Title: Swine Influenza surveillance in East and South East Asia: a systematic review

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Abstract:

The emergence of the human pandemic influenza A H1N1 virus in 2009 has called attention to the lack of surveillance data on swine influenza (SI) around the world. Circulation of influenza in swine presents an ongoing risk of the emergence of virus strains that can cause epidemics and pandemics in humans. Surveillance systems on SI need to be improved in high risk regions. East and Southeast Asia are important pig and poultry producing areas, where the majority of production takes place on small-scale farms with low biosecurity levels. This systematic review synthesizes data on SI virology, serology and epidemiology in East and Southeast Asia. Within a total of 467 retrieved references from PubMed and ISI Web of KnowledgeSM, a total of 74 research articles, literature reviews and conference papers have been selected. Surveillance results have been more frequently published since the 3 past years. Large unequalities between countries are underlined. The literature focuses mainly on virological data, while the serological and epidemiological situation of swine influenza in East and Southeast Asia remains poorly described. Greater investment is needed in SI surveillance, to improve our knowledge of circulating strains as well as the epidemiology and disease burden in the region.

Key words: Swine influenza; Southeast Asia; Surveillance; Cross-species transmissions; Emergence

Main text Introduction

Pigs are the main animal reservoir of H1N1, H3N2, and H1N2 influenza viruses. H1N1 and H3N2 strains have emerged in swine on several occasions consecutively with multiple cross-species transmissions from birds or humans (Brown 2000; Webby & Webster 2001). The first H1N2 viruses isolated were a reassortants between H1N1 and H3N2 (Brown 2000). All these 3 subtypes are spreading within swine population worldwide with a continuous evolution (i.e antigenic drift or reassortants), which increases the genetic diversity of swine influenza viruses (Brown 2000; Vijaykrishna et al. 2011; Webster et al. 1992).

Although the first three human influenza pandemics involved viruses of avian origins, the recent swine-origin H1N1 pandemic that emerged in 2009 (H1N1 pdm) convinced scientists that more attention needs to be paid to the pivotal role of pigs in the emergence processes of pandemic strains (Garten et al. 2009; Smith et al. 2009). Beyond their zoonotic potential and the pandemic risk influenza viruses need to be monitored because of their sanitary and economic impact on the swine supply chain, since they represent also a major swine pathology in developing countries, which requires systematic vaccination (Olsen et al. 2006).

Due to a lack of epidemiological, clinical and laboratory data on the swine influenza, the scientist communities agree that surveillance activities urgently need to be improved around the world, including East and Southeast Asia (OFFLU 2011; Smith et al. 2009; Van Reeth & Nicoll 2009).

Countries in East and Southeast Asia include Brunei, Cambodia, China (including Hong-Kong Special Administrative Region (SAR)), Indonesia, Laos, Malaysia, Myanmar, the Philippines, Thailand and Vietnam. According to statistics provided by the Food and Agriculture Organization of the United Nations Organization, this region produced approximately 515 million pigs in 2008, representing more than the half of the worldwide pig production. The pig production in East and Southeast Asia is characterized by a wide mixture of production types. The majority of producers are smallholders and semi-commercial, with their production aimed for home consumption and/or sale. Integrated production units are increasing in most developed countries within the region. The terms "small-scale", "mediumscale" and "large-scale" do not have any precise definition (ACIAR 2002). In the present review, we assume that a commercial system has more than 50 pigs per year reared in industrial system, backyard system has less than 50 pigs per year, a semi-commercial system is a mix between commercial and backyard (Liu et al. 2011). Backyard and semi-commercial system are characterized by a poor level of biosecurity and a mix of species, which could increase the risk of influenza virus persistence and emergence on swine farms (Olsen et al. 2006).

The aim of this systematic review is to make the synthesis of our current knowledge on swine influenza in East and Southeast Asia, in order to underline the needs in terms of surveillance in the region.

