of other sexually transmitted infections (STI), behaviours, and demographic changes in the populations most at risk.	Some countries use the term SGS to refer to surveys that include both biological and behavioural measures in the same individuals.
HIV and AIDS case reporting	Passive, routine reporting of numbers of HIV and/or AIDS cases diagnosed in the reporting period.	Some countries use data reported from HIV testing and counselling sites to derive HIV case numbers, rather than separate systems for HIV case reporting.
HIV sentinel surveillance (HSS)	Annual measures of HIV seroprevalence of selected risk populations. Data come from selected sites/locations that are repeated in subsequent rounds.	Sampling approaches vary and include: <ul style="list-style-type: none"> • sequential sampling among facility-based populations, e.g. ANC attendees; • convenience sampling in community settings with the intent to reach a broader representation of the population; and • cluster sampling or respondent-driven sampling. Some countries incorporate limited behavioural questions into their protocols and refer to this as HSS+.
Probability surveys	Probability sample surveys of selected risk populations in selected sites. Behavioural surveillance survey (BSS) protocols include extensive knowledge, attitude and behavioural questionnaires. If HIV and/or STI testing is added onto BSS, this is referred to as Integrated bio-behavioural survey (IBBS).	In Asia Pacific, BSS and IBBS are usually focused on key populations at higher risk, including proxy populations of male clients of sex workers and apply time location cluster sampling or respondent-driven sampling methodologies. The frequency of conducting BSS and IBBS varies in different countries, often depending on the availability of external resources from development partners.

Collated tables and documentation developed by the Asia Pacific-Regional Support Team and the HIV and AIDS Data Hub for Asia-Pacific were also used. The variation in use of terms to describe different surveillance activities across countries was a key challenge. For purposes of clarity, we used the terms HIV case reporting, HSS and probability surveys (includes behavioural surveillance survey [BSS] and integrated bio-behavioural survey [IBBS]) (Table 1).

RESULTS

Size estimation of key populations at higher risk

Resources for generating population size estimates have increased as the core uses of such data for programme planning, budgeting and monitoring of programme coverage have been recognized. More recently, size estimation exercises have also been recognized as a key component of the surveillance system and an integral part of understanding epidemic potential in “Know Your Epidemic” analysis.⁶

A large array of approaches are being used to generate size estimates in the region, most commonly mapping of key populations in certain locations and survey-based multipliers in conjunction with probability surveys of key populations at higher risk (Table 2). Since 2000, 14 countries have generated population size estimates using mapping techniques, while 10 have used the multiplier method. As solicitation points and partner-meeting venues are easier to define for sex workers and men who have sex with men (MSM), these populations are more often estimated using the mapping method. Almost twice as many countries have relied on multiplier-based approaches for estimating the population size of people who inject drugs (PWID) than those that use mapping. Six countries have used both mapping and the multiplier method in the same population to enable comparison of results between methods. National-level estimates of the size of key populations at higher risk are usually made by extrapolating local-level estimates from a few areas (Table 2).

Despite these efforts, a large number of countries still lack local size estimates of key populations at

Table 2. Use of different population size estimation methods for key populations at higher risk in Asia Pacific countries

Group	FSW	MSM	PWID
Mapping or rapid assessment and response	Afghanistan, Bangladesh, Cambodia, China, India, Indonesia, Malaysia, Mongolia, Myanmar, Nepal, Pakistan, Philippines, Sri Lanka, Thailand	Bangladesh, Cambodia, China, India, Indonesia, Mongolia, Nepal, Pakistan, Sri Lanka	Afghanistan, Bangladesh, India, Indonesia, Nepal, Pakistan
Multiplier	Bangladesh, China, Malaysia, Maldives, Myanmar, Philippines, Thailand	China, Lao People's Democratic Republic, Malaysia, Maldives, Myanmar, Philippines, Thailand	Bangladesh, China, Cambodia, Malaysia, Maldives, Myanmar, Nepal, Philippines, Thailand
Capture recapture		Cambodia	Cambodia, Thailand
Network scale-up			Thailand
Extensive extrapolation for national estimate	Bangladesh, China, India, Indonesia, Lao People's Democratic Republic, Nepal, Philippines, Viet Nam*		

FSW - female sex workers; MSM - men who have sex with men; and PWID - people who inject drugs.

* In Viet Nam, specific implementing partners have used mapping, enumeration, capture–recapture and multipliers in selected provinces, but not through a national/centrally coordinated effort.

higher risk in most geographic areas or feel dissatisfied with the level of reliability of the results from their size estimation efforts. Countries are interested in strategies for optimizing their size estimation activities, including:

- improving the quality of field implementation of the selected methods to reduce preventable bias;
- selecting locations for size estimation data collection more strategically to allow for improved extrapolation; and
- proactive coordination with organizations planning to implement probability surveys of key populations at higher risk to include useful multipliers for size estimation to the protocol at little additional cost.

HIV and AIDS case reporting

Of the 20 countries included in the review, 18 maintain functioning HIV case reporting systems. Many of these systems rely on routine monitoring data for HIV counselling and testing services as the primary source from which to obtain HIV cases disaggregated most commonly by age, gender and risk factor. This combining of routine data with passive surveillance systems is efficient but may result in the exclusion of collecting more detailed information about newly diagnosed HIV

cases, e.g. occupation, whether the person has a regular sex partner. Place of residence is another important characteristic to collect on HIV cases to identify emerging geographic pockets of the epidemic; however, some routine monitoring systems for HIV counseling and testing use the location of the testing site as an imperfect proxy for this information. On the other hand, a benefit of most routine monitoring systems for HIV testing and counseling is data on the number and types of people tested. The availability of these “denominators” are critical for determining whether trends in HIV case reports reflect changes in testing patterns rather than potential changes in the number of actual cases.

HIV sentinel surveillance

Globally, HSS originated as a relatively low-resource method for observing trends in annual HIV seroprevalence among clinic-based populations who provided blood specimens for other routine tests, i.e. syphilis screening among antenatal care (ANC) attendees. Data from ANC attendees are valuable in generalized epidemic settings, but are less useful in tracking the HIV epidemic in low-level and concentrated epidemic settings. Eleven countries in the Asia Pacific region have adapted HSS methods of sampling to measure HIV seroprevalence among key populations – Bangladesh, Cambodia, China, India, Indonesia, Mongolia, Myanmar, the Philippines, Sri Lanka, Thailand and Viet Nam.

Table 3. The surveillance “shift” in active surveillance for key affected populations

Primary method of surveillance	None	HSS only	BSS (alone or in addition to HSS)	IBBS (alone or in addition to HSS or BSS)
1990–1999	Afghanistan, Bhutan, Fiji, Lao People’s Democratic Republic, Maldives	China, Malaysia, Myanmar, Mongolia, Pakistan, Papua New Guinea, Philippines, Sri Lanka, Viet Nam	Bangladesh, Cambodia, Indonesia, Nepal, Thailand, India	
2000–2004	Afghanistan, Bhutan, Fiji, Maldives	Myanmar, Sri Lanka	Bangladesh, China, Timor Leste, India, Malaysia, Mongolia, Papua New Guinea, Philippines, Thailand, Viet Nam	Cambodia, Indonesia, Lao People’s Democratic Republic, Nepal, Pakistan
2005–2011			Bangladesh, Fiji (ANC attendees and male STI patients), Papua New Guinea (ANC, STI & TB patients), Sri Lanka	Afghanistan, Cambodia, China, India, Indonesia, Malaysia, Mongolia, Myanmar, Timor Leste, Thailand, Viet Nam <u>IBBS only:</u> Lao People’s Democratic Republic, Maldives, Nepal, Pakistan, Philippines <u>BSS only:</u> Bhutan

ANC - antenatal care; BSS - behavioural surveillance survey; HSS - HIV sentinel surveillance; IBBS - integrated bio-behavioural survey; STI - sexually transmitted infections; and TB - tuberculosis.

Nine of these countries also include seroprevalence measures among ANC populations (Bangladesh and the Philippines do not conduct HSS among ANC populations). A major challenge in conducting HSS among key populations is developing consistent approaches for sampling hidden, mobile groups who may not routinely come to health facilities for services. Over time, many countries have adopted community-based methods for sampling these groups; however, there are insufficient resources to apply rigorous approaches for representative, replicable samples in most countries. In some countries, the distinction in seroprevalence measures from HSS and probability survey efforts (i.e. IBBS) have become less clear (Table 3).

As new components of surveillance have been introduced and the numbers of HSS sites have increased, the available management and technical resources have been stretched. In some cases quality control and continuity of data have suffered. These inconsistencies can be difficult to reconcile when interpreting HSS trend data. Further exacerbating this problem, there has often been an absence of written reports documenting methods and results and potential quality control problems during the implementation of

surveillance activities.

Probability surveys

Many countries in the region have put considerable resources into conducting probability surveys of female sex workers (FSW), MSM and PWID to obtain representative measures of HIV, sexually transmitted infections (STI) and risk behaviour. Eight countries, including Bangladesh, China, Cambodia, India, Nepal, Pakistan, Thailand, and Viet Nam, now have more than three rounds of consecutive BSS or IBBS survey data for key populations at higher risk in selected sites.

Use of surveillance data

From the review of available documentation, it appears that the main use of surveillance data in the region is related to quantifying the burden of disease at the national level every two years using the Estimation and Projections Package⁷ and reporting on biennial United Nations General Assembly Special Session indicators at the national level.⁸ More recently, countries have begun to apply these models at the subnational level to better understand local epidemic patterns that

may better guide programming and help develop a more informed national picture of the epidemic (e.g. Viet Nam, Nepal, India and Indonesia).

Several countries have also used surveillance data for the purpose of impact evaluation of their national programmes generally, as well as of specific prevention programmes (e.g. 100% Condom Use Programme).

DISCUSSION

Over the past decade, HIV surveillance systems in the region have evolved from focusing primarily on HIV case reporting and annual seroprevalence measures from HSS to inclusion of a broad array of data collection activities. The types of data include population size estimates, behavioural surveys and integrated bio-behavioural surveys that are combined to inform the understanding of the epidemic and the response.

More recently, it appears that some countries are scaling down or streamlining their surveillance activities for HIV and AIDS; eliminating those which are perceived to return little usable data or substituting earlier activities with other sources of similar data, e.g. using HIV prevalence data from prevention screening of pregnant women in the place of HSS among ANC populations. The intention is to better direct limited surveillance resources and improve the quality and usability of the results. As many countries in the region are heavily dependent on external funding for HIV and AIDS programming,⁹ and there is uncertainty that current level of funding from development partners will continue,¹⁰ a decrease in the numbers and frequency of these resource-intensive surveys, such as probability surveys, in the future is likely. All countries would benefit from evaluating the design of their surveillance systems to clarify the utility of each surveillance component, including how different components work together to give a more in-depth picture of the epidemic in different regions of the country.

There is also a need to balance national analysis with subnational-level analysis and use of HIV and AIDS surveillance data. The substantial effort to generate national-level estimates and global reports, usually for donors, competes with the resources and time needed to conduct the same assessments at subnational-levels.

These subnational analyses can highlight variations within a country and may be more likely to generate insight to guide effective prevention strategies. Countries should be supported to make decisions driven by their local epidemic context with surveillance data that allows for this.

To improve subnational analysis and use of surveillance data, it is essential that data collection and data analysis be integrated in the same unit with year-round attention to both. Data analysts and users need to coordinate well from the beginning. A clear understanding of how the data can or will be used can motivate more streamlined and efficient systems of data collection locally. Involvement of subnational-level programme staff in efforts to synthesize, triangulate and interpret data into national-level indicators may enhance the robustness of the results and consensus by all partners. Commitment from donors and technical agencies to support approaches to engage subnational partners in data analysis is also essential.

This assessment was based on publically available information and through communication with M&E and surveillance advisers for HIV and AIDS in country. Therefore it is likely that some activities may have been missed.

From the information collected in this assessment we can conclude that HIV surveillance systems in the Asia Pacific region are maturing; however, there are still opportunities for improving the collection and utilization of the data to understand and respond to the HIV epidemic.

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Human resource challenges in scaling up the response to HIV in Papua New Guinea

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In Papua New Guinea, an estimated 0.9% of the adult population is infected with HIV, and the spread of the epidemic is geographically heterogeneous.¹ The seriousness of the epidemic presents many issues for the government, donors and nongovernmental organizations. One of the greatest challenges of the HIV response is that of human resources. This article highlights human resource issues specific to HIV in Papua New Guinea and raises a series of questions that need to be addressed.

The Australian Agency for International Development (AusAID) Review of HIV Training Programs in Papua New Guinea, conducted in 2009, noted that there had been no assessment of the quality and effectiveness of HIV training programmes or documentation of numbers trained.² The review demonstrated that there are multiple agencies involved at many different levels in the human resource response to HIV, and the review commented on the lack of coordination between agencies. The most significant recommendation was that training programmes needed to be re-oriented so that they are based on a strategic assessment of needs reflecting national and provincial priorities and focusing on new developments in the epidemic.

In 2011, the Independent Review Group on HIV delivered a report to the Papua New Guinea National AIDS Council Secretariat and the National Department of Health (NDoH) indicating that while health service staff in several provinces had maintained HIV service levels in 2010 relative to 2008 and 2009, there were significant human resource concerns.³ These included increasing STI and HIV patient loads with static or diminished staffing levels, insufficient space with occupational health risks for staff and patients alike and stock-outs of some drugs and repeated stock-outs of HIV test kits.

Ongoing restructuring of the NDoH has also meant the loss of key staff and insufficient funds to support supervisory activities. Additionally, there are problems emerging for Papua New Guinea in meeting recurrent costs and absorbing staff positions introduced by Global Fund-supported activities.⁴ The Papua New Guinea 2010 United Nations General Assembly Special Session country progress report indicated that the capacity to deliver prevention of parent-to-child transmission (PPTCT) services remains limited.⁵ The report also noted other staffing issues, including a lack of formal training for managers, and a limited understanding of PPTCT and variable interpretations of global PPTCT standards.

The only comprehensive study of the HIV workforce in Papua New Guinea is that of Buchanan-Aruwafu & Amos.⁶ The study found that half of the 141 health workers sampled had been educated more than 20 years before the baseline, with a quarter of health staff completing their education between 30 and 40 years before. Only a quarter had completed their education in the last eight years. Health staff interviewed reported that they had participated in a variety of courses in the previous year. These courses were stand-alone and not part of an ongoing and nationalized training course. The majority of health workers surveyed reported that the facility in which they worked lacked adequate staff. Many also reported that staff would arrive late for work, and some reported staff being absent for extended periods. Unscheduled staff absences, when there is already inadequate staffing, further contributes to staff frustration, the possibility of facility closure and the inability to provide health services. Facility closures occurred frequently due to shortages of medicine, staffing issues, water problems, criminal activities or tribal fighting.

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More than half of health workers in the study reported that staff did not receive enough supervision, with only three-fifths reporting that a doctor had visited their facility. While over half of health workers reported that their last supervisory visit was within the last month, a quarter had their last supervisory visit six months before. Two-thirds of health workers reported that they were not satisfied with their working conditions, and three-quarters were frustrated in their work. Not receiving pay on time or not having adequate drugs and medical supplies were identified by health staff as contributing significantly to feeling frustrated at work. Staff also reported that they did not feel safe from contracting HIV.

From the limited amount of available information in relation to the HIV workforce in Papua New Guinea it appears that a major concern is the potential for training recipients to enter the workforce with limited and variable sets of skills and with little likelihood of receiving ongoing support and supervision. There is concern that this can lead to a disintegrated service response and to staff operating with limited effectiveness.

There has been considerable direct investment in HIV workforce training in Papua New Guinea. It is recognized that greater integration of HIV workforce training, with, for example, trainings in Sexually Transmitted Infections Syndromic Management and Adolescent and Sexual Reproductive Health, is required in Papua New Guinea. Indeed, the Papua New Guinea National Health Plan 2011–2020 has the overarching goal of integration of all programmes within a strengthened primary health care framework.⁷

The redistribution of health workforce away from other health priorities toward HIV-programme planning needs to be further examined in Papua New Guinea. This has been noted as occurring in other countries, and with the imperative to continue and extend the provision of HIV-related services, specific tasks have been delegated to less trained staff and sometimes to community members.^{8,9} In some countries the response of task-shifting has been adopted, either formally delegated by policy and supported by task-specific training, or informally by community members taking on new roles.¹⁰ The potential of such strategies to effectively prevent HIV

transmission and to provide treatment and care services for people living with HIV requires investigation in the Papua New Guinea context.

In identifying the HIV workforce policy issues, it is clear that a number of policy options need to be addressed in Papua New Guinea, and these include:

- integration and coordination of national training plan and inputs towards achieving the HIV workforce goals of the Papua New Guinea National Health Plan 2011–2020,⁷ in particular Key Result Area 6, aiming to reduce the burden of communicable diseases;
- agreement on sets of workforce competencies needed for the prevention of HIV transmission and the provision of treatment and care in the cultural contexts of Papua New Guinea;
- assessment of task-shifting as a feasible strategy in the HIV response in Papua New Guinea;
- expansion of infrastructure and services as proposed in the recent Papua New Guinea Global Fund grant, especially those sections of the grant focused on health system strengthening through health workforce development at provincial and district levels;
- strengthening of management systems at the district level to support health workers in the field by ensuring appropriate supervision;
- strengthening of management systems at the national level to ensure that health workers' payments are timely and medical supplies are adequate; and
- coordination of HIV workforce training and management through national, provincial and district-level planning in Papua New Guinea.

There are considerable challenges facing the health workforce in relation to the HIV epidemic in Papua New Guinea. Developing HIV workforce training and competencies as well as improving infrastructure and management systems are just some of the key issues requiring further investigation.

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HIV and AIDS Data Hub for Asia Pacific: a regional tool to support strategic information needs

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The 2011 global commitments towards controlling HIV made by Asia-Pacific countries require considerable improvement in strategic information and response tracking. The HIV and AIDS Data Hub can serve as an important tool for stakeholders with its regional database of subnational indicators, web site and data synthesis capacity.

REGIONAL COMMITMENTS AND HIV STRATEGIC INFORMATION NEEDS

In 2011, countries across the world – including those in Asia and the Pacific – made bold new commitments towards the elimination of HIV, including several specific targets to be met by 2015.^{1–4}

In Asia and the Pacific, the renewed commitments are warranted by the estimated 4.8 million people living with HIV (14% of global infections) and the second highest death toll after Sub-Saharan Africa, with an estimated 310 000 AIDS-related deaths.⁵ The need to reach new targets by 2015 means, more than ever, that countries will have to prioritize understanding the progression of their HIV epidemics. Regular systems need to be in place for tracking trends and remedying gaps. Since epidemics in the region tend to be concentrated among key populations at higher risk, and are geographically disparate within countries, there is a need for better subnational data generation and analyses so that responses can prioritize appropriate groups and localities. Central and subnational data synthesis and triangulation units involving technical experts, policy-makers and communities are essential. Using resources effectively demands greater coordination among development partners and national partners in HIV interventions and guidance on new developments such as Treatment for

Prevention and the Investment Framework.^{6,7} There is already substantial regional experience in effective responses that reverse the epidemic. Increased sharing of lessons and innovative approaches among countries would be highly beneficial.

However, gaps still exist in HIV and behaviour surveillance, monitoring and evaluation and/or their quality and in subsequent analysis of data to guide programming. One-third of 26 countries assessed in Asia and the Pacific conducted HIV sentinel surveillance surveys among all their relevant key populations (sex workers, men who have sex with men, people who inject drugs) between 2008 and 2012; two-thirds of the 26 countries had done behavioural surveys. Although size estimations of key populations are now more available (20/24 countries assessed), questions remain in countries about their reliability. The proportion of AIDS spending on interventions among key populations is still low (median of 6% reported by 14 countries).⁸ Comparisons of country progress are hampered by diverse data collection methods and indicators, often tailored to meet reporting needs rather than inform programming. In many countries there is still a gap whereby strategic information generated by data analysts is not translated into key messages for policy-makers. Communities often do not have the evidence to participate in decision-making.

In this environment, there is need for a regional tool to support national and international partners with updated HIV data for policy advocacy and tracking of progress. The regional HIV and AIDS Data Hub for Asia-Pacific, with its openly accessible web site that is linked to a regional database and team of data analysts, is in a unique position to fill this role.⁹

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EVOLUTION OF DATA HUB FROM PROJECT TO SUSTAINABLE REGIONAL DATA RESOURCE

Initiated in 2006 by the United Nations Children’s Fund (UNICEF) East Asia and Pacific Regional Office (EAPRO), Asian Development Bank and the Joint United Nations Programme on HIV/AIDS (UNAIDS) Regional Support Team for Asia-Pacific (RSTAP) to promote evidence-informed advocacy and action, the web site was launched in 2008. The Data Hub also received technical support from World Health Organization (WHO) and the Fogarty Programme, University of California, Los Angeles. A Science and Technical Advisory Group of HIV experts guided early development and provided information and data validation. Technical and operational development was managed by EAPRO until 2011.

The three major aspects comprising the Data Hub are the regional database, data analysis team and web site with data products (Figure 1). Data are collected from published literature and national HIV web sites and from a network of country and regional partners. Data are vetted for accuracy and valid methods and conclusions by the team before being included in the regional database. The Data Hub, with its focus on subnational information on key populations and affected women and children, with gender- and age-disaggregated data where available, complements the global standardized

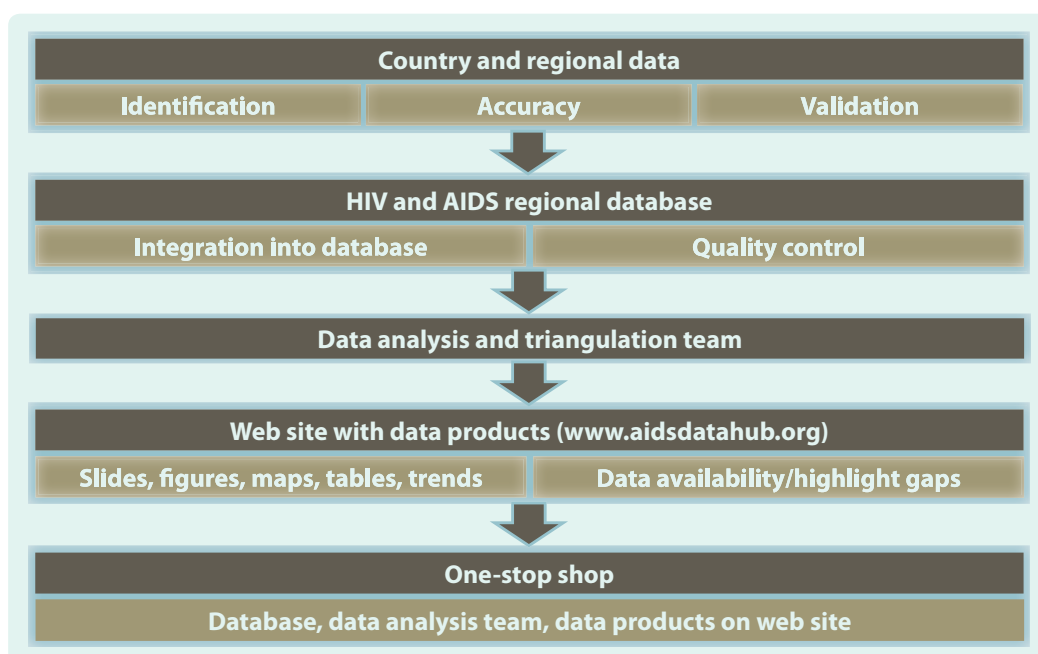
United Nations General Assembly Special Session (UNGASS) and health sector data.

The Data Hub team responds specifically to regional needs by compiling the epidemic and response-related data on Asian countries and the Pacific to generate useful strategic information products. These are downloadable on the web site and increasingly commissioned through direct communications with partners.

The web portal is the only regional site of its kind, with a large repository of data on 26 countries. The regional database now has 86 000 data points for 1400 indicators on HIV prevalence, vulnerability, risk behaviours, national response and socioeconomic impact collected from over 900 unique sources. The web site has a comprehensive online reference library with over 2500 downloadable documents. Also available are downloadable data spread sheets; country reviews of synthesized strategic information; thematic regional reviews; slides on “Data Availability,” “Economics of AIDS;” key information and maps; key presentations by experts; and a section for common tools, guidelines and training manuals. Over 10 000 unique visitors made approximately 15 000 visits to the site during the first quarter of 2012.

There are many examples of how the Data Hub products and/or the expertise of the data analysis team

Figure 1. How the HIV and AIDS Data Hub for Asia-Pacific works to generate strategic information products



add value to regional reports and key events that aim to improve HIV responses. The Data Hub has become an important reference source for UNAIDS cosponsors and civil society regional networks seeking data on specific themes or validation of data and for developing presentations for regional events. In collaboration with UNAIDS RSTAP, the data analysis team collated and analysed data for the regional report, "HIV in Asia and the Pacific: Getting to Zero." In February 2012, the Data Hub provided the strategic information for the regional brief and overview presentations at the United Nations Economic and Social Commission for Asia and the Pacific (ESCAP) Asia-Pacific High-Level Intergovernmental Meeting.

At the country level, several National AIDS Programme web sites provide a link to the Data Hub web site. The Nepal National Centre for AIDS and STI Control used Data Hub products in their 2010 Country UNGASS Progress Report.