Methods

Search strategy

Swine influenza is not an OIE notified diseases, except influenza viruses in pigs that fulfil the criteria of a new emerging disease (this was the case with pandemic H1N1/2009 up to

September 2010). Therefore, no official reports or notification on country status regarding swine influenza are available. In June 2011, we searched the GenBank database to identify strains of swine influenza especially of H1, H3, H5, H9 and other subtypes reported in each country of interest. In parallel, we searched the PubMed database, using the following search strategy:

#1: "swine" OR "pig*"

#2 "influenza" OR "flu" OR "H1*" OR "H2*" OR "H3*" OR "H4*"OR "H5*" OR "H7*" OR "H9*"

#3: "China" OR "Myanmar" OR "Cambodia" OR "Laos" OR "Thailand" OR "Vietnam" OR "Brunei" OR "Malaysia" OR "Indonesia" OR "Philippines" OR "Hong Kong" OR "Asia".
#4: #1 AND #2 AND #3

In order to account for proceeding papers, an additional search using the same strategy was performed with ISI Web of KnowledgeSM to extract meeting documents that were unlisted in MEDLINE® database. Finally some unpublished data were also extracted from technical reports and steering committee reports on the OIE/FAO Network of Expertise on Animal Influenza website (http://www.offlu.net/index.html). Although unpublished, this kind of information may be considered as expert opinions.

Selection criteria

Titles and then abstracts were reviewed using the following inclusion criteria: articles had to report primary virological or serological data on swine infections by the influenza virus in at least one country of interest. Experimental studies were excluded. Since the swine-origin H1N1pdm may be called "swine influenza" even in humans, the term "Veterinary science" was used to limit the search to animal health. Remaining articles reporting human infection were excluded. In a second step, the limit "Published in the last 10 years" was used to focus on the most recent references, which may underline current needs in terms of data and surveillance.

Data analysis

For each reference, the publication date, the country and the main topic (i.e virology, serology, both or epidemiology) were registered. For the most recent references, the source of data was categorized as monitoring (i.e systematic sample collection on healthy animals) included in surveillance program, SIV outbreak investigation, cross-sectional survey, pooled data provided by various databases, or not available. The following relevant variables were extracted from all selected articles and reports: the number of animal tested, the number of positive tests, the number of farm tested, the number of positive farm, laboratory assays including the subtype testing, the time and the location (i.e clinically affected farm, healthy farm, slaughterhouse, market) of sample collection, the age and farming system of collected pigs (i.e backyard, semi-commercial, commercial), epidemiological context (i.e details about neighbouring farms), and season of epidemic peak and season of the lowest virus activity in case of a longitudinal study. The isolation rate was computed for virological studies. The average value was also computed for each study design and compared using the Chi squared test. The seroprevalence of each subtype was also computed. When H1 and H3 subtypes were both tested, the seroprevalence of influenza type A was estimated. Confidence intervals and relative precisions were computed assuming an infinite population and dividing the standard deviation of each estimate by the estimate value.

Results

Selected articles

The initial PubMed research strategy retrieved 467 published articles, among which 242 were related to veterinary science. A total of 66 articles reporting virological or serological evidence of swine infection by an influenza virus in a country of interest were selected on the basis of their title and abstract. Two recent literature reviews on swine influenza in China were available (Liu et al. 2011; Yu et al. 2009). The additional search on ISI Web of KnowledgeSM retrieved 52 articles of conference proceedings, among which 7 matched with the selection criteria, all published in the last 10 years. As shown on Figure 1A, the number of articles has largely increased in the last 3 years. In total, 37 references were published before 2008 and the same number after 2008. Data were mainly provided by continuous monitoring and SIV outbreak investigations. The number of pooled data analyses has increased in the last 2 years. The most publishing country is China, including Hong-Kong SAR, with a total of 52 published articles followed by Thailand, with a total of 12 published articles (Figure 1B). Virology is the most frequent studied topic. In comparison, serological and epidemiological studies represent only 10% and 4% of references respectively (Figure 1C). *Virological situation*

We identified 4 different study designs where the virus was isolated. One approach consisted of systematic visits to slaughterhouses to collect samples in both healthy and formerly sick pigs. A second approach, also often related to national surveillance programs, consisted of single or repeated sample collection in randomly selected farms. Although selected farms were usually healthy, some specimens were collected from sick animals. Nine other studies published in China and Thailand were based on the particular approach involving the detection and reporting of outbreaks on pig farms, and corresponding viruses identified from sick animals. Finally, a single case study reported a high isolation rate of avian-origin SIV, obtained from outbreak investigation of AIV, during outbreaks of H5N1 HPAI in poultry in Indonesia (Nidom et al. 2010). The average isolation rates according to each approach are presented in Table 1. The isolation rate was significantly higher when samples were collected in clinically affected farms in comparison to other strategies (p < 0.05). However, the highest isolation rate was obtained in the study that investigated commercial farms near previous H5N1 outbreaks in poultry farms in Indonesia.

Up till now (July 2011), a total of 708 strains have been published in the GenBank database by Hong Kong SAR, 156 by People's Republic of China (21 by Taiwan), 61 by Thailand, 15 by Indonesia and 1 by Malaysia. Several strains collected during surveillance activities have been sequenced in Hong-Kong SAR through research on H1N1 pdm (Smith et al. 2009; Vijaykrishna et al. 2011). The relative distribution of each subtype is presented in Figure 2.