In 2011, partners commissioned a Data Hub Management Review to further increase its benefit for the region and to examine sustainability options. The Review acknowledged the Data Hub as a useful strategic information resource and made the following important recommendations on future directions within a three-year business plan:

- Adopting an ecosystem approach to involve regional partners (United Nations cosponsors, development and national partners, community networks, civil society and nongovernmental and private sector organizations) in a network using the platform to profile relevant information and evidence to guide responses. EAPRO has demonstrated the benefit of this approach by hosting the Asia Pacific Prevention of Parent to Child Transmission Task Force webpage on the Data Hub, which largely used data and slides prepared by the Data Hub at its launch.
- Concentrating on the regional focus and support to multi-country initiatives, with a shift from current products that anticipate regional and national partners needs to those that specifically meet expressed data requirements, with increased data triangulation and epidemic modelling.

- Providing a forum for the wealth of qualitative information generated by communities most affected by HIV.
- Tapping into the immense new technological potential to support data use, including interactive applications, data reporting and management tools.
- Facilitating the transition to a sustainable regional platform by having UNAIDS RSTAP host the platform due to its convening role in HIV strategic information and partnerships.

Now managed through UNAIDS RSTAP, the Data Hub will capitalize on its established position as the one-stop shop for subnational data and value-added analysis on HIV and AIDS in Asia and the Pacific by broadening its partnerships to increase its potential as an effective tool for stakeholders in measuring progress to limit the HIV epidemic by 2015.

Conflicts of interest

The authors are all part of the Data Hub data analysis team and this article was undertaken as part of routine activities.

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Uptake of interventions for preventing mother-to-child HIV transmission in 11 operational districts in Cambodia

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Introduction: To achieve the global goal of eliminating mother-to-child transmission of HIV, retention of HIV-positive women and their babies throughout the cascade of prevention of mother-to-child transmission of HIV (PMTCT) services is necessary. Little evidence has been published on coverage of the cascade in resource-limited settings. Along with PMTCT service expansion in Cambodia, a national routine reporting system was developed. This study examines coverage of six PMTCT interventions to improve our understanding of retention throughout the cascade.

Method: We developed indicators to monitor coverage of the six key interventions: (1) maternal antiretroviral treatment or prophylaxis; (2) delivery in a health facility; (3) infant ARV prophylaxis at birth; (4) infant co-trimoxazole prophylaxis at six weeks; (5) first infant DNA-PCR test at six weeks; and (6) second infant DNA-PCR test at 30 weeks. Programme data from April 2008 to December 2011 in 11 operational districts were used to identify those eligible for each intervention.

Results: Women eligible for maternal antiretroviral treatment or prophylaxis in the study were aged 18 to 48 with a median age of 30 years. Coverage of the six interventions were: (1) 79.9% (258/323); (2) 92.2% (236/256); (3) 69.9% (179/256); (4) 73.3% (184/251); (5) 85.7% (215/251); and (6) 61.6% (135/219). Among those eligible, 29.7% (65/219) received all six interventions.

Discussion: This study revealed critical gaps in PMTCT service delivery under routine conditions in Cambodia. Service optimization by reducing gaps will help eliminate HIV infection among infants and improve maternal survival. Further operational studies are needed to identify determinants of service uptake.

In 2010, an estimated 390 000 children globally were newly infected with HIV¹ with an estimated 22 000 children from the Asia Pacific region newly infected with HIV in 2009.² Over 90% of them were infected through mother-to-child transmission (MTCT). Without treatment, about half of children die before their second birthday.³ Without intervention, the risk of MTCT ranges from 20% to 45%. With specific interventions, the risk of MTCT can be reduced to less than 2% in non-breastfeeding populations and to 5% or less in breastfeeding populations. Despite the availability of effective interventions for prevention of mother-to-child transmission (PMTCT), much progress remains to achieve the global goal of virtually eliminating mother-to-child HIV transmission by 2015.⁴

In low- and middle-income countries, 35% of pregnant women received HIV testing and counselling in 2010, and only 48% of the estimated number of HIV-positive pregnant women received the most effective antiretroviral (ARV) regimens (excluding single-dose nevirapine) for PMTCT in 2010.¹ In sub-Saharan Africa, the region with the highest number of pregnant women living with HIV, the coverage of HIV testing and counselling increased in 2010 but only reached 42% (up from 35% in 2009).¹ In Asia and the Pacific, the coverage of HIV testing and counselling among pregnant women was even lower at 17% in 2009.⁵

In addition to HIV testing, counselling and ARV treatment or prophylaxis for pregnant women, the

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mother–infant pairs should be able to access a range of services throughout the PMTCT cascade including skilled care at birth, ARV and co-trimoxazole prophylaxis for infants and first and second DNA-PCR testing for infants. Opportunities to improve programme outcomes can be missed at each step of the PMTCT cascade. For example, in a study in Malawi, 55% of HIV-positive pregnant women were lost to follow-up by the 36-week antenatal visit, 68% by delivery and 81% by the six-month postnatal care visit.⁶ Similarly, according to a review paper, many newborn children are likely to be lost from care at each step of the early infant diagnosis process, “including infant presentation to care, test offer by healthcare professionals and test acceptance by parents/caregivers, specimen processing, result return to healthcare facilities and parents/caregivers, and linkage to care.”⁷ In view of this, it is important to examine regularly the coverage of each service in the PMTCT cascade using available routine programme monitoring systems to understand at which stages retention is insufficient (or where there are significant drop-offs). Few papers have been published on the gains in coverage of each service of the PMTCT cascade using available routine data, particularly in low- and middle-income countries in Asia.

In Cambodia, one of the resource-limited countries in Western Pacific Region, HIV was first detected in 1991 and the first AIDS patient was diagnosed in 1993. The epidemic peaked in 1998 with an estimated HIV prevalence of 2% among adults aged 15 to 49, but successful interventions have dramatically curbed the epidemic.⁸ It is estimated that prevalence had fallen to 0.6% by 2010. In acknowledgement of its efforts to halt and reverse the HIV epidemic, Cambodia received a Millennium Development Goal Award in 2010. Also, HIV treatment has been rapidly expanded and the ART coverage among overall HIV-infected people reached more than 90% by the end of 2008.⁹ Remaining challenges for Cambodia include addressing concentrated HIV epidemics among sex workers, people who inject drugs and men who have sex with men, and moving towards elimination of new paediatric infections.

For PMTCT, only 29% of pregnant women received HIV testing and counselling in Cambodia in 2008 and of the total identified HIV-positive women only 27% received ARV.⁹ At that time, most of the PMTCT services were available only at selected antenatal/maternity health facilities co-located with voluntary counselling and

testing sites. Subsequently, 179 (20%) of 903 health facilities providing antenatal care services also offered HIV testing and counselling. To improve the coverage of each step of the PMTCT cascade, the Cambodian Ministry of Health decentralized the HIV counselling and testing element of the PMTCT services to the health centre levels by adopting the Linked Response approach in two demonstration areas in 2008.¹⁰ The Linked Response aimed to strengthen existing reproductive health services and increase access to comprehensive HIV prevention, education, testing, care and treatment, including PMTCT services by establishing linkages between sexual and reproductive health and HIV services.

Following the successful demonstration of the Linked Response in the initial implementation areas, the approach was rolled out on a national scale, resulting in 921 (92%) out of 997 health facilities providing both antenatal care services and HIV testing and counselling to pregnant women. The coverage of HIV testing among pregnant women increased to 78.1% and that of ARV to 63.5% by 2011.¹¹ According to the HIV sentinel surveillance in 2010, the HIV prevalence among pregnant women at antenatal care was estimated to be 0.4%. Building on the progress made in PMTCT, the Royal Government of Cambodia expressed its commitment to achieving elimination of new paediatric infections.⁵ Increased understanding of the remaining gaps in PMTCT service coverage is crucial to obtain the universal coverage levels required to achieve paediatric infection elimination. In parallel with the roll-out of the Linked Response approach, the Ministry of Health has worked to develop a cohort monitoring system that captures the data on service delivery throughout the PMTCT cascade from pregnancy to infant HIV diagnosis. This cohort monitoring system is being successfully implemented in a subset of operational districts.

In this study, we aim to use this cohort data to describe the coverage of six key PMTCT interventions, namely: (1) maternal antiretroviral treatment and prophylaxis; (2) delivery in a health facility; (3) infant ARV prophylaxis at birth; (4) infant co-trimoxazole prophylaxis at six weeks; (5) first infant DNA-PCR test at six weeks; and (6) second infant DNA-PCR test at 30 weeks.

METHODS

This paper is based on routine programme data from April 2008 and December 2011 from the

11 operational districts where a complete set of data was made available from a total of 77 operational districts in Cambodia. Data were collected to measure the following indicators of the six key PMTCT interventions: (1) percentage of HIV-infected pregnant women identified who received ARV for PMTCT; (2) percentage of HIV-exposed infants who were delivered at health facilities; (3) percentage of infants born to HIV-infected mothers who received ARV prophylaxis at birth; (4) percentage of infants born to HIV-infected mothers who received co-trimoxazole prophylaxis at six weeks; (5) percentage of infants born to HIV-infected mothers who received the first DNA-PCR test at six weeks; and (6) percentage of infants born to HIV-infected mothers who received the second DNA-PCR test at 30 weeks.

The eligibility of the study participants for each of the six interventions was based on the National Guidelines for Prevention of Mother-to-child Transmission of HIV; the National Guidelines for the Prevention and Treatment of Opportunistic Infections among HIV-exposed and HIV-infected Children in Cambodia and the Standard Operating Procedures to Initiate a Linked Response for Prevention, Care and Treatment of HIV/AIDS, Sexually Transmitted Infection and Reproductive Health Issues.

All HIV-infected pregnant women identified during the study period were eligible for maternal ARV treatment or prophylaxis (Indicator 1) if they did not choose to have an abortion and their gestational age was at least 14 weeks by the time that the study ended. They included women who were reported as lost to follow-up or death. All infants born to HIV-infected women in the cohort served as denominator for Indicator 2 and Indicator 3. Infants born to HIV-infected women who reached six weeks of age by the time the study ended were eligible to receive co-trimoxazole prophylaxis (Indicator 4) and the first DNA-PCR test (Indicator 5). They included infants who were reported as lost to follow-up or death. Infants were eligible to receive the second DNA-PCR test (Indicator 6) if they reached 30 weeks of age by the time that the study ended. They included infants who were reported as lost-to-follow-up or death but did not include those who tested positive at the first DNA-PCR test.

The analysis was limited to the specified 11 operational districts among the total of 77 operational districts due to higher completeness and quality of data from these 11 sites compared with many

of the other operational districts where there were much greater challenges in obtaining timely and complete facility reports. These 11 operational districts have all benefited from supplemental technical and financial support from development partners for both programme implementation and data collection while some of the other operational districts have not received such support.

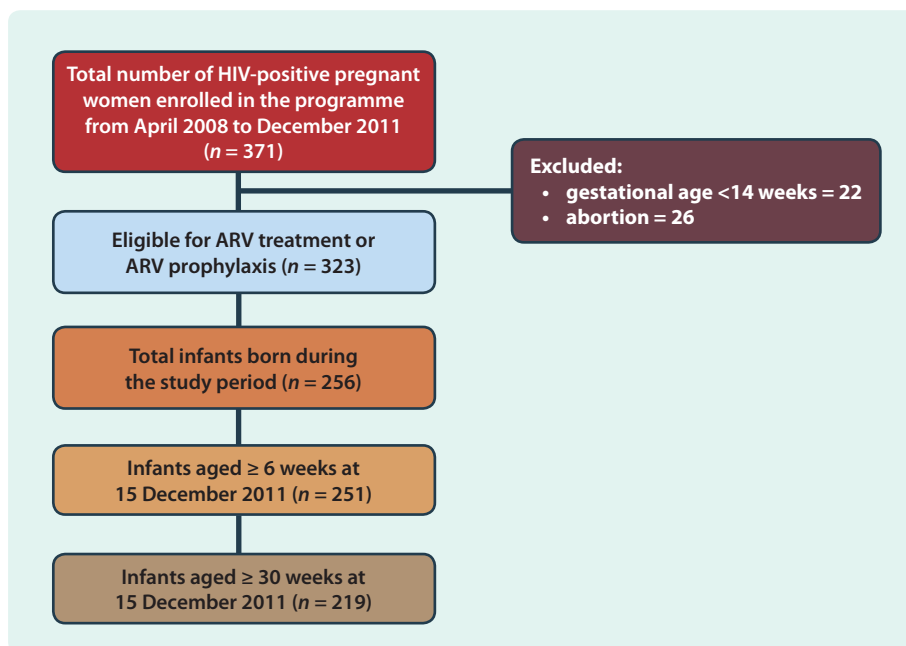
We extracted the routine programme data from the health facility registers. A total of 371 HIV-positive women including those diagnosed before the pregnancy or those newly diagnosed were enrolled into the programme. Of the women in the cohort, 323 were eligible for ARV treatment or ARV prophylaxis during pregnancy on the basis of their CD4 count and gestational age at diagnosis. Forty-eight women did not meet the criteria to receive ARV treatment or prophylaxis as they chose to have an abortion ($n = 26$) or their gestational age was less than 14 weeks ($n = 22$). A total of 256 children were born from 323 mothers who were eligible to receive ARV prophylaxis. Only 251 of these infants were eligible for co-trimoxazole prophylaxis and the first DNA-PCR test as they were at least six weeks old as of 15 December 2011. Of these 251 infants, 219 were eligible for the second DNA-PCR test at the age of 30 weeks (four children got HIV-positive result in their first DNA-PCR test at six weeks and 28 other children were not yet 30 weeks old) (Figure 1). A total of nine women died during the study period. All of these women received ARV treatment or prophylaxis and five gave birth to five babies. A total of 17 women were lost to follow-up throughout the cohort. Of these 17 women, 14 were lost to follow-up before treatment initiation.

For the analysis, we identified the number of HIV-positive women and children who received each of the above six interventions (numerator) and calculated coverage of these interventions using the total number of eligible HIV-infected women or children for each intervention as denominator (Figure 1).

RESULTS

All of the 323 eligible women were offered interventions to prevent HIV transmission from them to their children. Of them, 258 (79.9%) received ARVs (Figure 2). Women who were eligible for ARV treatment or prophylaxis included in the study were aged between 18 and 48 with a median age of 30 years old.

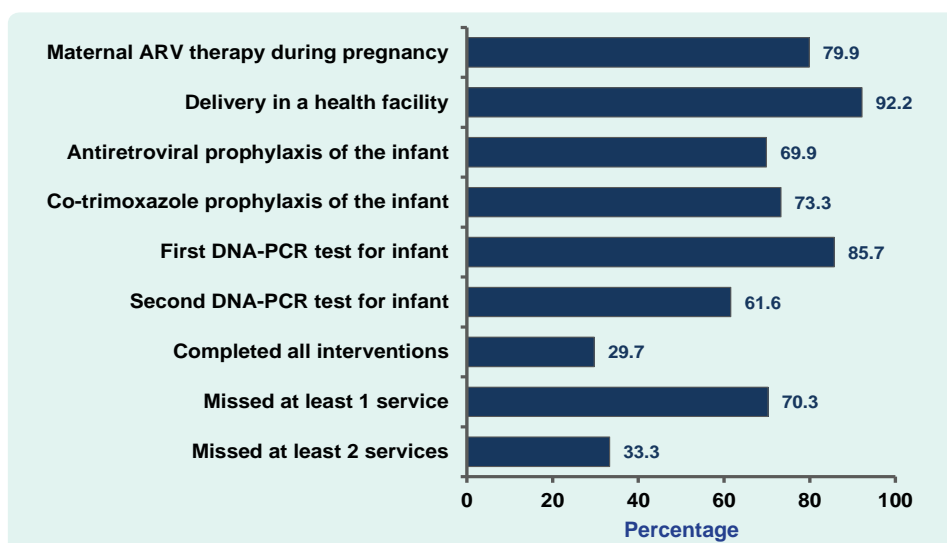
Figure 1. Cohort of HIV-positive pregnant women and their HIV-exposed babies enrolled in the PMTCT programme in 11 operational districts in Cambodia



By 15 December 2011, 254 women in the cohort had given birth to 256 infants, as two women had twins. Of the 256 infants, 236 (92.2%) were born in health facilities and 179 (69.9%) received ARV prophylaxis after birth. Out of 251 eligible infants, 184 (73.3%) received co-trimoxazole prophylaxis and 215 (85.7%) received the first HIV DNA-PCR test. Similarly, 135 (61.6%) of the 219 infants who were eligible for the second HIV DNA-PCR test received it.

Of the 256 mother–infant pairs in the cohort, 251 were eligible for all five infant interventions when the infants were six weeks old. Of them, 93 (38.6%) completed each of the interventions. A total of 219 mother–infant pairs were eligible for all six interventions by the time the study closed. Of these, 65 (29.7%) completed all interventions, while 154 (70.3%) missed at least one intervention. Of the 256 newborn infants, 19 (7.4%) died; the cause

Figure 2. Coverage of six key interventions of babies enrolled in the PMTCT programme in 11 operational districts in Cambodia



Note: The denominator for each indicator is the number of mothers or infants who were eligible for the intervention.

and date of death of these children was not recorded. Of the infants tested for HIV DNA, five were positive, including four positive at the first test (at six weeks of age) and one positive at the second test (at 30 weeks of age).

DISCUSSION

We identified critical service delivery gaps using the six coverage indicators of the PMTCT cascade in Cambodia. The Asia Pacific strategy for elimination of new paediatric infections defines the programme target for ARV coverage at 90% or above among the estimated total number of HIV-infected pregnant women and exposed infants by 2015.² The denominator in this study was not all estimated HIV-infected pregnant women but all women who were accessing services; therefore, the target figures of the ARV coverage for this study population must be higher than 90% to move towards elimination. Similarly, coverage of other non-ARV services should be greater than 90% although no international or national targets have been set for them. This study revealed that none of the six interventions in the PMTCT cascade in the 11 selected operational districts in Cambodia have achieved that level of coverage yet. Furthermore, we found that the majority of the mother–infant pairs did not complete all the interventions. The suboptimal coverage of the full PMTCT cascade highlights the need for significant improvement in linked HIV and reproductive health service delivery.

In this study, about 80% of the identified HIV-positive pregnant women received ARV for PMTCT. This coverage is higher than the coverage in Zomba District, Malawi¹² and in northern Uganda.¹³ In Malawi, a total of 75% of HIV-positive women who were not on ART received a single dose of nevirapine, while in Uganda, a total of 50% of HIV-positive women received either short-course zidovudine from the 36th week of pregnancy or single-dose nevirapine at the onset of labour or at least two hours before delivery. Although the uptake of ARV treatment or prophylaxis is higher among the HIV-positive women in our study than in others, further studies should explore the reasons behind this suboptimal access to ARV treatment or prophylaxis by HIV-positive pregnant women. The possible reasons may include lack of affordable transportation, mobility of the population, insufficient quality of counselling services in health facilities and fear of stigma and discrimination.

Over 92% of HIV-positive women who received ARV treatment or prophylaxis for PMTCT delivered at health facilities. This is an important achievement as this figure is much higher compared to the facility-based delivery rate (54%) in Cambodia among the pregnant women in the general population.¹⁴

Approximately 70% of the newborn children of HIV-positive women received the ARV prophylaxis. This result is much higher than the result of a study in Zimbabwe,¹⁵ in which only 31% of infants received ARV. However, the remaining 30% of the newborn children of this study who did not receive ARV prophylaxis were at high risk of acquiring HIV. It is documented that newborn children of HIV-positive women without ARV prophylaxis are more likely to get HIV infection from their mothers through breast feeding compared to those receiving ARV prophylaxis. Evidence shows that there is an incremental increase in the probability of mother-to-child HIV transmission of approximately 0.2% for each month of breastfeeding among those receiving triple ARV prophylaxis or treatment.¹⁶ The rate of transmission from mother to child with less effective regimens such as a single dose of nevirapine or no prophylaxis is as high as 1.57% among mothers with CD4 counts lower than 350.¹⁷

Among this group of HIV-exposed infants, about 73% received co-trimoxazole prophylaxis, reducing the risk of having opportunistic infections. Co-trimoxazole prophylaxis is safe and highly effective in reducing morbidity and mortality among HIV-positive children. The World Health Organization, therefore, recommended initiation of co-trimoxazole prophylaxis to all HIV-exposed infants at around six weeks of age.¹⁸ The infants who did not receive co-trimoxazole prophylaxis were at a higher risk of mortality in the absence of its preventive benefits.

Cambodian guidelines recommend HIV testing using DNA-PCR test (with dried blood spot) for all infants born to HIV-positive women at six weeks of age.¹⁹ However, about 14% of the children in our study did not receive the first test at six weeks of age. Similarly, about 38% of the newborn infants born to HIV-positive women did not receive the test at 30 weeks. This is a critical gap as such children may have missed the opportunity for early diagnosis in the event that they were infected by the virus during the postnatal period.

The most striking result of our study is that fewer than one-third of the HIV-positive women and their infants aged over 30 weeks completed all six key interventions of the PMTCT cascade. In a previous study in Malawi,¹² only 18% of HIV-positive women completed all the recommended strategies i.e. both mothers and newborn infants took single-dose nevirapine and they followed the recommended feeding option. Although the proportion of mother and infant pairs who completed all the PMTCT services is higher in our study than other studies, our results clearly highlight critical service delivery gaps as well as the need for further studies in identifying the correlates of the uptake of each step of the PMTCT cascade.

One of the limitations of this study was the small number of operational districts included in the study because of the higher completeness and quality of routine programme data in these operational districts compared with the other operational districts in the country. It is possible that the selected operational districts have stronger programmatic capacity in implementing the PMTCT programme than other areas due to additional support received from development partners. The results of this study, therefore, may not be generalizable to the whole country. In Cambodia, the Ministry of Health has been working to improve the routine monitoring system of the PMTCT programme throughout the country. The cohort monitoring system is being implemented with relative success in these 11 operational districts. However, many districts will require further support to improve completeness and quality of data recording. Through these efforts it will be possible for the national programme to analyse this rich programme data reflecting PMTCT coverage throughout the service cascade. While our data comes from only a small sample of the total number of operational districts, the results from this analysis provide a preliminary indication of coverage in Cambodia and a potential baseline against which to measure Cambodia's progress towards scaling up access to ARVs for HIV-infected pregnant women and, eventually, elimination of new paediatric HIV infections.

In conclusion, this study revealed the critical gaps in PMTCT service delivery under routine programme conditions in Cambodia. Optimization of PMTCT services by reducing such gaps will help to eliminate HIV infection among newborn infants and improve maternal survival. Further operational research is needed to identify the determinants of the uptake of the PMTCT services.

Conflict of interest

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Innovative data tools: a suite for managing peer outreach to key affected populations in Viet Nam

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Problem: The paper tools used to monitor outreach work in all major cities in Viet Nam had substantial writing requirements for each contact with difficulty maintaining confidentiality.

Action: This paper describes the development of a Unique Identifier Code (UIC), a field data collection notebook (databook) and a computer data entry system in Viet Nam. The databook can document 40 individual clients and has space for commodity distribution, group contacts and needles/syringe collection for each month.

Outcome: Field implementation trials of the UIC and databook have been undertaken by more than 160 peer outreach workers to document their work with people who inject drugs (PWID) and sex workers (SW). Following an expanded trial in Hai Phong province, there have been requests for national circulation of the databook to be used by peer educators documenting outreach to PWID, SW and men who have sex with men. The standardized UIC and databook, in a variety of locally adapted formats, have now been introduced in more than 40 of the 63 provinces in Viet Nam.

Discussion: This development in Viet Nam is, to our knowledge, the first example of the combination of a confidential UIC and an innovative, simple pocket-sized paper instrument with associated customized data-entry software for documenting outreach.

The HIV epidemic in Viet Nam remains in a concentrated stage with signs that it may have begun to stabilize over the last two years. There has been some decrease in HIV prevalence among people who inject drugs (PWID) and female sex workers (SW) in most provinces. According to the Viet Nam national 2011 sentinel surveillance, HIV prevalence among PWID and SW remains high, at 13.4% and 3%, respectively; Integrated Biological and Behavioural Surveillance 2009 data indicate that prevalence among men who have sex with men (MSM) also remains high at 16.7%.¹ The distribution of HIV cases largely follows the distribution of these three populations that are heavily concentrated in urban centres (though not absent in non-urban communities). The overall adult HIV prevalence (ages 15–49) remained at 0.45% in 2011.²

Since 2004, projects implementing broadly similar HIV prevention peer outreach targeting PWID and SW have expanded across Viet Nam to 60 provinces for the Needle Syringe Programme (NSP) and 63 provinces

for condom distribution.³ These outreach activities, designed to take HIV prevention education, behaviour change communication and HIV prevention commodities into the networks of key affected populations, have followed similar practices under each project, often being co-located in the same province, district or even commune, and reaching out to the same networks. At the end of 2011, these peer outreach workers numbered in excess of 6200 across the 63 provinces.³

Previous paper instruments to collect client contact data by peer outreach workers, under the variety of projects in Viet Nam, had problems with reliability of data recording, confidential monitoring of individuals and recording of commodity distribution and other services. There exist major practical challenges to harmonizing and collecting data for various coverage indicators at the provincial and national level while managing the data collection burden in the field.⁴

To improve the collection and reporting of these outreach data, we document the development of a suite

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of innovative data tools for managing peer outreach to PWID, SW and MSM in Viet Nam.

CONTEXT

The tools in use for peer outreach at the beginning of this project in 2008 were extremely varied, comprising paper notebooks of A5, A4 or even larger sizes. The data collected were loosely standardized but often included name, address, birthdate, mobile number and signatures for each contact where free commodities (needles/syringes, condoms) were distributed. Some projects attempted to use code numbers or names including codes for frequency of contact. Most outreach workers had their own informal notebooks from which they transferred data into official project books at home at the end of each day. These paper systems often involved serious breaches of client confidentiality and gave supervisory staff false confidence in the system's protection against service contact fraud and diversion of commodities.

The data collected by outreach workers were transferred to summary sheets at the district level, and both the number of contacts and of individuals were collated for provincial reports. There was no system to avoid double counting of individuals by different outreach workers or services, or for the accurate collating of total monthly individuals reached. The summary outreach data were usually collated on paper at each Provincial AIDS Center (PAC) from the district reports, for hardcopy transmission to Central Project Management Units in Ha Noi, as well as for entry into the Ministry of Health online HIV reporting system.

ACTION

Development of the Unique Identifier Code (UIC)

In 2008, Population Services International (PSI) in Viet Nam initiated development of a Unique Identifier Code (UIC) for their programmes with PWID and SW in Viet Nam.^{5,6} PSI undertook a test of several proposed UICs on large databases of names in university lists (>4000 student names in two cities) to identify the sequence of likely initials and numbers able to be generated from an individual's family name, location and age that could generate a de-identifying code with low duplication rates (less than 2.5% for example).

The aim of the search for such a unique identifier was to find a code that could be generated consistently by clients which would preserve their confidentiality and protect their privacy, yet which contained some data useful for client contact analysis (such as age and gender) and which could readily be standardized across several client services. The use of UIC would enable removal of double-counted clients and creation of more accurate coverage numerators.

Of the codes tested by PSI, a nine-digit easily self-generated code using letters and numbers was identified with a duplication rate of less than 1.5% in all cities and 0.9% overall. In collaboration with several development partners and the Viet Nam Authority of HIV/AIDS Control this code was refined to 10 digits incorporating the standard Ministry of Health three-letter code for each of the 63 provinces. The UIC could be collected over time as familiarity and trust developed; initially a nickname was used by the outreach worker.

The final field-tested code agreed as the national standard contains:

- (1) the first two letters of the father's familiar or common name;
- (2) the first two letters of the mother's familiar or common name;
- (3) the three letter code for the province of birth;
- (4) a code for identified gender (M = 1, F = 2); and
- (5) the last two digits of the year of birth.

Development of the databook

In a parallel process, a standardized data collection tool for the outreach workers (the databook) was developed. This process began with the collection and analysis of many outreach data collection tools from across the country and region. It was agreed that the new tool should be pocket-sized; be able to track at least 40 individual clients; require a minimum of written pen strokes to record each contact; and facilitate monitoring of outreach worker client workloads, service coverage and service intensity.

The initial versions of the databook were based on small handbooks used in a small number of provinces

every week, the outreach workers could easily total the commodities they distributed and activities conducted in the summary pages. For ease of supervision, the book provides at a glance an accurate measure of individuals contacted each month plus a good impression of intensity and nature of client contacts.

Although the databook may seem wasteful of paper or space, the benefits of ease of use, clarity, speed and accuracy, and the avoidance of the transcription of data burden generously outweigh this downside. The databook requires 12 books per year per outreach worker and therefore the programme cost is dependent on the quality of paper (12 A4 pages per book) and the size of print runs.

Post-implementation supervision of the outreach team leaders and workers has been used to ensure consistent recording detail and appropriate and accurate recording of UIC and service content. The databook has been readily used by low literacy peer outreach workers. It is fortunate that the ability to write letters and numbers is near universal in Viet Nam, which allows for easy recording of codes by peer outreach workers. There may be difficulties in less literate sub-populations.

Comprehensive training modules have been developed for use of UIC and the databook. All trainings, usually lasting one day, have been conducted in Vietnamese with systematic use of group discussion, examples and paper exercises. The databook, in a variety of (minimally) locally adapted formats, and the standardized UIC has now been adopted by two large donor-funded harm reduction projects, and are now progressively being used by outreach workers in more than 40 of the 63 provinces in Viet Nam.

During the expanded trial in Hai Phong there was considerable interest expressed by programme managers from other provinces for national propagation of these tools for their ease of documenting peer outreach to PWID, SW and MSM, and the distribution of commodities.

The software to manage the wealth of data collected by the outreach workers is also slowly being rolled out, yet programme managers can, using the databook, UIC and a simple spreadsheet, generate accurate client service data and low technology client lists to remove double counting.

DISCUSSION

This suite of tools for effective management and documentation of peer outreach client contacts in Viet Nam is, to our knowledge, the first example of the combination of confidential UIC and an innovative, inexpensive pocket-sized paper instrument with associated customized data-entry software for documenting outreach.

Initial reservations about obtaining UIC information from key affected populations, limited literacy of the peer outreach workers and coding difficulties have been overcome by the extremely hands-on nature of the training process and the follow-up supervision that emphasizes techniques for stepwise collection of UIC over time. Collection of the complete UIC was consistently more difficult from more mobile venue-based SW than other client groups.

In a new country context, rigorous testing of a proposed UIC using a large, detailed database of names will be necessary to ensure that the duplication rate of the code remains low (recommended less than 5%) with the training tailored to the local situation and literacy.

Conflicts of interests

None declared.

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An online framework for introducing STI point-of-care tests in Pacific island countries and areas

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Sexually transmitted infections (STIs) are an important public health issue in Pacific island countries and areas. Diagnosis is challenging, often requiring laboratory facilities and technical expertise rarely available. Patients seldom have results before they leave the health facility, with management primarily based on symptoms. As the delay between testing and treatment increases, so does the potential for complications of infection for the individual, the likelihood of STI transmission to other sexual partners and the chance the client will not return for follow-up. Effective tests that can be used at the point of care (POC) can conceivably overcome these consequences of delayed diagnosis. Such tests for STIs are becoming more available and affordable, with the potential to improve STI control.¹ However, the introduction of POC tests is complex,² requiring consideration of a range of implications to operationalize testing successfully and minimize potential harms.

The Burnet Institute was funded by the Secretariat of the Pacific Community to support ministries of health in the region to explore ways to integrate POC testing into existing STI management and control strategies. A participatory consultation process was undertaken with members of the Pacific Regional STI Working Group, selected ministry of health representatives and regional experts to develop an online 'toolkit' to provide a framework for health managers to critically appraise the suitability of POC testing for STIs in their country, to ensure a smooth introduction of the test if deemed appropriate, and to minimize harms. While there are several resources that describe these aspects in detail,³⁻⁵ they are often focused on a specific infection with formatting that precludes easy use by health managers in the Pacific.

The web-based framework consists of three sections that can be read as sequential steps or referred to individually as needed. This structure means that those seeking to review, strengthen or change their existing approach to STI testing may also find the toolkit useful. Section 1, Initial Assessment, provides advice on how to weigh the benefits and costs of introducing an STI POC test. It also includes background information on key definitions and technical concepts. Section 2, Piloting the STI POC Test, outlines the steps in preparing for and implementing a pilot test to determine how well the POC test performs in the local setting. This is an important stage before wider introduction of a POC test. Section 3, Scaling Up, briefly discusses the principles of using the POC test on a wider scale. The toolkit also includes downloadable tools to help health managers with particular steps and links to relevant printed and organizational resources. The challenges and complexities of introducing STI POC tests are highlighted with snapshots of lessons learnt from the region.

The online toolkit will be road-tested later this year to ensure that language, content and usability match the needs of users in the Pacific. The toolkit will be revised following the trial, and hosted on the Burnet Institute web site. Those wishing to have an advanced look at the toolkit can contact the authors at the e-mail address listed above; feedback is welcome.

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Sex, gender and emerging infectious disease surveillance: a leptospirosis case study

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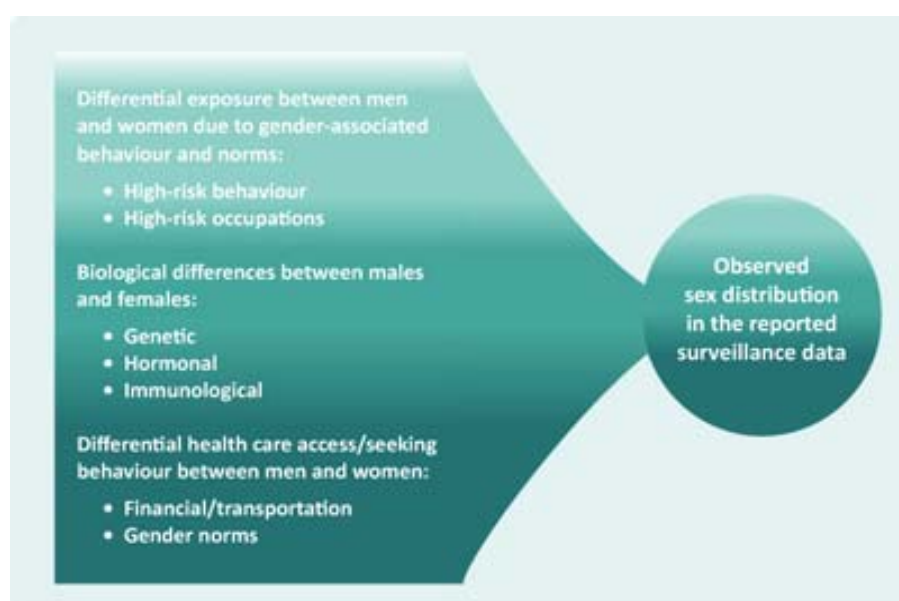
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Whatever the population, wherever the place, whenever the period, sex has been an essential demographic variable for surveillance. However, the distinction between “sex” and “gender” has not always been well understood or acknowledged by those of us engaged in public health surveillance. Sex refers to the biological and physiological factors that define males and females, while gender refers to socially constructed roles and attributes that a particular society considers appropriate for men and women.¹ While both sex and gender factors contribute to reported surveillance data, their full contributions are often not recognized. When such data are then used to ascertain sex/gender differential in disease risk without caution, the complete picture behind the observed distribution may be missed or misinterpreted. Using leptospirosis as a case example, we describe the importance of interpreting surveillance data with a

more gender-sensitive perspective, considering the various biological and social factors behind the reported numbers.

Leptospirosis is an emerging infectious disease with a high public health burden in the Asia Pacific region. Human infection is caused by the *Leptospira* bacteria and usually occurs through exposure to urine of an infected animal, contaminated water or soil. A commonly cited risk factor for the disease is male sex/gender,² and an excess of male leptospirosis cases observed in surveillance data is often ascribed to occupational/recreational exposures associated with male gender. However, it is often unknown how this observed distribution may be affected by sex differentials in disease severity or gender differentials in health care-seeking behaviour/access (Figure 1). These factors should be carefully considered when interpreting surveillance data.

Figure 1. Factors to consider when interpreting the observed sex distributions in reported surveillance data



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Traditionally, the excess of male leptospirosis cases observed in surveillance data has been explained through occupational/recreational exposures that put men in greater contact with leptospira-infected animals or contaminated water.^{1,3-5} For example, in the leptospirosis-endemic Philippines, from 1998 to 2001, among 840 clinically suspected seropositive cases, 87% of the cases were male and 70% were involved in outdoor activities, with 80% exposed to surface water or sewage. While there has been a considerable decrease in leptospirosis cases in Japan (attributed to occupational exposure control measures among rice-field workers), there continues to be an excess of male cases (16/20 cases reported from November 2003 to April 2005 were male), with the majority linked to male-dominated occupations (e.g. sewage work).⁵ Similar findings have been reported from New Zealand, where 774/878 (88%) reported cases from 1999 to 2008 were male and 72% of the cases were livestock workers or meat-processing workers.³

Recently, biological differences have been cited as a possible, alternative factor for the male excess in reported leptospirosis cases.^{6,7} Several European studies have found that, while the incidence of leptospirosis is higher in men, there is no sex difference in leptospirosis seroprevalence, indicating that there may be sex differentials in the clinical manifestation of leptospirosis.^{4,7} Indeed, a recent study from Germany found that male leptospirosis patients ($n = 263$), relative to their female counterparts ($n = 75$), had clinically more severe outcomes and higher case fatality (5% versus 1%, respectively) despite no significant differences in the type of exposure or time from onset of symptoms to treatment (4.5 days for both).⁷ In rural Lao People's Democratic Republic, while the proportion of persons engaged in agricultural work was found to be equal among males and females, leptospirosis seroprevalence was significantly higher among males (29%) than females (19%). When adjusted for previously reported risk factors for leptospirosis, such as barefoot walking and swimming, males were still significantly associated with higher seropositivity.⁸ In fact, there has been a growing recognition that biological differences between males and females based on genetic, immunological and hormonal factors may determine the susceptibility to disease and clinical outcomes.⁹ It is possible that females, when infected by leptospirosis (and all other things being equal), may have less severe sequelae than males, and surveillance data may be capturing the more

severe cases.⁷ In addition, a study conducted among leptospirosis patients in Sri Lanka revealed that male cases had significantly higher levels of leptospiremia than female cases (150 640 versus 5611 leptospira/mL, respectively).⁶

However, whether higher case numbers in males are due to a differential physiological response or to differentials in the dose received at the time of exposure, remains difficult to determine. Even when both genders are exposed to occupational/recreational risk factors, males may be receiving a higher dose due to greater frequency and/or duration of exposure. For instance, a study in Italy hypothesized that, among men and women both exposed to animals and/or leisure activities, the higher seropositivity among men (49/107; 46%) relative to women (47/180; 26%) may have been due to women being more cautious when in contact with animals or at leisure, thus receiving a lower dose.⁴ Being familiar with such gender-associated norms or behaviours of the population under surveillance is thus important, given the limitations in exposure measurement.

Whether the observed male excess in leptospirosis surveillance data is due to differential exposure, severity or both remains debatable, but both point to male gender as the higher risk group. However, gender differences in health care access or health care-seeking behaviour should also be considered. As surveillance data reflect only those cases that seek health care, any difference between the genders in health care accessibility (e.g. men have better access due to transportation or for financial reasons) or health care-seeking behaviour (e.g. men seek health care more often than women) would directly affect the surveillance data. For example, while there is an excess of male leptospirosis cases reported from India, a pattern traditionally linked to their greater occupational exposure,¹⁰ India is also among the lowest ranked nations in terms of gender equity.¹¹ As some Indian women have a lack of education and the financial means to access and use health care,¹¹ female leptospirosis cases may be underestimated in these settings. For example, among 143 patients affected by a leptospirosis outbreak in Orissa, India, while men compared to women had a higher attack rate (6.8% versus 4.9%, respectively) and proportion of cases hospitalized (50% versus 40%, respectively), the case fatality rate was significantly lower in males than in females (2% versus 16%, respectively).¹² Conversely, in other settings, there may be lower health

care-seeking behaviour by men, such that the incidence among men may be underestimated.¹³

Interpretations based on observed sex/gender distributions from surveillance data require careful thought, as there are important implications for public health actions. If the male excess in leptospirosis cases can be validly attributed to their occupational/recreational exposures, focusing public health efforts on reducing those exposures would be important. If, on the other hand, males have a more severe clinical outcome post-infection, emphasizing early and proper treatment for men might be important. However, if access to health care by women is known to be a concern for the population, one should interpret the reported sex distribution being mindful of such context. We hope that adopting a more gender-sensitive approach will assist all of us in public health practice to interpret surveillance data thoughtfully and to be mindful of the possible gender-related context of the reported numbers. Public health responses that follow such careful interpretation could enhance the efficiency and effectiveness of our actions.

Conflicts of Interest

None declared.

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How can we fight against antimicrobial-resistant bacteria in the World Health Organization Western Pacific Region?

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The public health community is faced with the global challenge posed by antimicrobial-resistant bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum β -lactamases (ESBLs)-producing enterobacteriaceae.¹ The need to address this issue prompted the focus of World Health Day 2011, which was entitled “Antimicrobial resistance: no action today, no cure tomorrow.”

In today's world of international travel, the globalization of drug-resistant bacteria is a pressing issue for public health professionals. In the World Health Organization (WHO) Western Pacific Region, as well as other regions in the world, more and more new types of antimicrobial-resistant bacteria have come to the forefront. An important example is New Delhi Metallo- β -lactamase 1 (NDM-1)-carrying enterobacteriaceae, which attracted attention in Europe in 2010 as imported cases associated with health care contact in India and Bangladesh. Although some NDM-1 cases were reported from Australia and Japan,² no outbreaks were reported in the Western Pacific Region.

In this perspective article, we consider four focus areas for countries in the Western Pacific Region to consider when strategizing their response to antimicrobial resistant bacteria.

(1) Surveillance of resistant bacteria

There is no formal framework for collaboration among surveillance programmes on antimicrobial resistance worldwide.³ Some countries in the WHO Western Pacific Region have national surveillance systems (e.g. Japan and Hong Kong [China]). The WHO Western Pacific Regional Office conducted the Regional Programme

for Surveillance of antimicrobial resistance from 1990 to 2000 and has recently established a new Working Group which has identified surveillance of resistance as a regional priority.³ According to the WHO Western Pacific Regional Office website, it annually accumulates drug resistance data from 14 focal laboratories in 13 countries based on their surveillance systems;⁴ however, no data is published on its website at the moment.

Constructing a standardized surveillance system in the Region would provide useful data to monitor and assess the pattern and frequency of resistant bacteria. Each country should establish and strengthen its reference laboratory and national surveillance programme. Building up standard methods and quality analyses in laboratories by using quality assessment schemes is crucial to establish multi-laboratory networks. WHONET, a free database software for management and analysis of microbiology laboratory data, would allow some measures of standardization. The surveillance system in European countries (European Antimicrobial Resistance Surveillance Network [EARS-Net]) is a useful model to enhance the international surveillance network among countries in the Western Pacific Region. Such a network would assist countries, especially when dealing with cross-border outbreaks of resistant bacteria. The WHO South-East Asia and the Western Pacific Regional Offices are collaborating to build up standard laboratory methods and surveillance systems to monitor resistant bacteria in both regions.

(2) Basic research of resistant bacteria

Basic research of drug-resistant bacteria, such as identifying responsible genes and enzymes, is crucial to

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understanding the mechanism of antimicrobial resistance and transmission. Among gram-positive bacteria, clonal spreading of community-associated MRSA (CA-MRSA) is an important topic. *Staphylococcus aureus* is one of the leading causes of bacterial infection worldwide. CA-MRSA have a different genetic profile to that of health-care-associated MRSA (HA-MRSA), yet are more virulent and transmissible than HA-MRSA.⁵ CA-MRSA infections are epidemic in some countries including Asian countries.⁶ Molecular typing (e.g. multilocus sequence typing [MLST]) provides information on distribution patterns that may translate to transmission routes of MRSA in communities. For instance, a combination of epidemiological, bacteriological and molecular methods showed the transmission tree and support control measures of an animal-origin MRSA epidemic in the Netherlands.⁷ Among gram-negative bacteria, ESBL-producing enterobacteriaceae is a pressing topic in the Western Pacific Region.⁸ The mechanisms of carbapenem resistance in enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are also receiving attention. Our group is trying to determine the distribution pattern of carbapenem-resistant *Acinetobacter baumannii* by using MLST.⁹

(3) Appropriate use of antimicrobials

Overuse and misuse of antimicrobials are considered to be major causes of the increase of drug-resistant bacteria.¹ Antimicrobial stewardship is a key component of a multifaceted approach to prevent emergence of antimicrobial resistance. Antimicrobial stewardship includes optimizing antimicrobial selection, dosing, routes and duration of therapy as well as limiting inappropriate antimicrobial use.

Detecting trends of antimicrobial consumption is necessary to estimate resistant selective pressure and enhance antimicrobial management in hospitals and communities. Antimicrobial usage is one of the major intervention points on antimicrobial resistance issues. Although there is no comprehensive surveillance systems of antimicrobial consumption in the Western Pacific Region, the European Surveillance of Antimicrobial Consumption (ESAC) collects data from either distribution or reimbursement systems in each country.¹⁰ A combination of surveillance of resistance and antimicrobials in the Western Pacific Region would be helpful to evaluate the association between antimicrobial usage and the trend of resistance.

Non-prescription antimicrobial use is frequent in some countries, especially in developing countries, and is considered a cause of antimicrobial resistance. According to surveys from Asian countries including China, the Philippines and Viet Nam, more than half of antimicrobials used were non-prescribed drugs.¹¹ There is also great concern about the poor quality of antimicrobials mostly in developing countries. Counterfeit, substandard or degraded antimicrobials are likely to worsen drug-resistance. Although counterfeit drugs with no active ingredient will not select drug resistant bacteria, those containing the wrong active ingredients with antibacterial effects may affect the emergence and spread of drug-resistant bacteria.

Antimicrobial use in livestock and fishery industries are also considered to have a potential impact on resistant bacteria among humans. Fluoroquinolone-resistant *Campylobacter* species in humans, for instance, are associated with fluoroquinolone use in poultry.¹² It is important to follow the harmful effect of these kinds of irregular antimicrobial uses on resistant bacteria. Tackling antimicrobial resistance requires an intersectional approach with effective coordination of action and an exchange of information among food, veterinary and health sectors in each country and relevant international organizations. Enhancement of collaboration between veterinary and human medicine would accelerate interdisciplinary and international action.

(4) Infection prevention and control practices

Basic infection prevention and control practices are essential to prevent the spread of drug-resistant bacteria in medical facilities. Standard precautions, including basic hand hygiene with soap and water or alcohol, are the most basic practices in the care of all patients. Contact precautions are recommended in the care of patients with antimicrobial resistant bacteria.¹³ Although these are crucial in both developed and developing countries, the risk of health care-associated infections seems to be higher in developing countries. Medical systems in developing countries are not always advanced enough to implement sufficient infection control practices.

WHO has published guidelines on hand hygiene in health care settings, how to organize training programmes and how to establish good practices among health care workers.¹⁴ The WHO Western Pacific Regional Office can

work with countries to step up their skills and resources to protect patients in medical facilities and provide appropriate support.

Each country in the Western Pacific Region should act now to prevent the increase and spread of antimicrobial resistant bacteria. WHO should provide support for national and cross-border actions in the Western Pacific Region. Now is the time to develop a comprehensive strategy using the four focus areas of this perspective article to effectively combat antimicrobial resistance.

Conflicts of interest

None declared.

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Analysis of fatal outcomes from influenza A(H1N1)pdm09 in Mongolia

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Introduction: While influenza A(H1N1)pdm09 usually causes mild illness in the majority of people, there have been reports of severe cases and deaths. As there is no documented evidence on fatal outcomes from influenza in Mongolia previously, we aimed to describe the epidemiology of fatal influenza A(H1N1)pdm09 cases to provide recommendations to assist the national influenza prevention and control strategy.

Methods: We selected influenza A(H1N1)pdm09-confirmed deaths in hospitals between 12 October 2009 and 31 January 2010 in Mongolia from the national influenza surveillance system. The mortality rate and case fatality rate (CFR) of influenza A(H1N1)pdm09-hospitalized deaths were calculated. Using country prevalence of pregnancy and chronic diseases, we calculated the relative risk of death from influenza A(H1N1)pdm09.

Results: There were 29 deaths with a mortality rate of 1.0 per 100 000 population during the study period, which was highest in children under five and the middle-aged population. Crude CFR was 2.2%. Of all fatal cases, 62% had at least one underlying condition. Most (62%) were provided antivirals, although none received these within 48 hours of symptom onset. Prevalence for pregnancy, cardiovascular and chronic liver diseases was five to 50 times higher in fatal cases compared to country prevalence.

Discussion: Mortality and crude CFR in our study was higher than in other studies. However, due to the diagnostic policy change during the epidemic, this estimate is likely to have overestimated actual case fatalities. Pregnancy, cardiovascular and chronic liver diseases were suggestive risk factors for death from influenza A(H1N1)pdm09. Strengthening hospital-based influenza surveillance is important in predicting severity of an epidemic and responding to influenza epidemics in a timely and appropriate manner.

Influenza A(H1N1)pdm09 emerged in Mexico and the United States of America in April 2009 and spread globally, affecting many countries of the world in 2009 to 2010. Although, the majority of people with influenza A(H1N1)pdm09 experienced mild illness,^{1,2} there were severe cases and even deaths. The efforts devoted to understanding the severity and impact of this novel influenza virus have demonstrated a generally low case fatality rate (CFR).³⁻⁵ Pregnant women and people with underlying medical conditions are known to be at increased risk of severe and sometimes fatal illness.¹

After the first case of influenza A(H1N1)pdm09 was identified on 12 October 2009 in Mongolia the epidemic peaked in November 2009, then cases gradually decreased below surveillance threshold starting the third week of 2010.⁶⁻⁸ There is no previously documented evidence on fatal outcomes from influenza in Mongolia. Analysing influenza fatal outcomes is important in understanding the severity and impact of influenza

and guiding prevention and control strategies. Thus, we aimed to describe the epidemiological and clinical characteristics of influenza A(H1N1)pdm09 fatal cases in Mongolia.

METHODS

Study design

We conducted a descriptive epidemiological study of laboratory-confirmed influenza A(H1N1)pdm09 cases reported through the national influenza surveillance system who died in hospitals between 12 October 2009 and 31 January 2010 in Mongolia. We excluded deaths reported to the surveillance system that occurred outside of hospitals due to the unavailability of case data. We selected this study period because the first confirmed A(H1N1)pdm09 case was reported on 12 October 2009 and the epidemic continued until the third week of 2010.

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National influenza surveillance is conducted in Mongolia throughout the year at over 150 designated sentinel influenza-like illness (ILI) surveillance sites across the country. Category-I surveillance sites include family group practices and district hospitals in the capital city and seven other population-dense and border provinces, as well as the Mother and Child Health Center and the National Center for Communicable Diseases in the capital city. ILI cases are reported daily and nasopharyngeal samples for virological analysis are collected from the cases. The number of samples collected depends on the outbreak or epidemic.

Category-II sites include family group practices and general hospitals in seven low population-dense provinces, two border point villages and two villages with over 10 000 population, as well as two tertiary hospitals and the National Cancer Center in the capital city. ILI cases are reported weekly and samples for virological testing are only collected when there is a suspected cluster of cases. Category-III surveillance sites include family group practices and province general hospitals of seven additional provinces that report ILI cases weekly.