The first emergence of swine influenza in East and Southeast Asia was reported in 1969 in Taiwan during the Hong-Kong human epidemic H3N2 (Kundin 1970). The human-like H3N2 swine influenza virus spread within the Asian swine population along several reassortants, especially with human seasonal, classical swine and avian viruses (Cong et al. 2010; Ngo et al. 2011; Yu et al. 2007). This subtype has been reported in Hong-Kong SAR (Vijaykrishna et al. 2011), in mainland China (Yu et al. 2007), in Taiwan (GenBank), in Thailand (Chutinimitkul et al. 2008; Takemae et al. 2008) and in Vietnam (Ngo et al. 2011). Today

surveillance results have led to contradictory conclusions, but this subtype may still spreading in China (Bi et al. 2010; Vijaykrishna et al. 2011).

The H1N1 subtype was first isolated in 1991 (Kupradinun et al. 1991; Vijaykrishna et al. 2011). The classical swine lineage remains the predominant one since its emergence until 2002 (Vijaykrishna et al. 2011). This lineage or clustering reassortants have been reported in China (Liu et al. 2011; Vijaykrishna et al. 2011), in Taiwan (Shieh et al. 2008) and in Thailand (Chutinimitkul et al. 2008; Takemae et al. 2008). The European avian-like H1N1 emerged in China in 1993 (Guan et al. 1996), long time before the first report of the Eurasian avian-like H1N1, which emerged in 2001 and became the predominant H1 lineage since 2005 in China (Vijaykrishna et al. 2011) and Thailand (Takemae et al. 2008). The US origin H1N2 has been reported since 2002 and is still circulating in China (Bi et al. 2010; Vijaykrishna et al. 2011; Xu et al. 2009) and Thailand (Takemae et al. 2008). In 2009, the emergence of the H1N1 pdm may involve some changes in the H1 distribution. This new virus has been isolated in China (Vijaykrishna et al. 2011) and in Thailand (Sreta et al. 2009). This lineage is currently spreading in swine, and the first reassortants with a swine influenza virus has been identified in Hong-Kong SAR (Vijaykrishna et al. 2010).

Pig infection with H5N1 and H9N2 avian-origin viruses have only been reported in Asia. The highly pathogenic avian influenza (HPAI) H5N1 subtype has been isolated several times in Chinese (Zhu et al. 2008) and Indonesian pigs (Nidom et al. 2010; Takano et al. 2009), with an evidence of a pig-to-pig transmission of an HPAI H5N1 avian-origin virus in Indonesia (Nidom et al. 2010). The avian H9N2 subtype has been reported in China and Hong Kong SAR on several occasions (Cong et al. 2008; Peiris et al. 2001; Yu et al. 2008a; Yu et al. 2011). The equine-origin H3N8 has been isolated once (Tu 2009).

Serological situation

Since a detailed review was performed in China in 2011 (Liu et al. 2011), we did not performed any additional analysis for this country. The synthesis of seroprevalence studies at individual level was thus computed on the basis of 9 references. The average seroprevalence of influenza type A could be extracted or computed on the basis of the literature review in China (Liu et al. 2011), 3 references in Thailand (Damrongwatanapokin, Parchariyanon & Pinyochon 2003; Kitikoon et al. 2011; Parchariyanon 2006), one reference in Malaysia (Suriya et al. 2008) and in Vietnam (Trevennec et al. 2011). As shown in the Table 2, the individual seroprevalence of influenza A ranges from 3.1% in semi-commercial pig farms in the spring in Vietnam (Trevennec et al. 2011) to an average of 61.4% in industrial pig farms in China (Liu et al. 2011). The totality of pigs was seropositive in the 2 farms tested in Thailand in 2011 (Kitikoon et al. 2011).

The proportion of each subtype were provided from the pooled data analysis in China, which tested H1, H3, H5, and H9 subtypes (Liu et al. 2011), from studies in Thailand on H1N1 and H3N2 subtypes (2 publications) (Damrongwatanapokin, Parchariyanon & Pinyochon 2003; Parchariyanon 2006) and Malaysia (1 publication), where H1N1 and H3N2 were tested (Suriya et al. 2008). The overall result indicates a higher proportion of H1N1 in comparison to other subtypes, which is consistent with virological data. There is an increase in seroprevalence of H1N1 over the 10 last years in China (Liu et al. 2011), whereas the H3N2 seroprevalence has been decreasing (Song et al. 2010), except in Thailand, where it remains the predominant subtype (OFFLU 2011).