An ILI case in the surveillance system is defined as a person with sudden onset of fever over 38 °C and cough or sore throat in the absence of other syndromic diagnoses. Data including detailed residence address, onset of illness, name of health care organization, date of presentation to health care, laboratory confirmation status and identified virus subtype are collected from each ILI case.

After the first laboratory-confirmed influenza A(H1N1)pdm09 case on 12 October 2009 in Mongolia, nasopharyngeal swabs were collected from all persons presenting to health care with an ILI. The swabs were sent to the virology laboratory of the National Center for Communicable Diseases for confirmation by real-time reverse transcription polymerase chain reaction (RT-PCR) using primers, probes and protocols supplied by the US Centers for Disease Control and Prevention.⁷ However, due to the rapid increase in the number of reported ILI cases within three weeks and the diagnostic capacity of the virology laboratory, the Ministry of Health changed the virologic diagnosis strategy to restrict laboratory testing to persons at risk for complications (pregnant women, young children with severe acute respiratory infection and people with chronic conditions).

Data collection and analysis

For the influenza A(H1N1)pdm09 deaths reported through the national influenza surveillance system, we retrospectively collected additional data by reviewing medical files using a pre-developed questionnaire. For each case, we collected socio-demographic data including education, employment, body weight and height, tobacco and alcohol use and clinical course of illness including signs, onset of illness, complications during the course of illness, underlying medical conditions and whether treated with antiviral medications.

The 2009 mid-term population data for age, sex and social variables including living areas, different household settings and employment were obtained from the National Statistics Office of Mongolia to calculate the population-based mortality rate of influenza A(H1N1)pdm09, defined as the number of fatal cases per 100 000 population during the study period.

As data on risk factors for non-fatal cases were not available, relative risks comparing fatal to non-fatal cases were unable to be calculated. Instead we compared the risk factors of the fatal cases to reported country prevalence data. Country prevalence data on smoking and alcohol use was obtained from the Mongolian STEPS Survey on the Prevalence of Non-communicable Disease Risk Factors – 2009,⁹ and the country prevalence of pregnancy and chronic diseases were obtained from monthly morbidity and mortality reports for September 2009 through February 2010 from the Health Department of Mongolia. Body mass index (BMI) was calculated from available height and weight data as body weight in kilograms divided by the square of height in metres.

All analyses were performed using EpiInfo 3.5.2. We compared the prevalence of tobacco use, alcohol drinking and BMI between the fatal cases and population prevalence using chi-squared tests. For pregnancy, cardiovascular diseases and chronic liver diseases, we calculated a prevalence risk ratio (RR) (with 95% confidence interval [CI]) by dividing the proportion of these conditions in the fatal cases to that in the general population.

As laboratory testing was restricted to high-risk persons after three weeks, the total number of cases was unknown. Therefore, the CFR was calculated by dividing

hospitalized deaths into all laboratory-confirmed cases for each study month, and reported as a percentage.

Ethics clearance was not required as our study was part of an emergency response to outbreak.

RESULTS

There were 1322 laboratory-confirmed cases including 29 confirmed fatal illnesses reported to the national influenza surveillance system between 12 October 2009 and 31 January 2010. Overall mortality rate was 1.0 per 100 000 population for this period. Crude case fatality rate (CFR) was 2.2%, ranging from 0.6% to 6.1% for the study months (Figure 1).

Demographic characteristics

Median age of fatal cases was 35, ranging from five months to 61 years. Population-based mortality rate was greatest in children under five (2.3 per 100 000 population), followed by persons aged 45–59 (1.7 per 100 000 population). Significant differences in mortality rates between females and males was not observed ($P = 0.4$) (Figure 1).

Although the highest mortality rate was in rural residents (1.5 per 100 000 population) followed by

urban residents (1.0 per 100 000) and provincial centres (0.3 per 100 000), a significant difference was not observed in mortality rates by geographical location ($P = 0.06$). When mortality rates per household types were compared, although traditional households had a rate of 1.4 per 100 000 compared to non-traditional households (0.7 per 100 000), a significant difference was not observed ($P = 0.07$). Of the 20 cases appropriate for the analysis of employment status (excluding children, soldiers, students and retired people), being unemployed had the highest and statistically significant ($P \leq 0.05$) mortality rate (12.0 per 100 000) over the employed group (0.8 per 100 000) (Table 1).

Clinical information

All cases (100%) presented with fever, as per the case definition, followed by cough (89.7%) and shortness of breath (65.5%), while the least common symptoms were sore throat (10.3%), diarrhoea (6.9%) and vomiting (6.9%). No cases manifested signs such as skin rash and sneezing.

All cases had medical complications, with pneumonia diagnosed in 27 (93.1%) and Acute Respiratory Distress Syndrome (ARDS) in 15 (57.1%) cases (Table 2).

Figure 1. Laboratory-confirmed cases and CFR of influenza A(H1N1)pdm2009 in Mongolia, 12 October 2009 – 31 January 2010

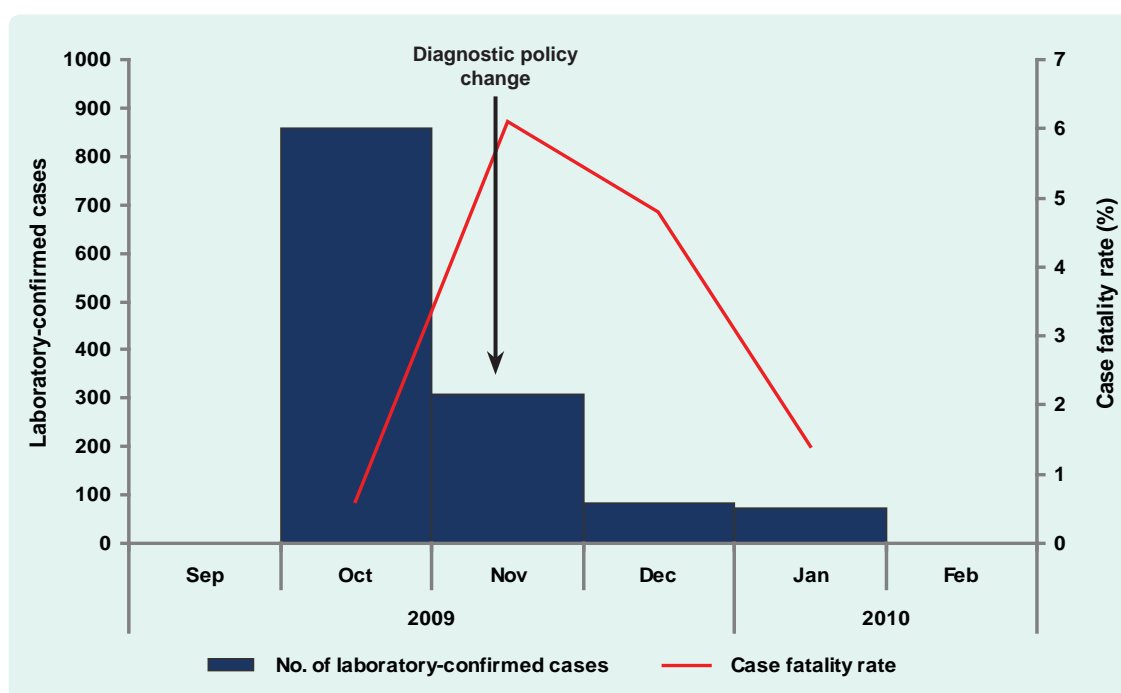


Table 1. Demographic characteristics and mortality rates from fatal cases of influenza A(H1N1)pdm09, Mongolia, October 2009 to January 2010

Variables	Cases		Mortality rate per 100 000	P-value
	n	%		
Age group				
Below 5 years old	6	20.7	2.3	
5–24	4	13.8	0.4	
25–44	12	41.4	1.4	
45–59	6	20.7	1.7	
60 years old and above	1	3.4	0.6	
Sex				
Male	12	41.4	0.9	0.40
Female	17	58.6	1.2	
Geographical location				
Urban	11	37.9	1.0	0.06
Provincial centre	2	6.9	0.3	
Rural	16	55.2	1.5	
Household type				
Non-traditional	10	34.5	0.7	0.07
Traditional*	19	65.5	1.4	
Employment				
Employed	8	27.6	0.8	< 0.05
Unemployed	12	41.4	12.0	
Other (children, soldier, student, retired)	9	31.0	-	
Education				
Primary & secondary school education	12	41.4	-	-
College	6	20.7	-	
University	5	17.2	-	
Children	6	20.7	-	

* Ger is the traditional household, which is a portable, felt-covered, wood lattice-framed dwelling, traditionally used by nomads in Mongolia. Most rural Mongolians and some parts of the population in the capital city still live in this traditional dwelling.

The median interval from symptom onset to initial presentation to health care was three days (range: 0–14 days) and cases were hospitalized for a mean of five days (range: 0–20 days) after symptom onset. Median time between onset of symptom and death was 9.5 days (2–25 days). In 18 cases (62.1%) Oseltamivir (Tamiflu) was given orally, but none of the cases received antiviral medication within the recommended 48 hours of symptom onset.

Comparison to population prevalence

Of the 21 cases for which data for analysis of tobacco and alcohol use was available, there was no significant difference for the prevalence of smoking (23.8% compared to 27.5%, $P = 0.7$) or alcohol drinking (28.6% compared with 38.6%, $P = 0.3$) between the fatal cases of influenza A(H1N1)pdm09 and the country prevalence.

Height and weight measures were available for 11 cases, of which 45.4% had an overweight BMI and

18.2% an obese BMI. This did not significantly differ from that of the Mongolian population at 27.3%⁹ and 12.5%,⁹ respectively ($P = 0.2$ and $P = 0.6$).

Of the cases, 62.1% had at least one underlying medical condition, with the most prevalent being cardiovascular diseases (CVDs) (24.1%), pregnancy (24.1%) and chronic liver diseases (17.2%) (Table 2). The prevalence risk ratio for CVDs was 5.6 (95% CI: 2.4–13.2), for pregnancy it was 50.4 (95% CI: 21.5–118) and for chronic liver diseases it was 14.3 (95% CI: 5.5–37.5) times higher than the prevalence in the population.

DISCUSSION

The overall mortality rate from influenza A(H1N1)pdm09 in Mongolia between 12 October 2009 and 31 January 2010 was 1.0 per 100 000 population. This is higher than the result from other countries such as 0.7 per million population in Viet Nam¹⁰ and 0.7 per million population in Japan.¹¹

Table 2. Symptoms, complications and underlying medical conditions of fatal cases of influenza A(H1N1)pdm09, Mongolia, October 2009 to January 2010 (n=29)

Signs and symptoms	Cases	%
Fever	29	100.0
Cough	26	89.7
Chest pain	8	27.6
Shortness of breath	19	65.5
General malaise	19	65.5
Myalgia	7	24.1
Headache	5	17.2
Sore throat	3	10.3
Diarrhoea	2	6.9
Vomiting	2	6.9
Runny nose	2	6.9
Others (nose bleeding, confusion, chills, skin rash, sneezing)	6	20.6
Complications	29	100.0
Pneumonia	27	93.1
ARDS	15	51.7
Disseminated intravascular coagulation	2	6.9
Liver dysfunction	6	20.7
Renal insufficiency	1	3.4
At least one underlying medical condition	18	62.1
Cardiovascular disease	7	24.1
Pregnancy	7	24.1
Chronic liver disease	5	17.2
Blood system disorder	3	10.3
Other conditions*	3	10.3
Chronic lung disease	2	6.9
Allergy	1	3.4

* Post surgery, multi-organ anomaly and low birth weight with rachitis

The mortality rate for influenza A(H1N1)pdm09 by age group in our study was highest in children under five followed by persons aged 45–59. Similar findings were observed in other studies. Result from a study in Japan indicated that severe complications were common in children under five and persons over 30 years of age.¹¹ A study in Germany observed a considerable number of severe cases of pandemic influenza among children.¹² The median age of patients who died in our study was 35, which is compatible to the age of fatal cases in other countries. The median age of patients who died in Viet Nam was 29 years,¹⁰ in England it was 39³ and a study in South Africa documented the median age of patients who died as 33 years.¹³

Of all deaths, 62% had at least one underlying medical condition, consistent with the 78% and 64% reported by Viet Nam¹⁰ and England.⁴ We found that

pregnancy, chronic cardiovascular diseases and chronic liver diseases were the most prevalent underlying medical conditions of those who died from influenza A(H1N1)pdm09. Death in people with these conditions increased by five to 50 times compared to the prevalence of these conditions in the general population. A study in the United Kingdom observed that pregnant women were over-represented among fatal cases compared with the general population and were at increased risk of death.^{2,3} Rapid deterioration and death among pregnant women have also been documented in other countries including the United States of America and South Africa.^{13,14} More than half of those who died in our study had received antiviral medications, but none received them within the recommended 48 hours after onset of symptoms. Other studies also observed delayed antiviral use in most severe and fatal cases.^{4,13}

Our study had several limitations. Data on hospitalized cases were not complete and were often missing information on the onset of disease and treatment aspects including specific timing and dosage of medication. Due to the diagnostic policy change to restrict virological testing to people at higher risk of complication, the denominator of laboratory-confirmed cases was underrepresented. This is reflected in the higher mortality and CFR in our study compared to the generally lower CFR observed in other studies^{3,10,11} and in northern hemisphere countries.¹² In addition, we calculated CFR crudely using confirmed deaths as the numerator and laboratory-confirmed cases as the denominator, so this is likely to overestimate the actual CFR. Lastly, the number of deaths was very small in our analysis.

In spite of these limitations, our study demonstrated the highest mortality in younger children and middle-aged adult population, which is comparable to other findings in different settings. In addition, we found that pregnancy and chronic diseases were suggestive risk factors of death from influenza A(H1N1)pdm09 in Mongolia.

To respond to influenza epidemics quickly and appropriately, hospital-based influenza surveillance should be strengthened. Timely analysis and feedback of severe and fatal cases is important in predicting the severity of the epidemics, which is one of the shortcomings of the ILI surveillance system in Mongolia. A hospital-based influenza surveillance system that will capture

possible influenza-associated hospitalizations and deaths is useful for monitoring trends and characterizing severe influenza-related diseases. Additional data on high-risk groups, outcomes and effectiveness of treatment, intervention and deaths can be collected from hospitals included in surveillance during an epidemic/pandemic period. This information can provide evidence on many issues including priority groups for vaccine and antiviral treatment, hospital bed management and estimating the severity of an epidemic.

Conflicts of interest

None declared.

Funding

None.

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Respiratory virus laboratory pandemic planning and surveillance in central Viet Nam, 2008–2010

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Introduction: Laboratory capacity is needed in central Viet Nam to provide early warning to public health authorities of respiratory outbreaks of importance to human health, for example the outbreak of influenza A(H1N1) pandemic in 2009. Polymerase chain reaction (PCR) procedures established as part of a capacity-building process were used to conduct prospective respiratory surveillance in a region where few previous studies have been undertaken.

Methods: Between October 2008 and September 2010, nose and throat swabs from adults and children (approximately 20 per week) presenting with an acute respiratory illness to the Ninh Hoa General Hospital were collected. Same-day PCR testing and result reporting for 13 respiratory viruses were carried out by locally trained scientists.

Results: Of 2144 surveillance samples tested, 1235 (57.6%) were positive for at least one virus. The most common were influenza A strains (17.9%), with pandemic influenza A(H1N1) 2009 and seasonal H3N2 strain accounting for 52% and 43% of these, respectively. Other virus detections included: rhinovirus (12.4%), enterovirus (8.9%), influenza B (8.3%), adenovirus (5.3%), parainfluenza (4.7%), respiratory syncytial virus (RSV) (3.9%), human coronavirus (3.0%) and human metapneumovirus (0.3%). The detection rate was greatest in the 0–5 year age group. Viral co-infections were identified in 148 (6.9%) cases.

Discussion: The outbreak in 2009 of the influenza A(H1N1) pandemic strain provided a practical test of the laboratory's pandemic plan. This study shows that the availability of appropriate equipment and molecular-based testing can contribute to important individual and public health outcomes in geographical locations susceptible to emerging infections.

Acute viral respiratory infections are an important cause of morbidity and hospitalization in Viet Nam where social and demographic conditions appear to heighten the risk of outbreaks capable of causing widespread disease and mortality. In Viet Nam, human infections with avian influenza A(H5N1) virus have occurred since 2003¹ and cases of severe acute respiratory syndrome (SARS) occurred in 2004. The socio-demographic and clinical features relating to these infections in Viet Nam have been previously described.^{2–7} Although SARS has not re-appeared, sporadic cases of human infection with avian influenza viruses continue to occur. As of November 2011, Viet Nam has recorded the third highest number of avian influenza cases and second highest number of related deaths globally.⁵ More recently, the rapid spread of the influenza A(H1N1) pandemic 2009 strain (hereafter referred to as A[H1N1]pdm09) into Viet Nam resulted in many thousands of laboratory-confirmed cases and 58 associated deaths during the first epidemic

wave.⁸ Common non-influenza respiratory viruses are also important causes of significant acute respiratory infection in the country.^{9,10}

The primary aim of this study was to assist the Virology Laboratory at the Nha Trang Pasteur Institute (NTPI) to develop laboratory preparedness for respiratory virus outbreaks, including the detection of common respiratory viruses and avian influenza viruses. Such laboratory capacity would provide early warning to Vietnamese public health authorities of an outbreak of infection of importance to human health, knowledge of which could be passed on to other countries in the region, including Australia. A second aim was to use the established polymerase chain reaction (PCR) methods to test respiratory samples collected from patients attending a local general hospital as proof of principle that staff training and transfer of technology were adequate. The surveillance period coincided with the occurrence of A(H1N1)pdm09, thereby enabling a

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practical assessment of the laboratory capacity that had been developed.

METHODS

Setting and study population

Specimens were collected from patients attending the Ninh Hoa General Hospital in Khanh Hoa province in rural south-central Viet Nam. The provincial capital city, Nha Trang, is located on the south-eastern coast, 38 km from the hospital. The region has a tropical climate with average temperatures ranging between 27°C and 33°C across two seasons: a dry season from January through August and a wet season from September until the end of December. The district population was 241 173 in 2009. In the same year, the 200-bed hospital treated a total of 19 516 patients, 927 with suspected pneumonia and 1654 with upper respiratory tract illnesses. The choice of the NTPI as the participating laboratory in Viet Nam was made by the Viet Nam Ministry of Health because laboratory capacity existed in the north (Ha Noi) and south (Ho Chi Minh City) but was less developed in the central regions of the country. Support to NTPI involved transfer of test methods and purchase of equipment suitable for rapid throughput testing. The established procedure required testing by locally trained Vietnamese scientists immediately on receipt of the samples, and same-day reporting.

Specimen collection

Nose and throat swabs were collected from approximately 20 consenting patients each week between October 2008 and September 2010 inclusive. All patients had symptoms consistent with respiratory infection. Sample numbers were increased to approximately 40 per week during the outbreak of A(H1N1)pdm09. The swabs were pooled into 1.5ml of viral transport media, stored on-site at 4°C and then transported at 4°C twice weekly to NTPI where PCR testing for common respiratory viruses was performed on the day of arrival by local NTPI-employed scientists. During the 2009 outbreak, specimens not related to surveillance were also received at NTPI but were only tested for A(H1N1)pdm09. The presence of bacteria and other non-viral agents capable of causing respiratory symptoms was not sought in any samples. Surveillance samples were not collected during Vietnamese Lunar New Year occurring in January 2009 and February 2010.

Nucleic acid extraction and reverse transcription

Viral nucleic acid was extracted from 200µl of sample using a QIAextractor robot (Qiagen, Valencia, CA, USA) and Qiagen DX reagent packs. The elution volume was 70µl. To control for the nucleic acid extraction, reverse transcription and PCR amplification steps, a non-human RNA virus (bovine viral diarrhoea virus [BVDV]) was spiked at low copy number into each sample before nucleic acid extraction and amplified using BVDV-specific primers. Reverse transcription was performed on 10µl of extract using random hexamer priming as previously described.¹¹

Respiratory virus detection by PCR

Respiratory viruses were detected using multiplex PCR assays based on methods reported previously.^{11,12} The viruses detected were: influenza A, influenza B, parainfluenza virus (PIV) types 1, 2 and 3, respiratory syncytial virus (RSV), picornaviruses (rhinoviruses and enteroviruses), adenoviruses, human metapneumoviruses (hMPV), and human coronavirus (HCoV) types OC43, 229E and NL63. Modifications to the published methods involved replacement of subtype-specific (H1 and H3) primers with primers specific for the influenza A matrix gene and the addition of primers to enable HCoV-NL63 detection. The primer sequences targeting the influenza A virus matrix gene and HCoV-NL63 are shown in **Table 1**. Differentiation of rhinoviruses from enteroviruses involved testing of picornavirus-positive specimens in an enterovirus-specific nested PCR as follows: 2.5µl of cDNA was added to a final first-round mastermix volume of 40µl with primers ENTC and ENTD (**Table 1**). Subsequent cycling conditions were 95°C for three minutes followed by 35 cycles of 30 seconds at 95°C, 30 seconds at 53°C and 30 seconds at 72°C, with final extension of five minutes at 72°C. Two microlitres of first-round PCR product were then transferred to a second round mastermix containing second-round primers ENTB and ENTC. Second round amplification was for 25 cycles at the conditions described above. The final PCR product was analysed on an agarose gel stained with ethidium bromide.

Subtyping of influenza A strains

Subtyping of influenza A viruses detected before the emergence of A(H1N1)pdm09 was performed using

Table 1. Virus, gene target and sequences of primers and probes

Virus (Target gene)	Method	First round primer/probe sequence (5' → 3')	Second round primer sequence (5' → 3')
Influenza A (Matrix)	Multiplex nested RT-PCR	FAMF1: CAGAGACTTGARRATGTYTTTGC FAMR1: GGCAAGYGCACCRGYWGARTARCT	FAMF2: GACCRATCCTGTCACCTCTGACT FAMR2: AYYTCYTTGCCCATGGAATGT
HCoV-NL63 (1b replicase)	Multiplex nested RT-PCR	CORF1: CTAATAAGTTAGTWCCWGGTATG CORR1: CACTATAACACTCAACYCKRG	CORF2: GTCCTCCTGGTAGTGGWAARTC CORR2: CACAKARSGAATCAACAGCAG
Enterovirus (5' -UTR)	Multiplex hemi-nested RT-PCR	ENTD: STCACC GGATGGCCAATCC ENTC: GGCCCTGAATGCGGCTAAT	ENTB: ATTGTCACCATAAGCAGCCA ENTC: GGCCCTGAATGCGGCTAAT
Influenza A (Matrix)	Real-time multiplex PCR	FLAMF: MGAGGTCGAAACGTAYGTTCTCT FLAMR: GTCTTGTCTTTAGCCAYTCCATGA FLAMP: CCCCTCAAAGCCGA	
Bovine viral diarrhoea virus (5' UTR-protease)	Real-time multiplex PCR	BVDVF: TCAGCGAAGGCCGAAAAG BVDVR: TGCTACCCCTCCATTATGC BVDVP: VIC-CTAGCCATGCCCTTAGT	
A(H1N1)pdm09 (HA)	Real-time PCR	ASwiF: GGAAAGAAATGCTGGATCTGGTA ASwiR: ACCCTTGGGTGTCTGACAAGTT ASwiP: CAGTCCACGATTGCAAT	
Avian (H5) influenza A (HA)	Real-time PCR	H5F: TGGTATGGGTACCACCATAGCA H5R: GGCTCAAACCTGAGTGTTTCATT H5P: CTGCAGACAAAGART	

a hemi-nested gel-based assay. During the 2009 outbreak, all samples were tested in two separate assays, a real-time PCR assay incorporating influenza A virus matrix and BVDV primers and the respiratory multiplex assay.¹¹ A(H1N1)pdm09 was confirmed in influenza-positive samples using a real-time PCR assay incorporating specific primers. Samples testing negative for the pandemic strain were then tested for influenza A(H3N2) or seasonal influenza A(H1N1) as previously described.¹¹ Identification of avian influenza H5N1 used a real-time PCR (primers and probe sequences shown in Table 1). The final reaction volume was 20 µl with a thermal profile of 20 seconds at 95°C followed by 45 cycles of three seconds at 95°C and 30 seconds at 60°C.

RESULTS

Specimens and patients

A total of 2144 surveillance specimens collected from individual patients were tested, with one quarter of these cases admitted to a hospital ward (Table 2). During the A(H1N1)pdm09 outbreak in 2009, the laboratory also received 1541 specimens from patients attending hospitals other than Ninh Hoa for influenza virus testing only (these results are not included as part of the surveillance study). Surveillance patients ranged in age from 0.1 months to 85 years (mean 13 years; median seven years). The majority were children aged five years and under (45.1%). There were more males than females (55% versus 45% [Table 2]).

Influenza virus detections

Of the 2144 surveillance samples tested, 1235 (57.6%) were positive for at least one virus (Table 2). The most common were influenza strains, more than half of which were A(H1N1)pdm09, first detected at the end of the dry season in 2009, then persisting through the wet season in that year (Table 2, Figure 1). This virus replaced an epidemic of A(H3N2) that occurred throughout the dry season in 2009. The A(H3N2) strain reappeared in 2010, peaking at the end of the dry season. A(H1N1)pdm09 infected mainly children and young adults, in contrast to influenza A(H3N2) infections, which mainly occurred in children under five-years-old (Table 3). Two large influenza B epidemics occurred during the study, peaking in the wet seasons of 2008 and 2010 but also circulating at low levels during the dry season in both years. Seasonal A(H1N1) strains were rarely detected. There was a single detection of non-pathogenic H5N1 in a three-year-old child (Table 3). This child had no known contact with poultry or other birds, but lived within one kilometre of an ostrich farm.

Of the 1541 non-surveillance samples tested during June to December 2009 for the pandemic strain, 637 (41%) were positive.

Non-influenza virus detections

Picornaviruses were detected throughout the two years of surveillance although only rhinoviruses circulated continuously (Table 2, Figure 1). Two large enterovirus

Table 2. Patient demographics and viruses detected from subjects treated as outpatients or inpatients, Khanh Hoa Province, Viet Nam, October 2008 to September 2010

Characteristic	Total		Outpatients		Inpatients	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Number of patients	2144	100.0	1606	75.0	538	25.0
Males	1177	55.0	856	72.7	321	27.3
Females	967	45.0	750	77.6	217	22.4
Age range (years)						
0–5	966	45.1	750	46.7	216	40.1
6–10	335	15.6	255	15.9	80	14.9
11–15	235	11.0	144	9.0	92	17.1
16–25	210	9.8	137	8.5	73	13.6
26–45	247	11.5	191	11.9	56	10.4
46–65	115	5.4	97	6.0	18	3.3
≥66	35	1.6	32	2.0	3	0.6
Virus-positive	1235	57.6	931	57.9	304	56.5
Virus-negative	909	42.4	679	42.3	230	42.7
Co-infected samples	148	6.9	111	6.9	37	6.9
Viruses detected						
Influenza A	384	17.9	234	14.6	150	27.9
A(H1N1)pdm09	200	9.3	101	6.3	99	18.4
A(H1N1)	18	0.8	13	0.8	5	0.9
A(H3N2)	165	7.7	120	7.5	45	8.3
A(H5N1)	1	0.1	0	0.0	1	0.2
Rhinovirus	266	12.4	211	6.2	55	10.2
Enterovirus	191	8.9	149	9.3	42	7.8
Influenza B	178	8.3	156	9.7	22	4.1
Adenovirus	114	5.3	89	5.5	24	4.5
Parainfluenza*	101	4.7	85	5.3	16	3.0
RSV	83	3.9	61	3.8	22	4.1
HCoV [†]	64	3.0	53	3.3	11	2.0
hMPV	7	0.3	6	0.4	1	0.2

RSV - respiratory syncytial virus; HCoV - human coronavirus; and hMPV - human metapneumovirus.

* PIV-1 (53.5%), PIV-2 (13.9%), PIV-3 (26.7%), PIV-not typed (5.9%).

† HCoV-OC43 (72%), HCoV-229E (4.7%), HCoV-NL63 (23.4%).

outbreaks were mainly confined to the dry seasons in 2009 and 2010 (Figure 1). A similar age distribution was seen for both virus types (Table 3).

Several respiratory viruses were detected only rarely, including adenovirus (5.3% of the total number of

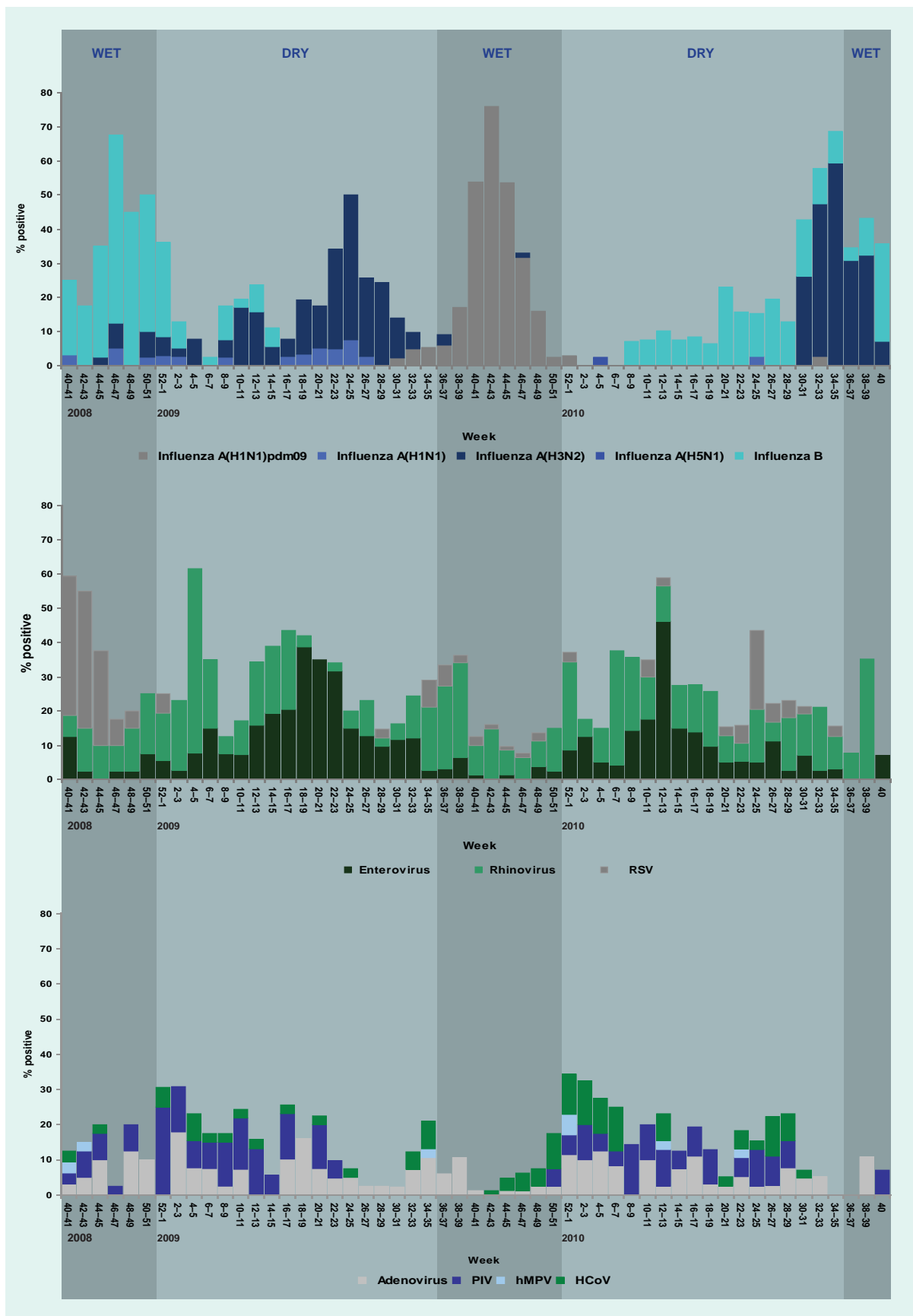
viruses detected), PIV (4.7%), RSV (3.9%), HCoV (3%) and hMPV (0.3%). Parainfluenza viruses, of which type 1 was the most common, circulated throughout both 2009 and 2010 (Table 2). RSV infections, which were not associated with an obvious seasonal distribution, occurred in the very young, adults of childbearing age

Table 3. Age group distribution of viruses detected in Khanh Hoa Province, Viet Nam, October 2008 to September 2010

Virus detected	Age groups (years)													
	0–5		6–10		11–15		16–25		26–45		46–65		≥ 66	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Positive cases	660	68.3	213	60.9	143	60.9	89	42.2	84	34.0	36	31.3	10	28.6
Co-infections	107	11.1	15	4.2	14	6.0	6	2.8	5	2.0	0	0.0	1	2.9
Negative cases	306	31.7	122	34.4	92	39.1	122	57.8	163	66.0	79	68.7	25	71.4
Influenza A	145	15.0	79	22.3	93	39.6	35	16.6	23	9.3	7	6.1	2	5.7
A(H1N1)pdm09	23	2.4	49	13.8	81	34.5	27	12.8	17	6.9	3	2.6	0	0.0
A(H1N1)	11	1.1	4	1.1	0	0.0	2	0.9	0	0.0	1	0.9	0	0.0
A(H3N2)	113	11.7	25	7.0	10	4.3	6	2.8	6	2.4	3	2.6	2	5.7
A(H5N1)	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Rhinovirus	140	14.5	33	9.3	27	11.5	22	10.4	31	12.6	10	8.7	3	8.6
Enterovirus	128	13.3	24	6.8	12	5.1	19	9.0	7	2.8	1	0.9	0	0.0
Influenza B	85	8.8	54	15.2	15	6.4	5	2.4	14	5.7	4	3.5	1	2.9
Adenovirus	93	9.6	10	2.8	3	0.0	4	1.9	1	0.4	2	1.7	1	2.9
Parainfluenza	69	7.1	20	5.6	3	1.3	3	1.4	2	0.8	3	2.6	1	2.9
RSV	66	6.8	4	1.1	2	0.9	2	0.9	5	2.0	2	1.7	2	5.7
HCoV	37	3.8	6	1.7	2	0.0	5	2.4	7	2.8	6	2.2	1	2.9
hMPV	6	0.6	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
Total	966		335		235		211		247		115		35	

RSV - respiratory syncytial virus; hMPV - human metapneumovirus; and HCoV - human coronavirus.

Figure 1. Fortnightly distribution and detection rates of respiratory viruses, Khanh Hoa Province, Viet Nam, October 2008 to September 2010



RSV - respiratory syncytial virus; PIV - parainfluenza virus; hMPV - human metapneumovirus; and HCoV - human coronavirus.

Table 4. Number and type of co-infections detected in 2144 samples tested, Khanh Hoa Province, Viet Nam, October 2008 to September 2010

	Flu B	ADV	RSV	EV	HRV	PIV	HCoV	hMPV	Flu B + RSV	EV + ADV	HRV + ADV
Flu A	1	1	1	5	23	2	2	0	0	1	0
Flu B		9	2	6	5	2	0	0	0	0	0
ADV			2	14	22	6	1	0	0	0	0
RSV				1	5	0	2	1	0	0	1
EV					0	4	6	1	0	0	0
HRV						9	7	1	1	0	0
PIV							1	1	0	0	0
HCoV								0	0	1	1

Flu A - influenza virus A; Flu B - influenza virus B; ADV - adenovirus; RSV - respiratory syncytial virus; EV - enterovirus; HRV - human rhinovirus; PIV - parainfluenza virus; HCoV - human coronavirus; and hMPV - human metapneumovirus.

and the elderly. HCoVs were also detected throughout the year across all age groups, albeit in low numbers. OC43 was the most common coronavirus, with a distribution that spanned the wet and dry seasons in 2008 through 2009 and 2009 through 2010 (Table 2, Figure 1).

There were 148 cases (6.9%) involving co-infection with at least two viruses (Table 4). Rhinoviruses (50.7% of all co-infections) and adenoviruses (39.9%) were most commonly involved.

DISCUSSION

The major aim of this study was to build permanent laboratory capacity that could provide early warning to public health authorities of an emerging epidemic of highly pathogenic avian influenza virus or other respiratory viruses. Over the two-year study period, 2144 samples were tested by locally trained Vietnamese scientists, with over half being positive for at least one virus. Viruses detected included influenza, most commonly A(H1N1)pdm09, as well as rhinovirus, enterovirus and adenovirus. The outbreak in 2009 of the influenza A(H1N1) pandemic strain provided an important opportunity for the laboratory to function under pandemic conditions, with an additional 1541 specimens received.

Two other studies of respiratory viruses have recently been undertaken in Viet Nam. Both involved hospitalized children living in either the central region where we conducted our investigation or in south Viet Nam.^{9,10} The study in the south was carried out over more than three years between 2004 and 2008, enabling the seasonal distribution of respiratory viruses

to be investigated. It revealed a similar pattern of circulation of influenza to that which we subsequently observed, with peaks occurring in the wet seasons and lower levels of circulation at other times. Although the study in south Viet Nam did not distinguish between the circulation of influenza A and B, our study showed that both virus types could be detected throughout the year and that conditions prevailing in the wet season favoured increased levels of circulation and infection.

The transmission of A(H1N1)pdm09 in central Viet Nam shared similarities and differences from that experienced in other geographical locations. In 2009 in Viet Nam, an established outbreak of A(H3N2) was quickly replaced by the pandemic virus, as observed in temperate climates including Australia, the United States of America and Europe.^{13–15} However, in contrast to the dominance of A(H1N1)pdm09 during subsequent winter influenza seasons in Australia in 2010 and Europe in 2010 and 2011,^{16,17} the pandemic virus only returned in very low numbers in and around Nha Trang in 2010. In the first post-pandemic influenza season in 2010, co-circulation of A(H3N2) and influenza type B was observed in this area of Viet Nam, more closely resembling influenza activity patterns observed in northern Asia, the United States of America and Canada.¹⁸

RSV and hMPV circulated only in the wet season in central Viet Nam, consistent with the previous study in the south of the country.¹⁰ In contrast, coronaviruses, rhinoviruses and adenoviruses circulated throughout the year. The adenoviruses were often associated with co-infections, making their clinical significance unclear. Parainfluenza virus circulation spanned wet and dry seasons.

Enteroviruses causing neurological disease,^{19,20} hand, foot and mouth disease and gastroenteritis have been reported in Viet Nam,^{19,21} but their association with respiratory syndromes has not been investigated. In our study, enterovirus circulation was restricted to the dry season in both study years. Identification of the enterovirus serotypes involved is currently being undertaken and is of interest since not all serotypes are thought to cause respiratory symptoms. A previous study involving hospitalized children in south Viet Nam also demonstrated the important role of enteroviruses in respiratory disease, but unlike our study did not fully reveal the role of rhinoviruses, probably because testing for type C rhinoviruses was not undertaken.¹⁰ In contrast, previous surveillance in Nha Trang revealed a significant number of cases attributable to rhinovirus infection but did not include testing that would most likely have indicated the importance of enteroviruses.⁹

A limitation of our study was that it was not primarily a clinical investigation and therefore we did not have access to detailed clinical information on the patients from whom specimens were collected. Hence, we can only make limited conclusions regarding the clinical impact of the viruses detected.

Overall only one quarter of patients from whom samples were obtained were admitted to a hospital ward. The exception was during the A(H1N1)pdm09 outbreak when more than half of the laboratory-confirmed cases were admitted. Following the first appearance of the pandemic strain in central Viet Nam, suspected cases appear to have been admitted as a precaution while information on the clinical severity of this novel strain was gathered over time.

Because our study involved both children and adults, in contrast to the two previously reported molecular-based studies in Viet Nam involving only children,^{9,10} we were able to show that the circulation and morbidity associated with common viruses such as influenza and less common viruses such as RSV, PIV and coronaviruses, had a wide age demographic. To some extent the intervention of A(H1N1)pdm09 hampered our efforts to comprehensively study the seasonality of respiratory viruses in this region of Viet Nam because the scale of the outbreak minimized the likelihood of detecting other circulating respiratory viruses. However, it did provide the opportunity for an assessment of a pandemic plan that had only been established in the

previous year. The detection of an influenza H5 virus, albeit a non-pathogenic strain, in a patient presenting with symptoms not suggestive of influenza infection, prompted an investigation of asymptomatic household contacts, each of whom returned negative results. During the 2009 influenza outbreak, locally trained medical, nursing and scientific personnel collected, transported and tested large numbers of specimens within a short turnaround time. Transfer of technology and the training of local scientists were the essential elements in this process. Our study shows that the availability of appropriate equipment and molecular-based diagnostic testing contributes to important individual and public health outcomes in geographical locations susceptible to emerging infections.

Conflicts of Interests

None declared.

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High-risk and multiple human papillomavirus infections among married women in Can Tho, Viet Nam

Lan Thi Hoang Vu*

Introduction: The two currently licensed human papillomavirus (HPV) vaccines are highly efficacious in preventing cervical pre-cancers related to HPV 6, 11, 16 and 18. Before implementing a large-scale HPV vaccine campaign in Viet Nam, information about the prevalence of infection with the HPV vaccine types is required. This study was done in Can Tho, the province with the highest prevalence of cervical cancer in the south of Viet Nam, to explore the distribution of other high-risk types of HPV among married women in this province.

Method: The study employed a cross-sectional design with multistage sampling. A total of 1000 participants were randomly selected, interviewed and given gynaecological examinations. HPV infection status and HPV genotyping test were completed for all participants.

Results: A broad spectrum of HPV types was reported in this study. The prevalence of cases infected with HPV 16 and/or 18 was 7%; the prevalence of cases infected with other high-risk HPV types was 6%. The highest prevalence for single and multiple infections, as well as for high-risk infections, was reported for the youngest age group (less than 30 years).

Discussion: While it is relevant to implement an HPV vaccine campaign in Viet Nam due to the high prevalence of infection with HPV 16 and/or 18, it is important to note that one can be infected with multiple types of HPV. Vaccination does not protect against all types of high-risk HPV. Future vaccine campaigns should openly disclose this information to women receiving vaccines.

Cancer of the cervix is the second most common cancer in women worldwide with about 500 000 new cases and 250 000 deaths each year.¹ Almost 80% of cases occur in low-income countries where cervical cancer is the most common cancer in women. Previous studies attributed the large decline of cervical cancer incidence in developed countries to their screening programmes and suggested that the high rate of cervical cancer mortality and morbidity in developing countries was due to ineffective or no screening programmes.² In 2010, Viet Nam had a total of 5644 cervical cancer cases (prevalence of 13.6 per 100 000 women).³

However, the prevalence rate in the south of Viet Nam is much higher, at about 26 per 100 000 women.^{3,4} The steadily increasing rate of this cancer in some provinces in the south has been observed in recent years. For instance, the crude rate of cervical cancer in Can Tho was only 15.7 per 100 000 in 2000 but increased to 25.7 per 100 000 in 2009.³

Studies have shown that infection with high-risk human papillomavirus (HPV) can lead to cervical cancer.^{5,6} Specifically, high-risk HPV types are detected in 99% of cervical cancers, and worldwide approximately 70% of cervical cancers are due to HPV types 16 and 18.⁷⁻¹⁰ In developed countries such as the United States of America, vaccines against HPV were recommended for routine use in females aged 11 to 12 years.¹¹ In Viet Nam, HPV vaccines have been offered since 2006. These vaccines are expensive for developing countries (US\$ 80 per dose with three doses required). These vaccines, however, prevent only four HPV types, two high-risk types (HPV 16, 18) and two low-risk types (HPV 6, 11).^{11,12}

Before implementing a large-scale HPV vaccine campaign in the south of Viet Nam, updated data on the prevalence and distribution of the vaccine types of HPV among women is required. During 2010 and 2011, a large-scale study was done in five provinces (Ha Noi, Ho Chi Minh City, Hue, Thai Nguyen and Can Tho) to

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explore the prevalence of HPV infection and its risk factors.^{13–15} The prevalence of cervical HPV infection ranged from 6.1% in Ha Noi to 10.2% in Can Tho. Most of the positive cases were infected with high-risk HPV, especially in Ha Noi and Can Tho where more than 90% positive cases were high-risk HPV. Furthermore, in Can Tho, more than 60% of women were infected with multiple HPV types.¹⁵

This study provides additional data to explore the distribution of HPV among married women in Can Tho in order to provide more detailed information for the cervical cancer prevention programme in this province.

METHOD

Study setting

Can Tho is located on the south bank of the Hau River, a major branch of the Mekong River. It is 169 km from Ho Chi Minh City, Viet Nam's largest city. Can Tho is the fourth largest city in Viet Nam and the biggest city in the Mekong Delta with an estimated population of 1 187 089. The majority of the population is living in urban areas (66%). The city is divided into nine districts and 85 communes. After 120 years of development, the city now is the delta's most important centre of economics, culture, science and technology.

Study population and enrolment

This study applied a cross-sectional design and multistage sampling as described elsewhere.^{13–15} The estimated sample size was 1050 women using a formula for sample size for a proportion estimate with relative precision with the following parameters: anticipated prevalence of HPV as 10%, relative precision of 0.25, design effect of 1.6 and estimated non-respondent rate of 10%. In the first stage, 21 communes were randomly selected from 85 communes in Can Tho. In the second stage, in each commune, 50 married women aged 18–65 were randomly selected from the list provided by the local women's union (this list contains the names of women currently living in the commune). Following an explanation about the objectives of the study, a written consent form for participation in the study was completed. The response rate was high (95.2%) and the final sample size was 1000 women. The main reason women declined to

participate was that they were uncomfortable with pelvic examination.

Information and specimen collection used the following steps. First, a personal interview was done to collect information on socio-demographic variables, obstetric/gynaecologic history and sexual lifestyle. After the interview, each participant was scheduled for a pelvic examination carried out by a gynaecologist. Samples of exfoliated cells from the ectocervix were collected with two wooden Ayre spatulas and were sent to the laboratory of the Viet Nam National Institute of Dermatology for HPV testing on the same day as the sample collections. The HPV genotyping protocol was described elsewhere.¹³ The protocol was reviewed and cleared by the Ha Noi School of Public Health Institutional Review Board (Ethical Approval Number 013/2010/YTCC-HD3).

Definition of infection with high-risk HPV types

High-risk HPV types are those that can cause cancer and include HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68 and 82. The low-risk group includes HPV 6, 11, 42, 43, 61, 70, 71 and 81. The current vaccines can prevent only high-risk types 16 and 18, and low-risk types 6 and 11. Infection with HPV 16/18 in this study refers to cases infected with either HPV 16 or HPV 18 or with both of these types.

RESULTS

Characteristics of population

Most women who participated in this study were aged from 30 to 49 years (64%). A total of 30 women (3%) reported a history of having been diagnosed with sexual transmitted diseases, with 5% reporting having more than two sexual partners within the last 24 months (**Table 1**).

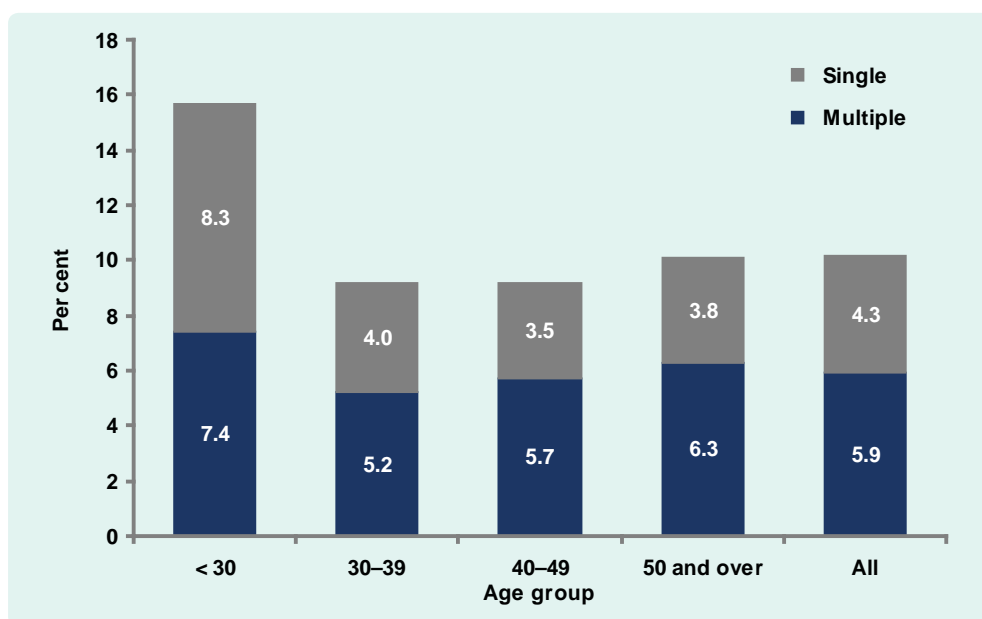
Single and multiple HPV infection

Most infected cases in this study had infections with multiple types of HPV, and this was shown for each age group (**Figure 1**). The prevalence of multiple HPV infection was highest among the youngest group at 7.4%. About 60% of the cases with multiple HPV infection were infected with more than two types of HPV;

Table 1. Demographical information of the study sample, Can Tho, Viet Nam, 2010–2011

Characteristics	Frequency	
	<i>n</i>	%
Age group	<30	121 12.1
	30–39	325 32.5
	40–49	318 31.8
	>50	237 23.7
Highest education attained	Primary	287 28.7
	Secondary	359 35.9
	High school	200 20.0
	Higher than high school	155 15.5
Occupation	Government officers	162 16.2
	Workers/handicraft	83 8.3
	Small trade	225 22.5
	Unemployed housewife/retired	334 33.4
	Other	197 19.7
History of sexual transmitted diseases	No	970 97.0
	Yes	30 3.0
Number of sexual partner within the last 24 months	1 sexual partner	950 95.0
	2 or more	50 5.0

Figure 1. Single and multiple HPV infection by age group, Can Tho, Viet Nam, 2010–2011



some cases were even infected with five or six different HPV types.

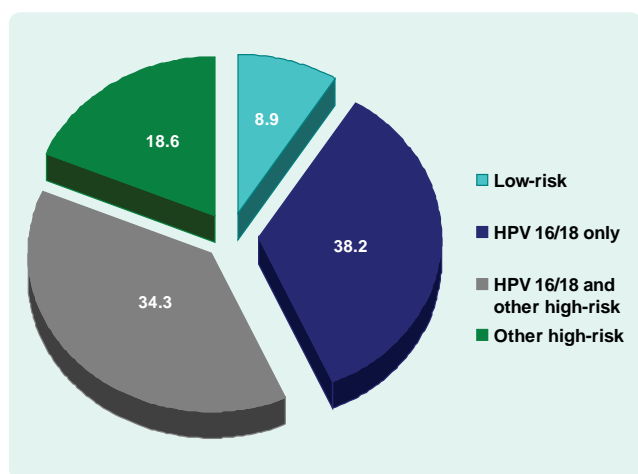
HPV16/18 and other high-risk HPV infections

In total, 73% of the positive cases were infected with HPV type 16/18; however, more than half of these cases were also positive with other high-risk types. More importantly, 19% of positive cases were not infected with HPV16/18 but with other high-risk types

(Figure 2). Overall, the prevalence of cases infected with HPV 16/18 was 7% and the prevalence of cases infected with other high-risk HPV types (including those infected with HPV 16/18 in addition to other high-risk infection types) was 6% (total 58 women).