Surveillance results over large samples indicate that H5N1 may spread at a very low level in swine populations in Vietnam and Thailand with a seroprevalence of 0.25% (n=3000) (Choi et al. 2005) and 1% (n=300) in Indonesia (Nidom et al. 2010; Santhia et al. 2009). Investigations on H5N1 AIV outbreaks in poultry did not detect systematic evidence of H5N1 infection in pigs (Parchariyanon 2006; Santhia et al. 2009; Song et al. 2010; Trevennec et al. 2011).

The H4 subtype has been measured only in one study in China and its relative seroprevalence appears to be important with up to 15% (Ninomiya et al. 2002). The H9 subtype seroprevalence has been evaluated only in China and was found in less than 3% of tested animals (Liu et al. 2011; Song et al. 2010).

The herd-level seroprevalence of swine influenza type A was computed for 3 countries: 17.1% in Vietnam (Trevennec et al. 2011), 60% in Taiwan (Shieh et al. 2008) and 83% in Malaysia (Suriya et al. 2008).

Risk factors

Variables extracted from selected references allowed us to identify some general risk factors of swine influenza. Seroprevalence of swine influenza in East and Southeast Asia has an epidemic peak during the fall and the winter season (Li et al. 2003; Shieh et al. 2008) and decreases in the spring (Trevennec et al. 2011), which is similar to the seasonal pattern described in Europe or America (Olsen et al. 2006). However, in Northern countries, multiple studies have shown that the disease can be observed all year round due to the total confinement of animals in industrial production type (Olsen et al. 2006). In East and Southeast Asia, since the majority of pigs is kept in open-houses (Bastianelli, Derail & Klotz 2007), we assume that the seasonality is an important pattern of the disease. The seroprevalence of influenza A is also associated with high level of animal densities (Liu et al. 2011).

Farm-level risk factors of swine influenza have been poorly investigated. A study, undertaken in Malaysia, identified farm size, purchase of pigs, presence of domestic pets and avian species on the farm site, and distance to the closest neighbouring farm as major risk indicators of swine influenza (Suriya et al. 2008). In Vietnam, seroprevalence is associated with breeding farms, which produce 20-40 pigs per year (Trevennec et al. 2011). Surprisingly, the presence of poultry on a farm was shown to decrease the risk of swine influenza infection. The authors suggest that instead of poultry, seropositive farms mainly have mammalian pets such as cats and dogs, which has already been found to increase the risk of swine infection by influenza viruses (Suriya et al. 2008). Poultry was not associated to the risk of swine influenza neither in a longitudinal survey in Chinese smallholders (Shu et al. 1996), nor in a crosssectional survey in semi-commercial system in Vietnam (Trevennec et al. 2011). Specific studies have also been conducted in pig farms during avian influenza H5N1 outbreaks in poultry in Taiwan (Shieh et al. 2008), Thailand (Parchariyanon 2006) and Indonesia (Nidom et al. 2010). Even though the avian influenza virus (AIV) has been isolated in pigs, no increase of seroprevalence was observed in swine (Nidom et al. 2010). In the framework of the pandemic H1N1/2009 in pig farms, epidemiological investigations are ongoing but to our knowledge, no result has been published up till now (OFFLU 2010).