In addition to HPV 16 and 18, there were 14 other high-risk HPV types identified in this study (Table 2). HPV 58 and HPV 52 were the most common of these high-risk types found in Can Tho,

Figure 2. Distribution of infection with HPV 16/18 and other HPV types, Can Tho, Viet Nam, 2010–2011



accounting for 22% and 13% of the positive cases, respectively.

Infection with high-risk/low-risk HPV by age group

Analysis by age group showed that (1) in all age groups, most cases were infected with high-risk HPV, which can lead to cancer; (2) the overall prevalence of HPV infection (i.e. including both low-risk/high-risk) was highest among the youngest group (i.e. less than

Table 2. Other types of high-risk HPV, Can Tho, Viet Nam, 2010–2011

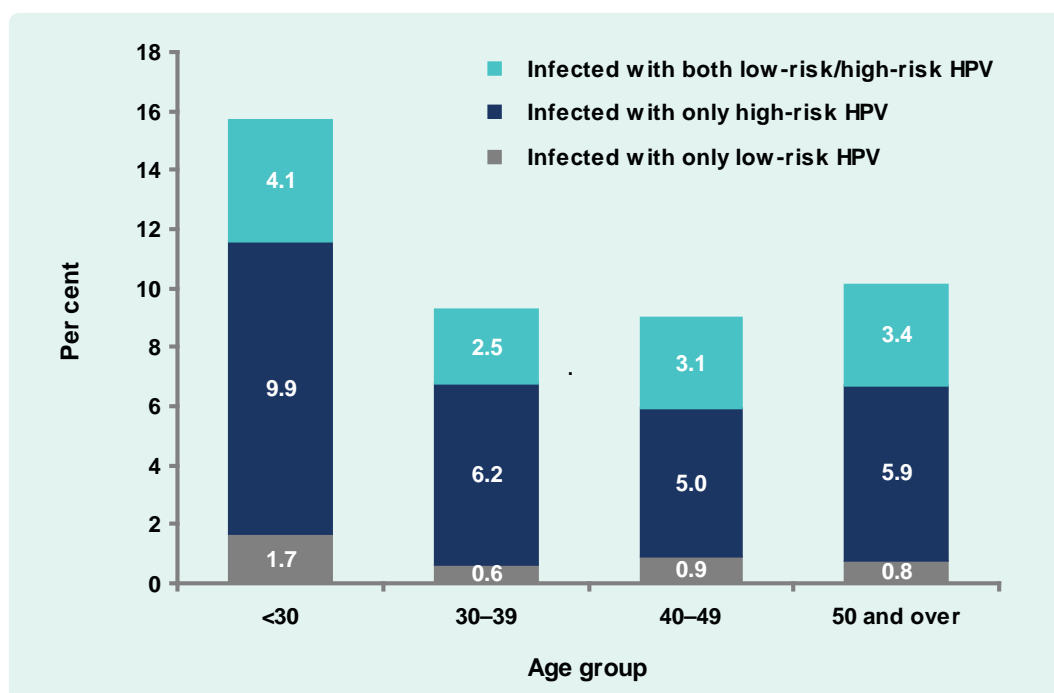
HPV type	Positive cases	% among positive	% among sample
HPV58	22	21.6	2.2
HPV52	13	12.7	1.3
HPV35	8	7.8	0.8
HPV45	6	5.9	0.6
HPV33	5	4.9	0.5
HPV31	3	2.9	0.3
HPV51	3	2.9	0.3
HPV56	3	2.9	0.3
HPV61	3	2.9	0.3
HPV53	2	1.9	0.2
HPV59	2	1.9	0.2
HPV62	2	1.9	0.2
HPV66	2	1.9	0.2
HPV68	2	1.9	0.2

30-years-old); and (3) the prevalence of infection with high-risk HPV was also highest among the youngest group (Figure 3).

DISCUSSION

A broad spectrum of HPV types was reported in this study. The prevalence of cases infected with HPV 16/18 was 7% and the prevalence of cases infected with other high-risk HPV types was 6%. The most common types of HPV infection were HPV 16 and 18, similar to

Figure 3. Single and multiple HPV infection by age group, Can Tho, Viet Nam, 2010–2011



previous studies in Viet Nam and other countries.^{16–18} HPV 58 was also found to be a common type among women in Can Tho, as reported in China, Thailand and The Philippines.⁶ The higher prevalence reported for Can Tho is consistent with the higher rate of cervical cancer in the southern compared to the northern provinces of Viet Nam. Previous studies had reported that the higher rate of cervical cancer in southern Viet Nam could be attributed to the ground combat militarization of South Viet Nam during the period 1955–1975.¹⁹

Similar to a previous study,¹⁴ the prevalence of overall HPV infection as well as the prevalence of high-risk HPV infection was highest among the youngest group (aged less than 30-years-old). This result demonstrates the increasing trend of HPV infection among the younger generation in Viet Nam as well as the need for effective cervical cancer programmes. A recent study suggested that the best control programme for cervical cancer in Viet Nam is to offer HPV vaccine to young girls and screening to older women. An 70% vaccination and screening coverage rate would reduce the lifetime risk of cancer by 20.4% to 76.1%.²⁰

Some health organizations in Viet Nam are considering two types of HPV vaccines licensed by the Food and Drug Administration (i.e. Cervarix made by GlaxoSmithKline and Gardasil made by Merck).¹² Cervarix protects against only HPV types 16 and 18, while Gardasil also protects against HPV types 6 and 11. It is important to note that one woman may be infected with multiple types of HPV at once. While 73% of the positive cases were infected with HPV 16/18, more than half of these were also infected with other high-risk HPV types that may also lead to cervical cancer and which cannot be prevented by currently available vaccines. Although it is relevant to implement an HPV vaccine campaign in Viet Nam due to the high prevalence of infection with HPV 16/18 in Can Tho, it is also important to inform the women who receive the vaccines that they are not protected against all high-risk HPV types and that they still need cervical cancer screening.

In developed countries, routine Pap smear and HPV tests are recommended for screening for cervical cancer. The Pap test is a method of examining cells from the cervix and is suggested every one to two years for most women aged 21 to 29 and every two to three years for most women aged 30 or older. For women

aged 30 or over, HPV tests can be done in addition to Pap smear tests.²¹ As with other developing countries, Viet Nam has not yet established a national policy and guidelines on cervical cancer screening.

Strict protocols to avoid biases were followed in this study: women were randomly chosen, all clinical examination and specimen collections were done by qualified gynaecologists and all samples were examined by a nationally qualified laboratory. The detection of HPV positivity using real-time polymerase chain reaction methods and the genotyping of HPV type using reverse dot blot method in this study also provided more precise results compared to the Hybrid Capture Tube Method applied in previous studies.¹⁷ However, it is important to note that this study covered only married women aged 18–65 so the results did not cover a subgroup of the population already sexually active but not yet married. This is a limitation of the study, but under the cultural and ethical norms of Viet Nam, it is very difficult to invite unmarried women to participate in a study with pelvic examinations. Women in Can Tho are also getting married at a later age, which further restricted the involvement of younger women in the study. Since the prevalence of HPV was higher in the younger age group in this study, and this group was under-represented due to the sampling frame, the actual prevalence in Can Tho might be higher than reported.

Since the findings of this study came from one urbanized province in the south of Viet Nam, caution must be taken in generalizing these findings to the entire Viet Nam population, especially to those in rural areas. In conclusion, a high prevalence of HPV infection, especially high-risk types, was observed in this study and this was higher for younger married women. As HPV infection has a high correlation with cervical cancer, this study emphasizes the need for both primary prevention of cervical cancer with HPV vaccines as well as secondary prevention with screening. Policy-makers in Viet Nam should consider making HPV vaccines and screening for cervical cancer routine practices.

Conflicts of interest

None declared.

Funding

None.

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Surveillance should be strengthened to improve epidemiological understandings of mosquito-borne Barmah Forest virus infection

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Introduction: Barmah Forest virus (BFV) is a mosquito-borne virus causing epidemic polyarthritis in Australia. This study used case follow-up of cases from the surveillance system to demonstrate that routinely collected BFV notification data were an unreliable indicator of the true location of exposure.

Methods: BFV notifications from June 2001 to May 2011 were extracted from the New South Wales (NSW) Notifiable Conditions Information Management System to study case distribution. Disease cluster analysis was performed using spatial scan statistics. Exposure history data were collected from cases notified in 2010 and 2011 to accurately determine travel to high-risk areas.

Results: Cluster analysis using address data identified an area of increased BFV disease incidence in the mid-north coast of NSW contiguous with estuarine wetlands. When travel to this area was investigated, 96.7% (29/30) cases reported having visited coastal regions within four weeks of developing symptoms.

Discussion: Along the central NSW coastline, extensive wetlands occur in close proximity to populated areas. These wetlands provide ideal breeding habitats for a range of mosquito species implicated in the transmission of BFV. This is the first study to fully assess case exposure with findings suggesting that sporadic cases of BFV in people living further away from the coast do not reflect alternative exposure sites but are likely to result from travel to coastal regions. Spatial analysis by case address alone may lead to inaccurate understandings of the true distribution of arboviral diseases. Subsequently, this information has important implications for the collection of mosquito-borne disease surveillance information and public health response strategies.

Mosquito-borne diseases are a growing concern in Australia, and an understanding of the spatial distribution of infection is required to refine surveillance strategies and public health interventions. Barmah Forest virus (BFV) disease is an arboviral disease endemic to Australia.¹ The virus was isolated from mosquitoes in 1974² and the first human cases were reported in 1986.³ The incubation period of BFV is probably seven to 10 days and symptoms of disease include rash, fever, arthralgia, myalgia and lethargy.^{4,5} BFV is a common cause of epidemic polyarthritis in Australia and carries important morbidity and economic impacts. It affects both genders and people of all ages. There is no specific treatment or vaccine available.⁶

New South Wales (NSW) uses a notifiable diseases register to record data on 57 communicable diseases

and medical conditions. Case demographics are entered into an electronic database at sites across the state when standardized clinical and laboratory case definitions are met. For the majority of notifiable conditions, including BFV disease,⁷ the case definition is based on a suggestive clinical picture and confirmatory laboratory findings. It is mandatory for laboratories to report notifiable disease detections and convey available patient information to public health authorities. Routinely collected data include the patient's name, date of birth, sex, residential address and suspected date of disease onset. Owing to the large number of disease notifications and the nature of collection, data quality and completeness is adequate for monitoring disease trends but may be insufficient to allow detailed analysis of risk and exposure. To obtain this information for BFV disease it was necessary to conduct case follow-up interviews.

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Seasonal BFV notifications in the Hunter New England Local Health District (HNELHD) of NSW (Figure 1) ranged from 60 to 173 between 2001 and 2011, with an average of 112 reports each season (incidence rate: 13.2 per 100 000).^{8,9}

There is some uncertainty regarding the natural reservoirs of BFV in Australia. Although low levels of neutralizing antibodies have been detected in kangaroos, wallabies, possums, horses, cats and dogs after experimental infection, the detected viraemia is considered too low for an insect vector to acquire the virus.^{10,11} The genetic similarity of BFV strains across Australia, as well as the pace in which they spread, suggests an avian or bat host.¹²

There is a diverse range of mosquito species confirmed as vectors of BFV. The majority of important vector species, such as *Aedes vigilax*, *Aedes procax*, *Aedes camptorhynchus* and *Verrallina funerea*, are associated with either coastal estuarine wetlands (i.e. saltmarsh and mangrove habitats) or brackish water environments (i.e. tea-tree and paperbark swamps).^{13–15} However, some species associated with freshwater habitats and urban environments, such as *Aedes notoscriptus*, *Culex annulirostris* and *Coquillettidia linealis*, may also be involved.^{13,16,17} Given the diversity of potential vector species and differences in the environmental drivers of mosquito population abundance within the different

habitats, it can be difficult to assess the regional health risks posed by BFV.

Although BFV disease has been documented in every state and territory of Australia, notifications occur predominantly on the Australian east coast, with sporadic inland cases.^{18,19} However, due to the limited knowledge of BFV's natural reservoir and a geographic distribution determined solely by the residential addresses of confirmed cases, the true distribution of the virus and thus the areas of risk are not definitively understood.

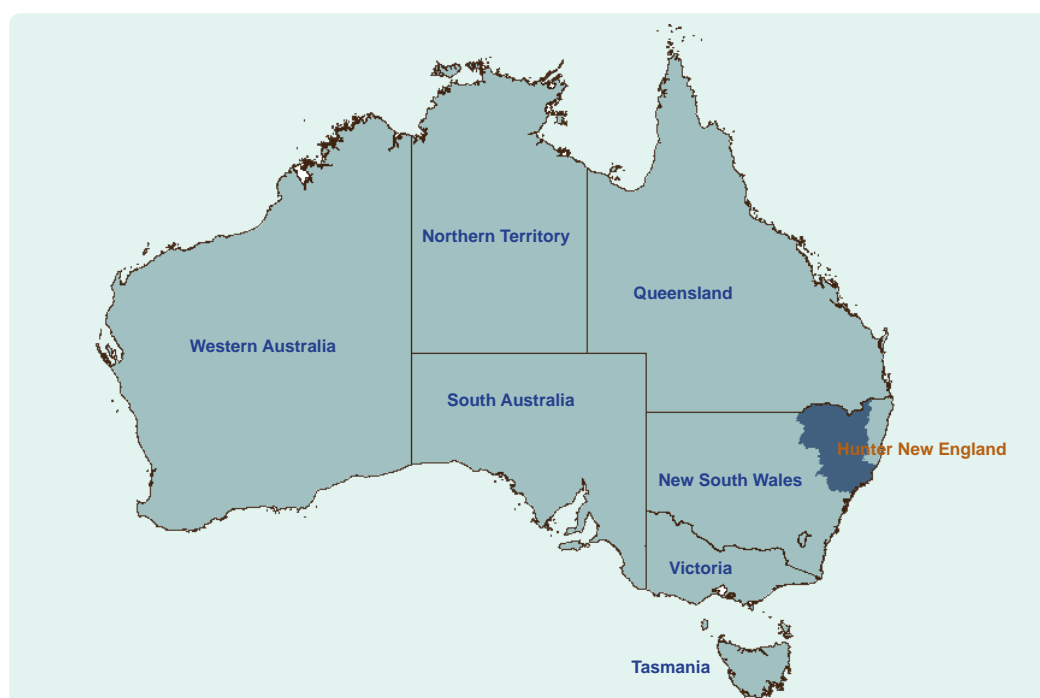
In this paper we aim to determine the likely risk exposure areas for BFV infection in the HNELHD of NSW, Australia by conducting structured interviews with all notified cases from June 2010 to May 2011 and to compare these identified risk exposure areas with those identified as having elevated standardized incidence rates when using routinely collected notification data from 2001 to 2010.

METHODS

Data acquisition

Notification data consisting of primary demographic information were extracted from the NSW Notifiable Conditions Information Management System for the period June 2001 to May 2011 and analysed using

Figure 1. Location of the Hunter New England local health district within Australia



MapInfo Professional version 10.0, a geographical information system.

Notification data were aggregated to local government area (LGA) level and the rates calculated, using population data obtained from the Australian Bureau of Statistics. Standardized incidence ratios (SIR) for each LGA were mapped to investigate the spatial distribution of BFV disease using the following formula:

$$\text{SIR} = \frac{\text{observed notifications}}{\text{expected notifications}}$$

$$\text{Observed notifications} = \frac{\text{notifications LGA}}{\text{population LGA}}$$

$$\text{Expected notifications} = \frac{\text{notifications HNELHD}}{\text{population HNELHD}}$$

$$\text{SIR} = \frac{(\text{notifications LGA}/\text{population LGA})}{(\text{notifications HNELHD}/\text{population HNELHD})}$$

Mapping and spatial analysis

The 1181 notifications between June 2001 and May 2011 were mapped to their residential address. Confidence intervals of 95% were applied to each SIR as the population in HNELHD is unevenly distributed. To identify disease clusters, incidence rates were calculated for each LGA, based on notification data and the 10-year seasonal mean of the underlying population. The data were analysed using Kulldorff's Circular Spatial Scan Statistics in SaTScan, version 8.0, using a purely spatial analysis with a discrete Poisson model and scanning for high incidence rates with a maximum cluster size of 50% of the population.

Case interviews

Cases notified in HNELHD area of NSW from June 2010 to May 2011 were interviewed by telephone about their travel history and possible exposure to mosquitoes during the incubation period of their infection (defined as four weeks).

Ethics approval

The Hunter New England Human Research Ethics Committee indicated that ethics approval was not required as this was regarded as a routine public health surveillance activity for a notifiable disease.

RESULTS

Spatial analysis of notifications from 2001 to 2011

Using routine notification data for the 10-year period, and applying 95% confidence intervals, there were statistically increased SIRs in three LGAs: Port Stephens, Great Lakes and Greater Taree, all of which contain large coastal lakes (Figures 2 and 3).

The spatial analysis performed with SaTScan detected one significant cluster of notified BFV cases (p -value < 0.01). This cluster, with a radius of 109 km, spanned an area of 37 277 km² and covered the LGAs of Greater Taree, Gloucester, Great Lakes, Walcha, Dungog and Port Stephens. SaTScan calculated the 10-year average as 61.0 annual notifications, compared to only 21.2 expected. This cluster showed a relative risk of 5.0, which means that people living in this area are five times as likely as the average population to contract BFV.

Case follow-up

Between June 2010 and May 2011, 62 BFV disease notifications were received for HNELHD. One case was accidentally reported twice. Contact details were available for 45 cases. The interviews revealed that two patients did not meet the case definition and were excluded. Ten cases could not be contacted and three refused to be interviewed. Thirty confirmed cases were interviewed, a 70% response rate (30/43).

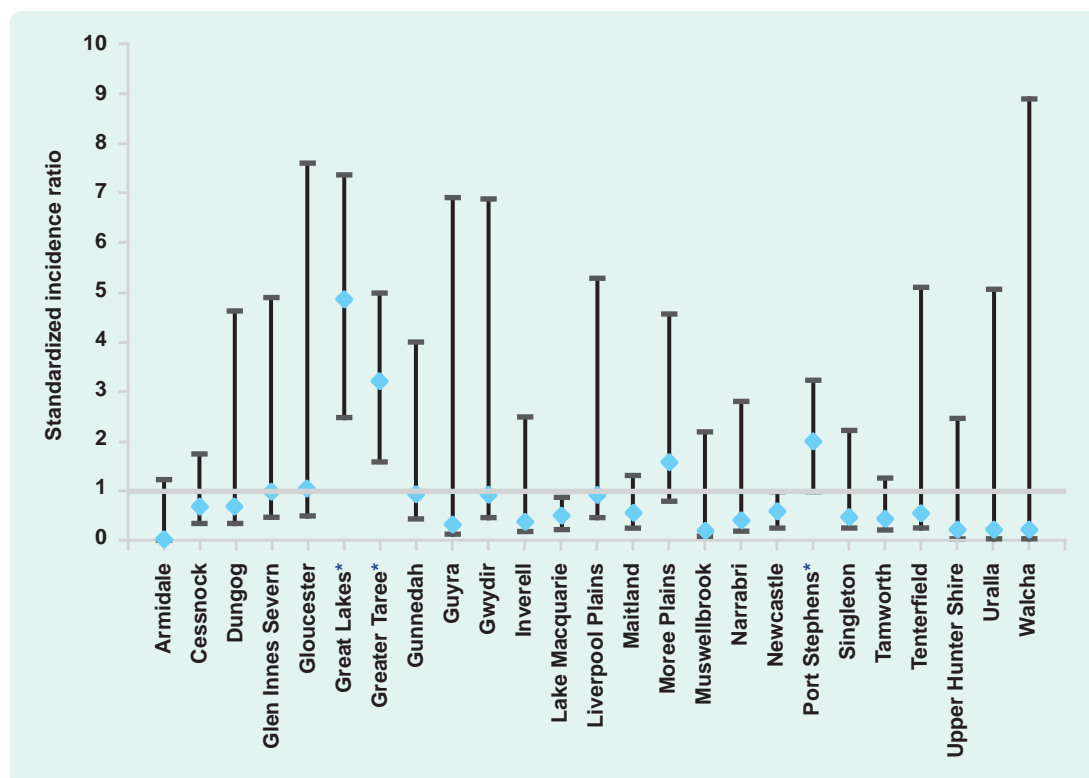
Location of exposure

Travel history obtained from respondents indicated 96.7% (29/30) either lived in coastal LGAs ($n = 22$) or conducted outdoor activities in these areas during the four weeks before disease onset ($n = 7$). From those living in non-coastal areas, 87.5% (7/8) reported having been exposed to mosquitoes in coastal LGAs. The remaining case was unable to provide a connection with the coastal areas during the incubation period but admitted poor travel history recall.

DISCUSSION

In keeping with the indication from 10 years of routine notification data, the majority of BFV disease cases of

Figure 2. Standardized incidence ratios of Barmah Forest virus per 100 000 population by local governmental areas, with 95% confidence interval ranges, Hunter New England local health district, 2001–2011



* Areas with statistically significantly increased incidence rates.

HNELHD in the 2010/2011 season were reported from the relatively densely populated central NSW coastal strip. While sporadic notifications were reported from inland areas, most of interviewed cases (96.7%) either lived in coastal LGAs or reported spending time in these areas shortly before contracting BFV. This finding is reassuring, suggesting that there has not been an extension of the range of competent disease vectors inland. Some mosquito species found inland may transmit BFV, for example *Culex annulirostris*, which is associated with freshwater habitats.²⁰ However, the abundance of this species is highly dependent on rainfall and, as a consequence, the local disease risk directly associated with this species may be variable. These results are in agreement with the findings of a recent Queensland study that used geostatistics to demonstrate higher incidence rates of BFV in coastal LGAs compared to inland areas.¹⁸

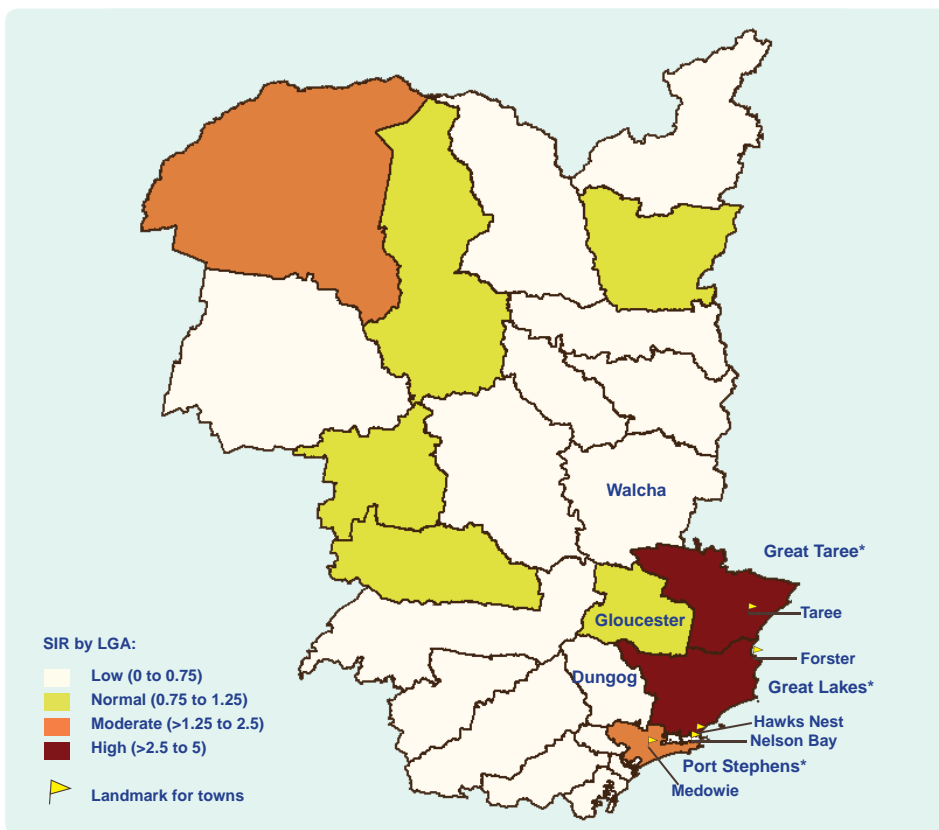
This is the first time a strengthened surveillance approach that investigated the true distribution of BFV has been reported. The current understanding of BFV distribution is based on the commonly observed coastal clustering of disease notifications, as well as the knowledge of distribution and competence of BFV vector

species, but this has not explained inland cases. Studies that concentrate on the spatial allocation of notified cases using residential address data to plot incidence may misrepresent the true location of exposure and lead to an inaccurate understanding of the disease distribution and epidemiology. This may be particularly relevant to mosquito-borne diseases and other diseases that have vectors or intermediate hosts.

The results of this study have implications for future surveillance strategies and the communication of public health messages. The detection of abundant mosquito populations and/or the isolation of BFV (as well as other mosquito-borne pathogens) from collected specimens may trigger public health warnings promoting personal protection measures. This study suggests that these messages should be broadcast more widely than just to the coastal population, particularly during holiday periods when recreational travel to the coast may increase.

Serological diagnosis of BFV is subject to certain limitations including high false-positive rates and the need to confirm recent infection through collection of two serum specimens to demonstrate seroconversion.⁵

Figure 3. Standardized incidence ratios of Barmah Forest virus disease per 100 000 population by local government area, Hunter New England local health district, 2001–2011



* Local government areas with increased standardized incidence ratios after applying 95% confidence intervals.

Confirmatory testing for IgM seroconversion is rarely conducted as only a single positive IgG test is necessary to be classified as a BFV case. This may compromise diagnostic certainty, and to limit this influence, the clinical features experienced by patients were carefully checked in addition to the laboratory diagnosis to ensure that their symptoms were compatible with a recent BFV infection.

The 2010–2011 season produced only 62 notifications, of which 30 patients were interviewed. The small sample size may impair general representativeness. We restricted our sample to those people who had been infected between June 2010 and May 2011 to reduce the possibility of recall bias. The majority of interviews were conducted within three months of the disease notification.

CONCLUSION

Geomapping in conjunction with spatial scan statistics using residential address data may be convenient for providing crude information on BFV disease clustering,

but assuming that the home address approximates the site of exposure is fraught with problems. For diseases with an environmental association like mosquito-borne diseases, it may provide a false impression of the risk areas and epidemiology.

Telephone interviews confirmed that almost all recently notified BFV cases occurred in close proximity to estuarine wetlands and other coastal brackish water habitats, which are increasingly being favoured for housing development.

We suggest a revision of the arboviral surveillance system in Australia to include collection of information on travel history and risk exposure. Spatial surveillance that considers exposure location, as used in this study, may be of particular value for other vectorborne diseases where accurate information regarding viral transmission is lacking. Understanding the spatial patterns of infection rather than assuming coherence of case allocation and disease distribution may improve knowledge regarding the disease ecology and allow more targeted public health interventions.

Conflicts of interest

None declared.

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A community-based sero-epidemiological study of hepatitis B infection in Lianyungang, China, 2010

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Introduction: The 2010 targets of the China Hepatitis B Prevention Programme were a prevalence of hepatitis B surface antigen (HBsAg) less than 1.0% for children less than five years old and less than 6.0% for the total population. This survey assessed the prevalence of Hepatitis B infection in Lianyungang, Jiangsu province, China in 2009–2010.

Methods: Multistage sampling was used with 2372 subjects among 17 selected villages. Blood specimen collection and testing by enzyme-linked immunosorbent assay (ELISA) were completed using the following markers for hepatitis infection: HBsAg and antibody to HBsAg (anti-HBs); hepatitis B e antigen (HBeAg) and antibody to HBeAg (anti-HBe); and hepatitis B core antibody (total anti-HBc). The data were analyzed with Epi Info, version 3.3.2.

Results: The prevalence of HBsAg was 2.4% (95% Confidence Interval [CI]: 1.8–3.0; Adjusted Prevalence [AP] 2.9%); anti-HBs prevalence was 51.1% (95% CI: 49.1–53.1; AP 49.2%) and total anti-HBc prevalence was 41.7% (95% CI: 39.8–43.7; AP 45.5%). The prevalence of HBsAg and total anti-HBc positivity increased from young to older age groups, yet the prevalence of anti-HBs positivity decreased from young to older age groups ($P < 0.001$ for all). There was no difference in the prevalences of HBsAg and anti-HBs among females and males ($P = 0.108$ and 0.089), but females had a higher prevalence than males for total anti-HBc positivity ($P < 0.001$).

Discussion: This survey showed that in 2010 the prevalence of HBsAg among children aged less than five years was lower than the national target of 1.0% and that the prevalence of HBsAg for the total population was lower than the national target of 6.0%.

Lianyungang is one of the thirteen municipal cities in Jiangsu Province with four rural counties and four urban districts with a population of 4 852 400.¹ In Lianyungang, the reported incidence of acute hepatitis B declined from 24.7 per 100 000 in 1997 to 9.9 per 100 000 in 2008, a decrease of 59.9%. For those aged less than 15 years, the reported incidence of acute hepatitis B declined from 12.5 per 100 000 in 1997 to 0.6 per 100 000 in 2008, a decrease of 95.2%.²

According to the China Children Immunization Programme, a child must be vaccinated with three doses of the hepatitis B vaccine before reaching 12 months of age. A child with the three-dose vaccination (first dose within 24 hours of birth, second at over one month and third at over six months; each dose is 5 μ g) can be reported as immunized. The hepatitis B vaccine became part of the immunization system in Lianyungang

in 1992; free hepatitis B vaccination for newborn infants was carried out in 2001. From 2001 to 2009 the reported immunization coverage rate among children aged from 12 to 24 months in Lianyungang for each year was always more than 99%.^{3,4}

China launched a hepatitis B catch-up immunization programme among children less than 15 years old in 2009. The target groups were those who had not completed a three-dose vaccination series or who had never received hepatitis B immunization. By 2010, Lianyungang had completed the catch-up immunization of hepatitis B vaccine for children less than 15 years old.

A national serological investigation of hepatitis B infection in China was conducted during the period 1992–1995 and showed that the prevalence for hepatitis B surface antigen (HBsAg) was 9.8%; in Lianyungang it was 2%–7%.⁵

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The China Hepatitis B Prevention Programme targets for 2010 were a prevalence of HBsAg lower than 1.0% for children less than five years old and a prevalence of HBsAg lower than 6.0% for the total population.⁵ As the reported incidence of hepatitis B does not represent the prevalence for positive hepatitis B markers, it was necessary to conduct a sero-epidemiological study to assess the prevalence of positive hepatitis B markers among residents of Lianyungang.

This study aimed to determine the prevalence of positive hepatitis B markers in Lianyungang and assessed whether the national targets for 2010 were achieved. This sero-epidemiological investigation was carried out from 10 November 2009 to 15 April 2010.

METHODS

Hepatitis B markers and test methods

The hepatitis B markers tested in this study were hepatitis B surface antigen (HBsAg) and hepatitis B surface antibody (anti-HBs); hepatitis B e antigen (HBeAg) and hepatitis B e antibody (anti-HBe); and hepatitis B core antibody (total anti-HBc).

HBsAg positivity indicates that the person is potentially infectious. Anti-HBs positivity indicates that the person obtained the antibody to HBsAg by vaccine or infection; anti-HBs is very useful to prevent hepatitis B infection or clear HBsAg. HBeAg positivity is associated with relatively high infectivity. Anti-HBe positivity indicates that the infectivity of hepatitis B is lower than that in the period of HBeAg positivity. Total anti-HBc positivity indicates past or current hepatitis B infection.

A 5 ml blood specimen was collected from an arm vein with a vacuum blood tube (2 ml peripheral blood was collected from children under three years old). The blood serum was centrifuged in gel tubes within five hours of collection and then sent to the laboratory for testing.

Enzyme-linked immunosorbent assay (ELISA) was used to test the hepatitis B markers with reagents. The HBsAg, anti-HBs, HBeAg and anti-HBe diagnostic reagents kits were from Beijing Kewei Clinical Diagnostic Reagents Co, Ltd; the total anti-HBc diagnostic reagents kits were from Shanghai Kehua Bio-Engineering Co, Ltd.

The Model 680 microplate reader by BIO-RAD was used (Bio-Rad Laboratory, Inc, Hercules, California, USA). A sample was considered positive for HBsAg, anti-HBs and HBeAg when the value of the optical density (OD) was ≥ 1 (cutoff value); it was negative when the value of OD was < 1 (cutoff value). A sample was considered positive for anti-HBe and total anti-HBc when the value of OD was ≤ 1 (cutoff value); it was negative when the value of OD was > 1 (cutoff value). Blank tests were implemented at the same time.

HBsAg, anti-HBs and total anti-HBc were tested in the first step to obtain the prevalence for HBsAg positivity, the prevalence for anti-HBs positivity and the prevalence for total anti-HBc positivity. We also tested for HBsAg-positive samples, HBeAg and anti-HBe. For those that were negative for HBsAg and/or anti-HBs we advised them to obtain the hepatitis B vaccine from clinics or hospitals.

Sample

The estimated sample size in this sero-epidemiological investigation was 2460, based on the prevalence of HBsAg carriers (9.1%),⁶ a relative precision of 10% and a confidence level of 90%, allowing for 10% loss. The sample size was distributed to each of the four rural counties and four urban districts according to the proportion of population in Lianyungang, China in 2010 (Table 1).

Initially four rural counties were randomly selected – Ganyu, Donghai, Guanyun and Guannan. Within these four counties, stratified cluster samplings were done in three strata according to the cumulative hepatitis B cases identified by the China National Diseases Reporting System in these four counties during the period 1 January 2006 and 31 December 2008. The three strata were: more than 20 cases (high), 10–20 cases (middle) and less than 10 (low). One town per stratum was identified in each county by simple random sampling totalling 12 towns. Then one village was identified in each town in the same way, finally 12 villages were identified in three strata in four counties. The sample size was distributed to three villages in each county; for example, there was a sample size of 556 in Ganyu County; 556 divided by three resulted in a 185 sample size distributed to each village (Table 1). Simple random sampling was done in the urban districts (Lianyun, Xinpu, Haizhou and Kaifa) due to few communities and

Table 1. Sample size distribution by country or district, Lianyungang, China, 2010

County or district	Population		Sample size	Selected villages or communities	Sample size per village	Target no. of households per selected village	Tested sample	
	N	%					N	%
Ganyu	1 097 618	22.6	556	3	185	62	531	22.4
Donghai	1 175 967	24.2	596	3	199	66	586	24.7
Guanyun	1 104 475	22.8	560	3	187	62	551	23.2
Guannan	752 266	15.5	381	3	127	42	372	15.7
Lianyun	143 630	3.0	73	1	73	24	70	3.0
Xinpu	361 212	7.4	183	2	92	31	181	6.7
Haizhou	149 703	3.1	76	1	76	25	71	3.0
Kaifa	67 529	1.4	34	1	34	11	30	1.3
Total	4 852 400	100.0	2 460	17	145	48	2372	100.0

few hepatitis B cases, so five communities were selected in four districts according to the sample size (Table 1). A total of 17 villages or communities were selected.

Households were allocated a random number, and were then recruited based on the order of these random numbers. The selected persons must have lived with others in a housing unit for more than 12 months. It was estimated that there were three members in each household in this area, so the total estimated households were 820 (2460/3).

All persons living within the sampled villages or community had a chance to be selected. However, persons who resided or worked in institutions were not eligible to participate in the investigation. An institution is a collective setting, for example, homes for the elderly or children, hostels, dormitories and military barracks, factories. All participants were advised they had the right to participate or withdraw from the investigation. Consent to participate and permission for a blood draw were obtained through a signature (or a fingerprint) on the consent form. The subjects were informed of their test results by telephone or mail or the participants could get their test results by calling the Lianyungang Center for Disease Control and Prevention. Prior to subject notification the results of HBsAg positivity were kept confidential to avoid discrimination when the test results were disclosed. All sensitive personal information collected during this investigation was kept confidential, including details of tattoos, sexual activity and orientation and drug use.

Ethics

We obtained approval from the Jiangsu Province Center for Disease Control and Prevention ethics committee before starting the sero-epidemiological investigation.

Data collection and analysis

A registration form was used to record the participant's name, age, address, telephone number, blood collection date, physical status and the results of the blood tests. Excel 2003 was used to set up the database and report the results of the blood tests. The data were analysed using Epi Info, version 3.3.2, including chi-squared tests and tests for trend which could take into account the study design. Prevalence figures were adjusted for age and reported as adjusted prevalence (AP).

RESULTS

Participants

The total number of participants who agreed to a blood draw was 2372, giving a response rate of 96.5%. Non responders were either not interested in participating in the investigation or unavailable/unable to be found.

When compared to the Lianyungang population in 2009, the proportion of survey participants in the 20–29 year age group was lower (16.1% compared to 6.3%) and the proportions of study participants

Table 2. Comparison of study participants with the 2009 Lianyungang population by age group

Age (years)	Study participants		Lianyungang population, 2009
	n	%	
0–4	135	5.7	5.4
5–9	515	21.7	6.8
10–14	397	16.7	9.9
15–19	106	4.5	8.0
20–29	149	6.3	16.0
30–39	213	9.0	16.5
40–49	292	12.3	13.6
50–59	293	12.3	10.8
Over 60	272	11.5	13.0
p - value			< 0.001
	2372	100.0	100.0

in the 5–9 year and 10–14 year age groups were higher (6.8% and 9.9% compared with 21.7% and 16.7% respectively) (Table 2). These differences were significantly different ($P < 0.001$).

Prevalence of hepatitis B infection

HBsAg prevalence among the 2372 survey participants was 2.4% (95% CI: 1.8–3.0); anti-HBs prevalence was 51.1% (95% CI: 49.1–53.1); total anti-HBc prevalence was 41.7% (95% CI: 39.8–43.7). When adjusted for age, the prevalence of HBsAg, anti-HBs

and total anti-HBc (AP) were 2.9%, 49.2% and 45.5%, respectively (Table 3).

A total of 57 HBsAg-positive specimens were tested again: 10 specimens were HBeAg-positive and anti-HBc-positive, 35 specimens were anti-HBe-positive and anti-HBc-positive, and another 12 specimens were both HBeAg and anti-HBe-negative and anti-HBc-positive. Three female specimens were HBsAg-positive and HBeAg-positive; two of the women were less than 20 years old, and one was over 60 years.

Distribution by person

The prevalence of HBsAg among children less than five years old was 0.7% (95% CI: 0.0–2.2 (Table 3). The prevalence of HBsAg among the < 15-year-old age group was 0.8% (95% CI: 0.2–1.3), lower than that in other groups. The trend for prevalence of HBsAg and total anti-HBc positivity increased from the young to older age groups ($P < 0.001$ for both), yet the trend for prevalence of anti-HBs positivity decreased from young to older age groups ($P < 0.001$) (Table 3).

The prevalences of HBsAg and anti-HBs among females and males were no different ($P = 0.108$ and 0.089). The prevalence for total anti-HBc positivity among females was 45.0% (95% CI: 42.3–47.7), significantly higher than that in males ($P < 0.001$) (Table 3).

Table 3. Seroprevalence of hepatitis B infection by age group and sex, Lianyungang, China, 2010

Age (years)	N	HBsAg-positive			Anti-HBs-positive			Total anti-HBc-positive		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
0–4	135	1	0.7	0.0–2.2	80	59.3	51.0–67.5	22	16.3	10.1–22.5
5–9	515	5	1.0	0.1–1.8	307	59.6	55.4–63.8	132	25.6	22.9–29.4
10–14	397	2	0.5	0.0–1.2	224	56.4	51.5–61.3	114	28.7	24.3–33.2
15–19	106	3	2.8	0.0–6.0	59	55.7	46.2–65.1	32	30.2	21.4–38.9
20–29	149	6	4.0	0.9–7.2	73	49.0	41.0–57.0	63	42.3	34.3–50.2
30–39	213	4	1.9	0.1–3.7	104	48.8	42.1–55.5	104	48.8	42.1–55.5
40–49	292	13	4.5	2.1–6.8	134	45.9	40.2–51.6	166	56.8	51.2–62.5
50–59	293	12	4.1	1.8–6.4	119	40.6	35.0–46.2	183	62.5	56.9–68.0
Over 60	272	11	4.0	1.7–6.4	112	41.2	35.3–47.0	174	64.0	58.3–69.7
AP *(%)			2.9			49.2			45.5	
p-value			< 0.001			< 0.001			< 0.001	
Sex										
Female	1289	25	1.9	1.2–2.7	638	49.5	46.8–52.2	580	45.0	42.3–47.7
Male	1083	32	3.0	1.9–4.0	574	53.0	50.0–56.0	410	37.9	35.0–40.7
p-value			0.108			0.089			< 0.001	
Total	2372	57	2.4	1.8–3.0	1212	51.1	49.1–53.1	990	41.7	39.8–43.7

* AP – Adjusted prevalence for age using Lianyungang population in 2009.

Table 4. Sero-prevalence of hepatitis B infection by county, Lianyungang, China, 2010

Counties	N	HBsAg-positive			Anti-HBs-positive			Total anti-HBc-positive		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
Rural										
Ganyu	531	14	2.6	1.3–4.0	284	53.5	49.2–57.7	205	38.6	34.5–42.7
Donghai	586	6	1.0	0.2–1.8	305	52.0	48.0–56.1	213	36.3	32.5–40.2
Guanyun	551	20	3.6	2.1–5.2	240	43.6	39.4–47.7	264	47.9	43.7–52.1
Guannan	372	12	3.2	1.4–5.0	233	62.6	57.7–67.6	201	54.0	49.0–59.1
Urban										
Lianyun	70	2	2.9	0.0–6.8	31	44.3	32.6–55.9	38	54.3	42.6–66.0
Xinpu	161	1	0.6	0.0–1.8	61	37.9	30.4–45.4	43	26.7	19.9–33.5
Haizhou	71	1	1.4	0.0–4.1	48	67.6	56.7–78.5	8	11.3	3.9–18.6
Kaifa	30	1	3.3	0.0–9.8	10	33.3	16.5–50.2	18	60.0	42.5–77.5
p-value			0.250			0.020			< 0.001	
Total	2372	57	2.4	1.8–3.0	1212	51.1	49.1–53.1	990	41.7	39.8–43.7

Distribution by place

The county with the highest prevalence of HBsAg was Guanyun County at 3.6% (95% CI: 2.1–5.2); the lowest was Xinpu District at 0.6% (95% CI: 0.0–1.8). The county with the highest prevalence of anti-HBs was Guannan County at 62.6% (95% CI: 57.7–67.6); the lowest was Kaifa District at 33.3% (95% CI: 16.5–50.2). The county with the highest prevalence for total anti-HBc positivity was Kaifa District at 60.0% (95% CI: 42.5–77.5); the lowest was Haizhou District at 11.3% (95% CI: 3.9–18.6) (Table 4).

There was no significant difference in the prevalence of HBsAg between all rural counties combined and all urban counties combined ($P = 0.250$), but there was a significant difference in the prevalence of anti-HBs between all rural counties combined and all urban counties combined ($P = 0.020$) and a significant difference in the prevalence of total anti-HBc between all rural counties combined and all urban counties combined ($P < 0.001$) (Table 4).

Distribution within rural counties by cumulative hepatitis B stratum

Sampling in the four rural counties was completed using stratum based on cumulative hepatitis B case numbers. There was no significant difference in the prevalence of HBsAg between high, middle and low cumulative number of reported hepatitis B case areas ($P = 0.360$); but there was a significant difference in the prevalence for anti-HBs positivity with the middle cumulative hepatitis B case areas having a higher prevalence than the high and low stratum ($P < 0.001$). The prevalence of total anti-HBc positivity in high cumulative reported hepatitis B case area was 46.0% (95% CI: 42.3–49.6), which was not significantly higher than in middle and low cumulative reported hepatitis B case areas ($P = 0.175$) (Table 5).

DISCUSSION

This sero-epidemiological investigation of hepatitis B infection among a community-based population in

Table 5. Seroprevalence of hepatitis B infection in rural counties by cumulative reported hepatitis B cases strata, Lianyungang, China, 2010

Stratum*	N	HBsAg-positive			Anti-HBs-positive			Total anti-HBc-positive		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
High	729	15	2.1	1.0–3.1	346	47.5	43.8–51.1	335	46.0	42.3–49.6
Middle	646	21	3.3	1.9–4.6	408	63.2	59.4–66.9	274	42.4	38.6–46.2
Low	665	16	2.4	1.2–3.6	308	46.3	42.5–50.1	274	41.2	37.5–44.9
p-value			0.360			< 0.001			0.175	
Total	2040	52	2.5	1.9–3.2	1062	52.1	49.9–54.2	883	43.3	41.1–45.4

*Stratum: high - more than 20 cases, middle - 10–20 cases and low - less than 10 cases.

Lianyungang showed a prevalence of HBsAg of 2.4% (AP 2.9%). This was lower than that in the 2002 national investigation (9.1%),⁶ in the 2008 national serosurvey (weighted prevalence 7.2%)⁷ and in the 2006 Jiangsu investigation (4.8%).⁸ The prevalence of HBsAg among children less than five years old was 0.7%, which was lower than the 1.0% goal set by the China Hepatitis B Prevention Programme during the period 2006–2010.⁵ However, the confidence interval for this 0.7% was 0.0–2.2, which is higher than the goal.

From 2001, free hepatitis B vaccination for newborn infants started in Lianyungang. This government-funded programme has made great achievements in the past 10 years. The reported coverage rate of hepatitis B vaccination has increased to over 99% for children less than 10 years old.^{3,4} The high coverage rate of hepatitis B vaccination has increased the prevalence for anti-HBs positivity among children less than 10 years old to over 59% (387/650), higher than other age groups. The prevalence of anti-HBs for all survey participants was 51.1%, which is higher than in the 2002 national investigation (39.90%, AP 37.48%),⁶ and similar to in the 2008 national serosurvey (weighted prevalence 50.1%)⁷ and in the 2006 Jiangsu investigation (50.34%).⁸ The prevalence of anti-HBs for those aged 0–4 years was 59.3%, which was lower than that reported in another Chinese serosurvey (69.8%).⁹

The high coverage rate of hepatitis B vaccination has lowered the hepatitis B infection. The positivity for HBsAg among children less than 10 years old in this study was 0.9% (6/650), lower than that in other age groups; the positivity for total anti-HBc among children less than 10 years old was 23.7% (154/650), lower than that in the age groups over 20 years old, but the prevalence of total anti-HBc for all survey participants was 41.7%, higher than that in the 2002 national investigation (20.2%, AP 21.6%),⁶ and that in the 2008 national serosurvey⁷ (weighted prevalence 34.1%) but lower than that in the Jiangsu investigation (49.8%).⁸

Analysis by cumulative hepatitis B case stratum showed that the prevalence of anti-HBs positivity in the middle stratum (10 to 20 cases between 1 January 2006 and 31 December 2008) was higher than the high and low strata (more than 20 and less than 10 cases respectively, $P < 0.001$). There was no

significant difference in the prevalence of HBsAg between the three areas ($P = 0.360$) and for total anti-HBc ($P = 0.175$). Therefore, the cumulative hepatitis B cases from the China National Diseases Reporting System in four rural counties during 2006 and 2008 did not really represent the hepatitis B infection level in a certain area, specific to the prevalence of positive hepatitis B markers.

From the coverage survey data for Lianyungang, we see high vaccine coverage over multiple years. This probably directly led to the decreasing burden of disease seen in the children tested in this study.

Our study had a response rate of 96%; however, the age distribution of the study sample was significantly different to that of the Lianyungang population. During the investigation many senior students and migrant workers aged 20–40 years old were not at home, so these age groups were underrepresented. We did adjust prevalence estimates for age to account for this.

CONCLUSION

This sero-epidemiological investigation showed the prevalence of HBsAg among children less than five years old had been controlled to less than 1.0%; the prevalence of HBsAg for all the population, at 2.4% was less than 6%. These data indicate that the hepatitis B immunization programmes has been effective in Lianyungang in the past few years.

Conflicts of interests

None declared.

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Influenza B outbreak in a primary school in Adelaide, Australia, 2011

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Introduction: This report describes a 2011 seasonal influenza B outbreak in a metropolitan primary school in Australia with 179 students.

Methods: Epidemiological, microbiological and environmental investigations were undertaken. A retrospective cohort study was conducted using a questionnaire that included demographic data, details of illness, chronic health conditions and vaccination status. Influenza-like illness (ILI) was defined as fever plus cough and/or sore throat. Analysis of ILI was undertaken with the chi-squared test and Fisher's exact test.

Results: Seventy-two questionnaire respondents (75%) reported illness during the outbreak – 43 with ILI, giving an attack rate of 45%. There was no association between ILI and age or chronic lung disease. Six (6%) students were vaccinated against influenza before the outbreak; although four became ill, none satisfied the ILI case definition. Seven students were positive for influenza B including two confirmed as B/Brisbane/60/2008-like; one student was positive for rhinovirus and another for metapneumovirus. The recommended influenza vaccine matched the circulating influenza strains.

Discussion: This cohort study estimated a high ILI attack rate and demonstrated low influenza vaccine coverage within the setting of a primary school. Gastrointestinal symptoms, in addition to constitutional and respiratory symptoms, were common.

Seasonal influenza outbreaks can cause substantial health burden, through both morbidity and mortality in all age groups, that can overwhelm health services.¹ Influenza in children who attend school or childcare is central to the community spread of influenza and epidemic amplification.²⁻⁴ Despite this, there is limited information in the peer-reviewed literature on the behaviour of seasonal influenza outbreaks in day schools.⁵⁻⁷

Influenza is a notifiable disease in South Australia (SA). Doctors and laboratories are required to report suspected or confirmed influenza to the Communicable Disease Control Branch (CDCB) of the South Australian Department for Health and Ageing;^{8,9} however, this is likely to under-represent the true extent of influenza infection in the community.

In SA, seasonal influenza usually peaks over the winter and spring (June to November) months.¹⁰ An average of 61 cases per month were notified from January to April 2011. In 2011, 4790 influenza cases were notified.¹¹

On Thursday, 26 May 2011, CDCB was notified by the principal of an Adelaide metropolitan primary

school (students aged five to 10 years) of a large number of unwell students (106 out of 179 students since 23 May 2011) and one unwell staff member. The illness was reported as one-to-two day gastroenteritis-like illness with headache, vomiting and fever (but no diarrhoea), respiratory symptoms in some students, as well as reports of transmission within families. There had been no recent excursions or camps, no combined assemblies and the school did not have a canteen. On the advice of CDCB, the school sent home information regarding the outbreak and placed notices with advice to stay home if unwell.

An investigation was initiated by CDCB to further characterize the illness by symptomatology and etiology and to estimate the attack rate and vaccine effectiveness within this school cohort.