Discussion

Data on swine influenza in East and Southeast Asia have been provided in greater quantity and quality over the last 3 years. This increase may be due to greater investment and improvement of surveillance networks on influenza viruses in domestic animals in some countries and a higher interest of the scientific community for swine. Both are direct consequences of the H5N1 HPAI crisis in 2005 and the recent emergence of H1N1 pdm in 2009. The later may be also the reason for which number of synthesis articles or reviews, such as pooled data analyses, has increased in 2009-2010. Nevertheless, published data are provided by a small number of countries, especially China and Thailand. The map of the region (Figure 2) highlights the limited knowledge on viral circulation in the whole region, especially in the centrally located countries. There were no data on swine influenza in Cambodia, Myanmar and Laos although it is likely that these countries are as affected as their neighbours. Varying levels of economic development partially may explain this observation as this is linked to surveillance capacity. In regards to virological results, there have been several emergences of swine influenza in the region, and also many evidences of multiple introductions of North American and European strains. Inter and intra-continental surveillance of gene flows will benefit the region. Furthermore, the isolation of avian origin viruses in pigs underlines the importance to monitor cross-species transmissions of influenza viruses from human or from avian species in this region. This literature review shows low isolation rates and underlines that a virological surveillance requires large sample collections. An option to increase the isolation rate is to collect in clinically affected farms. Unfortunately, no clear case definition of a suspect farm remains and swine infection may be asymptomatic. Furthermore, since the influenza virus is a major agent of porcine respiratory disease complex (PRDC) and may be associated with other pathogens, such as the Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) (Nakharuthai et al. 2008; Yu et al. 2008b), this virus cannot be monitored as a unique pathogen and a global surveillance system of respiratory syndromes on pig farms is required. Such clinical surveillance requires heavy investments to set up an efficient surveillance network, able to report clinical cases on time and to manage large sample collections from collection to the analysis. Some countries will have fewer resources at their disposal than others, and may meet various barriers in the field. Firstly the effective participation of swine workers to report clinically affected animals may vary greatly with the industry sector, which is constituted in East and Southeast Asia of about 80% of small-scale production systems and 20% of medium to large-scale production systems (ACIAR 2002; Cocks P. et al. 2009). In the small-scale and familial production sector, pigs do not represent a major source of familial income (ACIAR 2002; Cocks P. et al. 2009). The lack of diseases awareness due to a weak technical level and the lack of concern for biosecurity may be frequent, causing under-reporting. In the medium to large-scale commercial sector, even though the awareness of swine workers is supposed to be higher (Cocks P. et al. 2009), they may be reluctant to report symptoms to the authorities, which may incur much heavier economic losses (weak or no compensation). Secondly, the lack of reference laboratories with swine influenza expertise is well recognized in East and Southeast Asia (OFFLU 2011), and virological assays, such as real-time PCR, virological isolation or sequencing are not available in all countries (Inui 2007). Given these concerns, the clinical and virological surveillance program of swine influenza and emerging influenza viruses in swine in East and Southeast

Asia must include a capacity building component and the development of partnerships between laboratories for the sharing of expertise and eventually to organize shipments.

In brief, virus isolation is essential to track gene flows, to improve diagnosis, and to produce vaccines. However, in developing countries, where technical capacities and financial resources may be limited, we identify 3 main critical points to develop an efficient surveillance network: the risk of under-reporting of clinical cases, the lack of laboratory capacities and difficulties to manage large amount of samples, including collection, storage and analyses. Surveillance of swine influenza needs to be based on simple, low-cost activities adapted to the context and capacities of each country.

Serologic surveillance is often thought of a limited value because of the endemic status of swine influenza, as well as the use of vaccination in some countries. Thus, positive results are not specific of emergence and we must add that serological test interpretations are challenged by cross-reactivity. This explains why serological studies may be negletected in comparison to virological studies. Nevertheless, the large majority of pig farms in East and Southeast Asia do not vaccinate against influenza. Serological assays give thus the evidence of a past exposure to the pathogen. This may be useful to monitor diseases in species with a short production cycle, since the population is frequently replaced. We suggest that the serological tool may be exploited in East and Southeast Asia, because it offers the opportunity to perform large number of tests easily, rapidly and at low cost.

A serious lack of knowledge about the disease determinants, including farming-systems, commercial practices and environment, was observed. Further studies need to be conducted to identify i) the annual and seasonal pattern of the seroprevalence, ii) the relative proportion of circulating subtypes and iii) at-risk populations. These information will help i) to target the virological surveillance on at-risk time and location, ii) to identify emerging subtypes using adapted serological testings and iii) to plan a sentinel surveillance based on serological profiles. Studies on these various surveillance options are on going and will be discussed after completion.

Conclusion

Published literature on swine influenza in East and Southeast Asia has improved our recent knowledge on virology in the last decade. Improvement of surveillance systems is essential to better track the virus in the whole region, in order to identify inter and intra-continental gene flow. However, molecular analyses require high laboratory capacities and large sample collections. In East and Southeast Asia, surveillance networks are unequally efficient depending on the country. Facing to limited-resource, there is a need to develop modern and high cost-effectiveness alternative strategies. In a context of weak infrastructure and of a lack of laboratory capacities, serological data would help to improve surveillance activities by detecting some past and recent emergences. Adapted diagnostic tools and modern statistical skills should be developed.

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Tables

Table 1: Virological surveys on Swine Influenza in East and Southeast Asia published in the last 10 years.

Type of study	Country	Isolation	Virus	Tested	Subtype	Reference
		rate				
Monitoring in	China	1.69%	84	4957	H_9N_2, H_3N_2	(Peiris et al. 2001)
slaughterhouse	Thailand	0.56%	2	359	H_3N_2	(Parchariyanon 2006)
	Mean	1.62%	86	5316	-	
Monitoring in	Thailand	0.56%	2	359	$H_1N_1, \qquad H_1N_2,$	(Thawatsupha et al.
healthy farms					H_3N_2	<u>2003)</u>
	China	0.44%	9	2024	H_1N_1 , H_3N_2 ,	<u>(Li et al. 2003)</u>
	China	0.81%	16	1085	other	$(I_{i} et al 2004)$
	Cillia	0.0170	10	1905	$H_1N_1, H_1N_2, H_2N_2, H_5N_1, H_5N_1, H_5N_2$	<u>(L1 ct al. 2004)</u>
					H_9N_2	
	China	0.00%		500	H_1N_1 , H_3N_2	<u>(Yu et al. 2007)</u>
	Taiwan	0.00%		881	H_1N_2, H_3N_1	(Shieh et al. 2008)
	China	0.52%	10	1920	H1N1, H3N2,	<u>(Tu et al. 2009)</u>
					H3N8, H5N1	
	China	1.67%	2	120	H1N2	(Xu et al. 2009)
	China	0.82%	29	3546	H1N1, H1N2,	<u>(Bi et al. 2010)</u>
					H3N2	
	Thailand	1.89%	20	1061	H1N1, H3N2,	(OFFLU 2011)
					pH1N1 2009	
	Mean	0.80%	88	11015	-	
SIV outbreak	China	1.92%	4	208	H_9N_2	<u>(Yu et al. 2008b)</u>
investigation	China	4.16%	15	361	H_9N_2	(Cong et al. 2008)
	Thailand	2.83%	3	106	H_3N_2	<u>(Nakharuthai et al.</u>
	China	1.020/	4	200	LIONO	$\frac{2008}{2008}$
	China	0.46%	4	208 650	П9IN2 ЦМ ЦМ	(1 u et al. 2008a)
	China	100.000/	2	2	$11_{11}1_{1}, 11_{11}1_{2}$	(O: Dong & Ly 2000)
	Theiland	100.00% 5.820/	с С	5 120		(Uskehereensuk et al
	Thananu	5.8570	7	120	1131\2	<u>(Lekenaroensuk et al.</u> 2010)
	Thailand	10.00%	2	20	Pandemic	(Sreta et al. 2010)
					H1N1/2009	
	Vietnam	0.90%	(NA)		H1N1, H3N2,	(OFFLU 2011)
					pH1N1 2009	
	Mean	2.45%	41	1676	-	
AIV outbreak	Indonesia	7.41%	52	702	H5N1	(Nidom et al. 2010)
investigation						

Country	Virus	Sample	Proportion	Relative	Age	Farming	Time	Influenza	Type of study	Reference
			of positive	precision		system		context		
China	Type A	32311	20.24%	0.04%	All	Commercial	Annual	NA	Pooled data	(Liu et al. 2011)
	H1	11168	31.14%	0.03%		(various			analysis	
	H3	10139	28.60%	0.03%		densities)				
	H5	5945	1.30%	0.17%						
	H7	1440	0.00%							
	H9	3619	2.38%	0.13%						
East China	Type A		16.78%		_					
South West	Type A	-	19.9%		_					
China					_					
South China	Type A	-	61.4%							
Thailand	Type A	85	100.00%	0.00%	NA	Commercial	Annual	Pig-to-human	Investigation of	(Kitikoon et al. 2011)
								transmission	human influenza	
									in 2 pig farms	
	Type A	553	28.57%	0.03%	Fattening	Commercial	May-	AIV outbreak in	AIV outbreak	(Parchariyanon
	H1N1	553	7.96%	0.07%			October	poultry	investigation	2006)
	H3N2	553	20.61%	0.04%						
	Type A	859	43.89%	0.02%		Commercial	Winter	NA	Cross-sectional	(Damrongwatanapok
	H1N1	367	19.89%	0.04%	Sow	(high density			study	in, Parchariyanon &
	H1N1	136	80.88%	0.01%	Fattening	area)				Pinyochon 2003)
Malaysia	Type A	727	24.35%	0.03%	NA	Commercial	NA	NA	Cross-sectional	(Suriya et al. 2008)
	H1N1	727	12.24%	0.05%					study	
	H3N2	727	12.10%	0.05%						
Indonesia	H5N1	300	1.00%	0.20%	NA	Commercial	November-	AIV outbreak in	Long-term	(Nidom et al. 2010)
							March	poultry	surveillance	
	H5N1	344	0.00%	-	NA	Backyard	December	AIV outbreak in	Cross-sectional	(Santhia et al. 2009)
								poultry	study	
Vietnam	Type A	609	3.12%	0.11%	Fattening	Semi-	April	AIV serology in	Cross-sectional	(Trevennec et al.
						commercial		poultry	study	2011)
	H5N1	3175	0.25%	0.39%	NA	Semi-	September	AIV outbreak in		(Choi et al. 2005)
						commercial	-June	poultry		

Table 2: Serological surveys on swine influenza in East and Southeast Asia in the last 10 years.