METHODS

Epidemiological investigation

Due to confidentiality issues, a list of children who attended the school was unable to be provided to CDCB. Initially, the school contacted parents of ill children and requested they contact CDCB. From this, preliminary

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telephone interviews were conducted with parents of 10 ill children to determine demographic details, symptoms, management and details of ill contacts. Active case finding was also conducted by telephoning local medical practitioners. Doctors who notified local children with laboratory-diagnosed influenza were contacted to obtain clinical history. Parents of locally residing children aged five to 10 years with notified influenza were contacted to determine the school attended.

An anonymous questionnaire was distributed to the school on Monday, 6 June 2011. The paper-based questionnaire was delivered to each classroom with an explanatory letter requesting that the questionnaire be completed by parents or caregivers up until Friday, 24 June 2011. It also included CDCB contact details for parents or caregivers with any comments or questions. The questionnaire was also available as an online questionnaire with a link provided in the explanatory letter.

The questionnaire included questions on demographics, details of illness (onset date, symptoms, health care seeking behaviour, management and diagnosis), chronic health conditions and vaccination status. There were 20 questions and it was estimated the questionnaire would take approximately 10 minutes to complete. The questionnaire was open to all students and staff.

Influenza-like illness (ILI) was defined as fever plus cough and/or sore throat as reported in the questionnaire. A descriptive analysis of ILI cases and cases that reported illness not consistent with ILI was undertaken. Attack rates were calculated as the number of students with ILI divided by total student respondents. Due to small numbers, a separate analysis of the 10 staff questionnaires was not undertaken.

Data analysis was performed using Stata 10 software. The relationships between ILI and class and ILI and age were analysed with a chi-squared test. Influenza vaccine effectiveness and the relationship between ILI and chronic lung disease was analysed using a Fisher's exact test.

Microbiological investigation

Throat or nasal swabs were requested from the initial sample of 10 ill schoolchildren. Swabs were collected

either by a collection centre of the state's public health laboratory (SA Pathology) or by the family general practitioner. Swabs were analysed at SA Pathology. Ribonucleic acid (RNA) was extracted from patient samples using the MagMAX™ automated extraction platform and the MagMax Total nucleic acid extraction kit (Life Technologies, Carlsbad, California, United States of America). Two hundred microlitres (μL) of patient sample and $25\mu\text{L}$ of extraction/inhibition control were used in each extraction and eluted into $100\mu\text{L}$ of kit buffer. The real-time polymerase chain reaction (PCR) assays used for the amplification and detection of influenza A and B were modified versions of the Centers for Disease Control and Prevention (CDC) real-time reverse transcription PRC (rRT-PCR) Protocol for Detection and Characterization of Influenza (version 2007). The inhibition control, a synthetic oligo cloned into the Pgem-t easy vector (Promega, Fitchburg, Wisconsin, United States of America), was amplified in a separate reaction. Additional testing for adenovirus, parainfluenza 1, 2 and 3, respiratory syncytial virus, rhinovirus and human metapneumovirus were performed as single duplex or triplex reactions (Mark Turra unpublished data). The assays were carried out in a single $12.5\mu\text{L}$ (final volume) influenza A and B multiplex reaction, using the Invitrogen SuperScript III platinum One-Step Quantitative RT-PCR system (Life Technologies, Carlsbad, California, United States of America) and $2.5\mu\text{L}$ of eluted RNA. The RNA was amplified using the LC480 real-time cycler (Roche, Basel, Kanton Basel, Switzerland) using the following cycling parameters: $50\text{ }^\circ\text{C}$ for 15 minutes, $95\text{ }^\circ\text{C}$ for 10 minutes followed by 45 cycles of $95\text{ }^\circ\text{C}$ for 15 seconds, and $60\text{ }^\circ\text{C}$ for 45 seconds. The second derivative max analysis provided by the LC480 software was used for interpretation of results. Results were interpreted as detected, equivocal or negative (Mark Turra, SA Pathology, personal communication, 5 June 2012).

Five specimens were sent to the Victorian Infectious Diseases Reference Laboratory (a World Health Organization [WHO] Collaborating Centre for Reference and Research on Influenza) for culture to determine subtyping and vaccine match.

Laboratory results were unable to be linked to questionnaire answers as the questionnaires were completed anonymously; therefore, laboratory-confirmed cases were reported separately. Information obtained from the laboratory, doctor notification and/or preliminary interviews on onset dates and symptoms were collated.

Environmental investigation

CDCB staff, along with two local council environmental health officers, visited the school on Monday, 30 May 2011.

RESULTS

Epidemiological investigation

Questionnaire responses were returned for 100 (55.9%) of the 179 students at the school. In two instances, two questionnaires were completed on the same questionnaire paper; since it was impossible to distinguish the individual responses, the four students were excluded. Therefore a total of 96 (53.6%) questionnaires were analysed.

Valid questionnaires were returned for 53 males (mean age 7.5) and 43 females (mean age 7.8) of which 37 males (69.8%) and 35 females (81.4%) reported being unwell. A total of 43 students, 25 males (47.2%) and 18 females (41.9%), reported ILI, giving an attack rate of illness of 75.0% and an attack rate of ILI of 44.8%. Students with ILI had a mean age of 7.5 years compared with 7.8 years for those without ILI. There was no association between ILI and age ($P > 0.05$)

or ILI and class ($P > 0.05$). There was no apparent relationship between date of ILI onset and age or class (data not shown).

An epidemic curve of the ill cases is shown in **Figure 1**. The first three ILI cases were all in the same class with subsequent rapid spread to all other classes in the school. All but three cases occurred within a 20-day period (15 May until 3 June 2011). The peak ($n = 7$) occurred on 23 May 2011. Illness duration was longer in students with ILI compared with those without ILI (**Figure 2**).

Among the 43 students with ILI, constitutional and respiratory symptoms were most common with students reporting the following symptoms: tiredness ($n = 38$), cough ($n = 38$), anorexia ($n = 38$) and sore throat ($n = 36$). Tiredness ($n = 17$), headache ($n = 13$) and rhinorrhea ($n = 12$) were the most common symptoms in students who were unwell but did not satisfy the ILI case definition. Thirty-one students with ILI (72.1%) reported abdominal pain, vomiting and/or diarrhoea (**Table 1**).

A total of 41 students (42.7%) presented to health care workers as a result of the illness, including 35 cases with ILI (81.4% of all ILI cases). Antibiotics

Figure 1. Epidemic curve by onset date, Adelaide, Australia, 2011

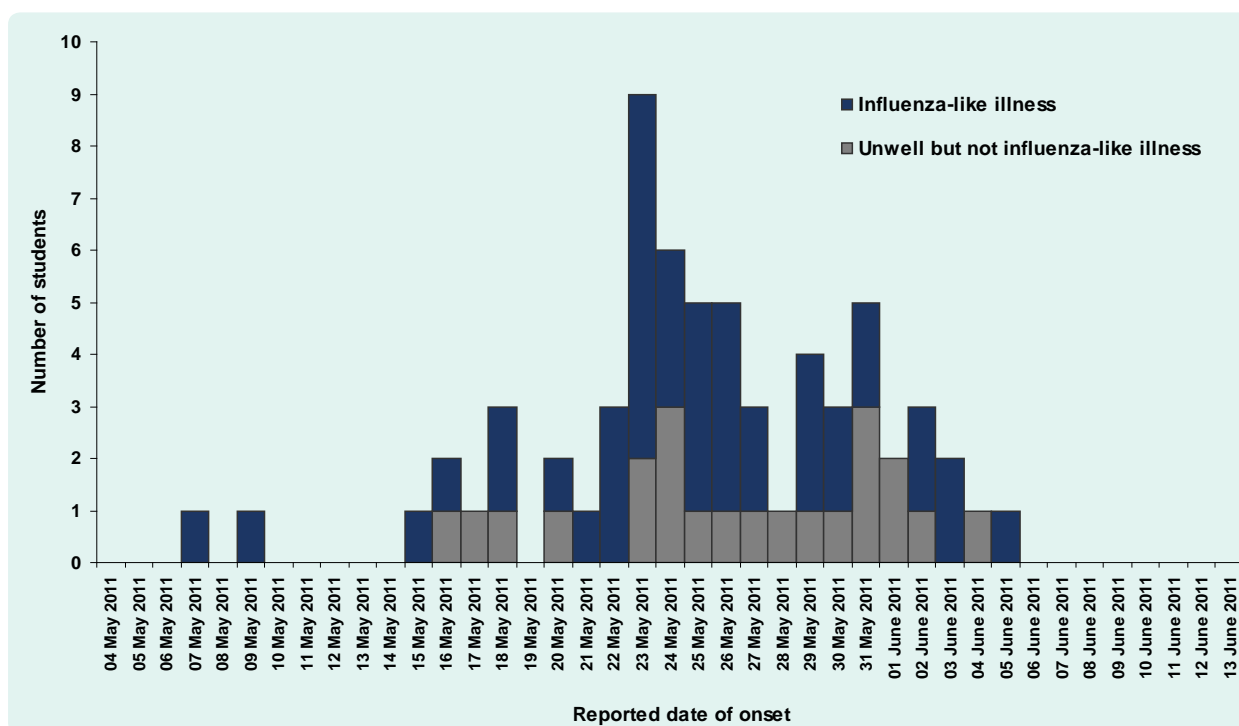


Figure 2. Reported duration of illness in questionnaire respondents who had been unwell, Adelaide, Australia, 2011

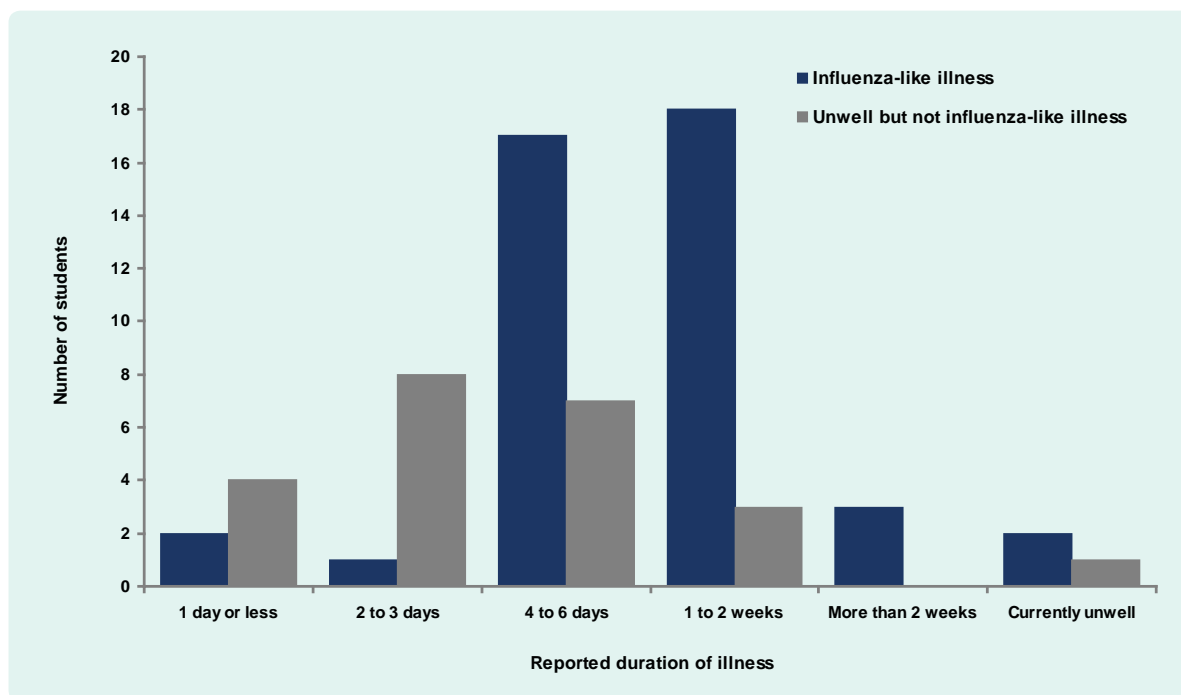


Table 1. Reported symptoms in questionnaire respondents who had been unwell, Adelaide, Australia, 2011

Symptoms	Illness met ILI case definition (n = 43)	Unwell but illness did not meet ILI case definition (n = 29)	Number of respondents
Fever	43	8	67
Tiredness	38	17	65
Cough	38	10	63
Anorexia	38	8	62
Sore throat	36	10	62
Headache	32	13	62
Rhinorrhoea	32	12	62
Abdominal pain	23	9	62
Nausea	19	3	57
Muscle aches	18	0	54
Vomiting	11	2	53
Diarrhoea	7	1	49
Epistaxis	2	1	51

were recommended by health care workers for 19 ILI cases.

Lung conditions (e.g. asthma) were the most commonly reported chronic illness among questionnaire respondents (n = 10, 10.4%). There was no association between ILI and chronic lung illness (relative risk [RR]: 0.93, 95% confidence interval [CI]: 0.44–1.95, P = 1.00).

Ninety-four students responded to the question regarding vaccination with six (6.4%) reporting vaccination in 2011 before illness onset in the school and an additional two reporting vaccination as a result of the outbreak. Four of these reported illness in this outbreak, although none satisfied the ILI case definition. The risk difference for ILI in respondents vaccinated in 2011 before the outbreak was -0.66 (95% CI: -0.78 to -0.54, P = 0.05, RR: indeterminate as no cases

Table 2. Date of onset, symptoms and swab type in students with confirmed influenza B, Adelaide, Australia, 2011

Onset date	Reported symptoms	Swab type	Swab collection date
25 May 2011	Fever, headache, cough, anorexia, diarrhoea	Throat	1 June 2011
26 May 2011	Fever, nausea, sore throat, lethargy, headache, cough	Throat	31 May 2011
27 May 2011	Fever, sore throat, cough, rash, aches, abdominal pain, lethargy, rhinorrhea	Nasal	31 May 2011
28 May 2011	Fever, sore throat, headache, cough, aches	Throat	2 June 2011
30 May 2011	Cough, influenza-like illness	Nasal	2 June 2011
31 May 2011	Influenza-like illness	Unknown	31 May 2011
1 June 2011	Fever, cough, cold-like symptoms	Throat	3 June 2011

in immunized), although given the small numbers this should be interpreted with caution.

Microbiological investigation

On 1 June 2011, the first throat swab was confirmed as influenza B. By outbreak conclusion on 15 June 2011, seven students were swab-positive for influenza B, one student for rhinovirus, and one student for metapneumovirus; one student was swab-negative. Two of the influenza specimens were confirmed as B/Brisbane/60/2008-like (included in the 2011 vaccine) and three specimens were unable to be cultured. Cases with confirmed influenza B satisfied the ILI case definition (Table 2).

Environmental investigation

Discussion with school staff identified that cough, lethargy and fever were predominant symptoms. Infection control practices including cough etiquette, hand washing, cleaning practices and staying home if unwell were discussed. 'Wash, wipe, cover' posters that promoted infection control were sent to the school. Events involving mixing with other schools were postponed.

The school had seven classes: reception (first year of school); two combined reception/year one classes; a year two class; a combined year two/three class; a combined year three/four class; and a combined year four/five class. There were between 17 and 30 students per class. The two classes where the outbreak appeared to initiate shared a double classroom with removable partition. There was one toilet block. There was a single playground for all students with mixing among year levels.

Daily updates on absentee numbers were obtained from the school, with 40, 44, 43, 28, 31, 26 and 23 students absent on 26 May, 27 May, 30 May, 31 May, 1 June, 2 June and 3 June, respectively. By 9 June 2011, absentee numbers had returned to background (two absent).

DISCUSSION

This outbreak investigation of influenza B in a primary school demonstrated a high attack rate of illness and of ILI. There was no association between ILI and age or chronic lung disease, a low self-reported influenza vaccination rate (6.4%) and no reported ILI in respondents vaccinated for influenza prior to the outbreak.

The attack rate of ILI in this study (44.8%) was lower than the age-specific ILI attack rate of 70%–80% reported in a primary school seasonal influenza A outbreak,⁵ but higher than the 34% attack rate reported in another primary school influenza outbreak⁶ and the 13% attack rate reported in a secondary school.⁷ Variability in attack rate in reported studies may reflect seasonal differences in influenza virus behaviour, environmental conditions and population exposure history.

The attack rate of any illness in student respondents in this study was 75.0%. The cause of illness in unwell students who did not satisfy the ILI case definition is unknown; however, as influenza can be asymptomatic or mildly symptomatic, it is possible that these students had influenza.² High absentee numbers occurred for more than two weeks with a peak on 27 May 2011 with 44 students absent (24.6% of total students).

The majority of students with ILI had gastrointestinal symptoms in addition to respiratory symptoms.

This has also been reported in a school outbreak of influenza A (e.g. nausea in 61% and vomiting in 45% of students).⁶ Gastrointestinal disorders have also been reported as being significantly more common in children with influenza B compared with influenza A (64% versus 39%, $P = 0.03$).² The atypical presentation of influenza in children may contribute to the spread of influenza in the community through reduced recognition of influenza as the cause of illness as occurred in this outbreak.²

In this study, 10.4% of children were reported to have chronic lung illness (including asthma), which is similar to the percentage given in the National Health Survey 2004–2005.¹² There was no association between ILI and chronic lung illness in this study. This may be due to the small number of cases and consequent variability of estimates; an alternative explanation is that there was no association between development of ILI and pre-existing chronic lung disease, only with development of severe ILI.¹³

The inactivated trivalent influenza vaccine is used in Australia. The vaccine used at the time of the outbreak was against the following strains: A/California/7/2009 (H1N1)-like virus, A/Perth/16/2009 (H3N2)-like virus and B/Brisbane/60/2008-like virus.¹⁴ Hence, the vaccine matched the strain seen in this outbreak. None of the six questionnaire respondents vaccinated in 2011 against influenza before this outbreak developed ILI. This corresponds to a vaccine effectiveness, from questionnaire data, of 100% against ILI. However, the use of proxy report without validation, the small size of the school and a response rate of 53.6% may have resulted in a falsely elevated estimation of vaccine effectiveness and so this result should be interpreted with caution. It is possible that use of ILI as a proxy for influenza underestimated influenza through vaccine-associated alteration of the influenza symptom profile.¹⁵ This may result in a differential presentation of influenza with an increased number of vaccinated students with asymptomatic or atypical influenza infection which did not meet the ILI definition, compared with a more typical presentation in unvaccinated students.¹⁵

In Australia, influenza vaccine is recommended for anyone from six months of age who wishes to be protected against influenza; however, it is provided free for children with specified chronic illnesses.¹⁶

To the authors' knowledge there is no formal estimate of influenza vaccine coverage in children in Australia, although non-peer-reviewed literature estimated influenza vaccine coverage in children at 10%.¹⁷ Our study found a self-reported influenza vaccination rate for students of 6.3% before the outbreak and 9.6% after the outbreak. This so provides an estimate for vaccine coverage for school-aged children in 2011. Despite the recent H1N1 influenza pandemic, our study found low estimated influenza vaccine coverage in this age group. Influenza vaccine coverage may have been influenced by media reports of side-effects associated with Fluvax and Fluvax Junior vaccine in 2010.^{17,18} Further studies to estimate influenza vaccination coverage in Australian children are required.

This study has several limitations. Questionnaire results were obtained by proxy from parents or caregivers with no validation of responses, which may have resulted in measurement error. There was possibility of selection bias as caregivers of ill students may have been more likely to respond, and there was considerable variation in response between classes. The small size of the school and response rate resulted in small numbers on which to base conclusions regarding vaccination coverage and effectiveness. Several questionnaires were incomplete, particularly regarding symptoms with several respondents only answering questions in the affirmative and leaving other subparts blank. Some parents or caregivers may have been from a culturally and linguistically diverse background and been unable to complete the questionnaire or complete it accurately; however, given the anonymous nature of the questionnaire and the use of the school to distribute the questionnaire, it is impossible to determine the effect. It is possible, although unlikely, that respondents completed more than one questionnaire, as questionnaires were not identification coded. The study strengths included documentation of an outbreak of seasonal influenza in a school including information on symptoms and vaccination history and a reasonable response rate to the cohort questionnaire.

This cohort study has characterized an influenza B outbreak in a school. As such, it has estimated the attack rate, influenza vaccine coverage and influenza effectiveness within the setting of a primary school-aged cohort in addition to characterizing ILI in children, which commonly included gastrointestinal symptoms.

Conflicts of interest

None declared.

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Western Pacific Surveillance and Response

Instructions to Authors

Aim of Western Pacific Surveillance and Response

To create a platform for sharing information to improve surveillance of and response to public health events in the Western Pacific Region.

Objectives

- To produce a web-based publication on surveillance and response activities in the region that has high exposure and is freely accessible.
- To promote information sharing on experiences and lessons learnt in surveillance and response for public health events in the Western Pacific Region and globally.
- To build capacity in communicating epidemiological findings in the Western Pacific Region.
- To highlight new and relevant technical or guidance documents and meeting reports published by the World Health Organization, Western Pacific Regional Office.

Audience

Western Pacific Surveillance and Response (WPSAR) is aimed at people studying, conducting research or working in surveillance of and response to public health events both within the region and globally.

Scope

WPSAR covers all activities related to the surveillance of and response to public health events. Such activities may be implementation or evaluation of surveillance systems, investigations of public health events, risk assessments both in rapid responses and policy development, outbreak investigations and research on routine public health activities. Public health events may be in any of the following areas; communicable diseases, natural disasters, bioterrorism and chemical and radiological events.

Frequency

Journal articles will be published an article at a time building up to an issue every quarter. This means that articles will be uploaded onto the website after the review and editing process therefore allowing timely dissemination. Printed copies of the journal are available for areas with limited internet access on request after the end of each quarter.

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WPSAR follows the guidelines from the Uniform Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee for Medical Journal Editors (ICMJE, <http://www.icmje.org/>).

Format for Manuscripts

Please submit all articles in double spaced 12 point Arial font in a Microsoft® Office Word file or a compatible file in English.

The format of the article will depend on the type. There are letters to the editor, perspectives, case reports/case series, lessons from the field, surveillance reports, surveillance system implementation/evaluation, risk assessments, original research, outbreak investigations report, news items and meeting/conference reports.

Letters to the Editor

A letter commenting on a previously published article OR a letter commenting on the theme of the issue.

- Word limit: ≤ 500 words
- ≤ 5 references
- ≤ 1 illustration

Perspectives

An unstructured article discussing an issue regarding surveillance of and response to public health events. The scope of the discussion must be clearly defined.

- Word limit: ≤ 1000 words
- ≤ 10 references
- ≤ 1 illustration

Case Report/Case Series

An unstructured article describing an unusual case or series of cases of public health significance. Sub-headings may be used to increase the readability of the article.

- Unstructured abstract of ≤ 250 words
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An article describing an issue faced in field epidemiology and the experience in trying to overcome the issue.

- Structured article with an abstract of ≤ 250 words and sections for problem, context, action, outcome and discussion
- The abstract should also be structured with problem, context, action, outcome, and discussion
- Word limit: ≤ 2000 words
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Surveillance Reports

An article of a summary and interpretation of surveillance data for a given period of time. A description of the surveillance system and the limitations of the data collected must be included.

- Unstructured abstract of ≤ 250 words
- Word limit: ≤ 2000 words
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- ≤ 10 figures/graphs/pictures

Surveillance System Implementation/Evaluation

An article describing the implementation of a new surveillance system or an evaluation of an existing surveillance system used to detect public health events.

- Unstructured abstract of ≤ 250 words
- Word limit: ≤ 2000 words
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An article detailing a risk assessment of a public health threat or event which may be planned or rapid.

- Structured article with an abstract and sections for introduction (including risk question/s), risk assessment methodology, results, discussion and recommendations.
- The results should include the assessment and/or characterization of the hazard, exposure and context, as well as the level of risk/risk characterization. The limitations must also be discussed. Risk management may be included in the discussion.
- The abstract should also be structured with objectives, method, results, and discussion
- Word limit: ≤ 3000 words
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Original research articles may include epidemiological studies including outbreak investigations.

- Structured article with an abstract of ≤ 250 words, introduction, methods, results and discussion
- The abstract should also be structured with introduction, methods, results, discussion
- Word limit: ≤ 3000 words
- ≤ 40 references
- ≤ 5 figures/graphs/pictures

Outbreak Investigation Report

An article describing the investigation of an outbreak. The detection, investigation and control measures should be included.

- Structured article with an abstract of ≤ 250 words, introduction, methods, results and discussion
- The abstract should also be structured with introduction, methods, results, discussion
- Word limit: ≤ 1500 words
- ≤ 15 references
- ≤ 2 figures/graphs/pictures

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News items and meeting and conference reports will not undergo peer review. Please contact the Editor at WPSAR@wpro.who.int if you intend on submitting such an article.

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Refer to the article type for the limit on illustrations (graphs, tables or diagrams). Please insert all illustrations at the end of the manuscript with a title. The illustration must be referred to in the text and must be able to be understood on its own. Use Microsoft® Office Excel for graphs and Microsoft® Office Word for tables and diagrams. Additionally, please provide a Microsoft® Office Excel spreadsheet of the data used to create a graph. Footnotes for illustrations should have superscript letters assigned and an explanation provided below the illustration.

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Reference the most recent and relevant publications. Please use Vancouver style referencing. Sample references can be viewed online: http://www.nlm.nih.gov/bsd/uniform_requirements.html.

Place the bibliography at the end of the article text and not as footnotes. Write journal names in full. Use superscript sequential numbering in the text. Place the number after any punctuation. For example:

These results are consistent with the original study.¹¹

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A

- Study design
- Data collection
- Data analysis
- Data interpretation
- Writing the article

B

- Drafting the manuscript
- Critically revising the manuscript

C

- Final approval of the manuscript for submission

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