Figures legends:

Figure 1: References published on swine influenza in East and Southeast Asia in June 2011 retrieved on PubMed and ISI Web of Knowledge, according to the source of data (A), the country of origin of data (B) and the main topic (C).

Figure 2: Swine influenza in East and Southeast Asia. Isolated subtypes (GenBank), herd-level and individual seroprevalence of swine influenza type A lastly published in China (Liu et al. 2011), Taiwan (Shieh et al. 2008), Malaysia (Suriya et al. 2008), Thailand (Parchariyanon 2006) and Vietnam (Trevennec et al. 2011).





B: Distribution of references per country (n=74)

C: Distribution of references per topic (n=74)

■ China ■ Indonesia ■ Malaysia ■ SEA ■ Thailand ■ Vietnam ■ Vietnam-Thailand











Appendix 1: Selected article for the literature review from PubMed database and Conference proceedings provided by ISI Web of Knowledge SM

Reference number	Source	Year publication	Торіс	Country	Title	Description	Details
1	PubMed	2011	Virology	Thailand	Brief report: molecular characterization of a novel reassorted pandemic H1N1 2009 in Thai pigs.	Kitikoon P, Sreta D, Nuntawan Na Ayudhya S, Wongphatcharachai M, Lapkuntod J, Prakairungnamthip D, Bunpapong N, Suradhat S, Thanawongnuwech R, Amonsin A.	Virus Genes. 2011 Mar 26. [Epub ahead of print]
2	PubMed	2011	Serology	Thailand	Serological evidence of pig-to-human influenza virus transmission on Thai swine farms.	Kitikoon P, Sreta D, Tuanudom R, Amonsin A, Suradhat S, Oraveerakul K, Poovorawan Y, Thanawongnuwech R.	Vet Microbiol. 2011 Mar 24
3	PubMed	2011	Both	China	Seroprevalence and genetic characteristics of five subtypes of influenza A viruses in the Chinese pig population: a pooled data analysis.	Liu W, Wei MT, Tong Y, Tang F, Zhang L, Fang L, Yang H, Cao WC.	Vet J. 2011 Feb
4	Conference	2011	Both	China	Surveillance of influenza viruses in swine in Hong Kong abattoir: methods and feasibility	Ma, E.S.K., Ho, P.L., Cheung, C.Y., Tse, T.M., Chan, A., Vijaykrishana, D., Poon, L.L.M., Guan, Y. & Peiris, J.S.M. 2011	Influenza Other Respi Viruses, vol. 5, pp. 74-6.
5	PubMed	2011	Virology	Vietnam	Isolation of novel triple-reassortant swine H3N2 influenza viruses possessing the hemagglutinin and neuraminidase genes of a seasonal influenza virus in Vietnam in 2010.	Ngo LT, Hiromoto Y, Pham VP, Le HT, Nguyen HT, Le VT, Takemae N, Saito T.	Influenza Other Respi Viruses. 2011 Jun 13. doi: 10.1111/j.1750- 2659.2011.00267.x. [Epub ahead of print]
6	Conference	2011	Sero- epidemiology	Vietnam	Swine influenza in Vietnam: preliminary results of epidemiological studies	Trevennec, K., Mortier, F., Lyazrhi, F., Huong, H.T., Chevalier, V. & Roger, F. 2011	Influenza Other Respi Viruses, vol. 5, pp. 71-3.
7	PubMed	2011	Virology	China	Long-term evolution and transmission dynamics of swine influenza A virus.	Vijaykrishna D, Smith GJ, Pybus OG, Zhu H, Bhatt S, Poon LL, Riley S, Bahl J, Ma SK, Cheung CL, Perera RA, Chen H, Shortridge KF, Webby RJ, Webster RG, Guan Y, Peiris JS.	Nature. 2011 May 26

8	PubMed	2011	Virology	China	Isolation and genetic analysis of a novel triple-reassortant H1N1 influenza virus from a pig in China.	Xu M, Huang Y, Chen J, Huang Z, Zhang J, Zhu Y, Xie S, Chen Q, Wei W, Yang D, Huang X, Xuan H, Xiang H.	Vet Microbiol. 2011 Jan 27
9	PubMed	2011	Virology	China	Genetic diversity of H9N2 influenza viruses from pigs in China: a potential threat to human health?	Yu H, Zhou YJ, Li GX, Ma JH, Yan LP, Wang B, Yang FR, Huang M, Tong GZ.	Vet Microbiol. 2011 Apr 21
10	PubMed	2010	Virology	China	Novel swine influenza virus reassortants in pigs, China.	Bi Y, Fu G, Chen J, Peng J, Sun Y, Wang J, Pu J, Zhang Y, Gao H, Ma G, Tian F, Brown IH, Liu J.	Emerg Infect Dis. 2010 Jul
11	PubMed	2010	Virology	China	Reassortant between human-Like H3N2 and avian H5 subtype influenza A viruses in pigs: a potential public health risk.	Cong Y, Wang G, Guan Z, Chang S, Zhang Q, Yang G, Wang W, Meng Q, Ren W, Wang C, Ding Z.	PLoS One. 2010 Sep 7
12	PubMed	2010	Virology	Thailand	First whole genome characterization of swine influenza virus subtype H3N2 in Thailand.	Lekcharoensuk P, Nanakorn J, Wajjwalku W, Webby R, Chumsing W.	Vet Microbiol. 2010 Oct 26
13	PubMed	2010	Virology	China	Genetic correlation between current circulating H1N1 swine and human influenza viruses.	Lu L, Yin Y, Sun Z, Gao L, Gao GF, Liu S, Sun L, Liu W.	J Clin Virol. 2010 Nov
14	PubMed	2010	Virology	China	[Isolation identification and genetic analysis of an H1N1 subtype isolate of swine influenza virus].	Lu W, Zhang XH, Wang XD, Wu H.	Bing Du Xue Bao. 2010 Sep
15	PubMed	2010	Both	Indonesia	Influenza A (H5N1) viruses from pigs, Indonesia	Nidom CA, Takano R, Yamada S, Sakai- Tagawa Y, Daulay S, Aswadi D, Suzuki T, Suzuki Y, Shinya K, Iwatsuki-Horimoto K, Muramoto Y, Kawaoka Y.	Emerg Infect Dis. 2010 Oct
16	PubMed	2010	Virology	China	[Phylogenetic analysis based on hemagglutinin and neuraminidase genes between swine influenza virus and human influenza A/H3N2 virus strains isolated in Zhejiang province].	Qiu LP, Lu YY, Xu CP.	Zhongguo Yi Miao He Mian Yi. 2010 Apr

17	PubMed	2010	Serology	China	Serological surveillance of influenza A virus infection in swine populations in Fujian province, China: no evidence of naturally occurring H5N1 infection in pigs.	Song XH, Xiao H, Huang Y, Fu G, Jiang B, Kitamura Y, Liu W, Liu D, Gao GF.	Zoonoses Public Health. 2010 Jun
18	PubMed	2010	Virology	Thailand	Pandemic (H1N1) 2009 virus on commercial swine farm, Thailand.	Sreta D, Tantawet S, Na Ayudhya SN, Thontiravong A, Wongphatcharachai M, Lapkuntod J, Bunpapong N, Tuanudom R, Suradhat S, Vimolket L, Poovorawan Y, Thanawongnuwech R, Amonsin A, Kitikoon P.	Emerg Infect Dis. 2010 Oct
19	PubMed	2010	Virology	Thailand	Genetic variations of nucleoprotein gene of influenza A viruses isolated from swine in Thailand.	Thippamom N,Sreta D,Kitikoon P,Thanawongnuwech R,Poovorawan Y,Theamboonlers A,Suwannakarn K,Parchariyanon S,Damrongwatanapokin S,Amonsin A.K	Virol J. 2010 Aug 9
20	PubMed	2010	Virology	China	Reassortment of pandemic H1N1/2009 influenza A virus in swine.	Vijaykrishna D, Poon LL, Zhu HC, Ma SK, Li OT, Cheung CL, Smith GJ, Peiris JS, Guan Y.	Science. 2010 Jun 18
21	PubMed	2010	Virology	China	[Molecular genetic evolution analysis of new A(H1N1) influenza virus].	Zhao L, Liu YH, Liu YH, Wang FL, Lin J, Han CH, Ma M, Ding YL, Ding XN, Wang JL, Yang LF, Pan J, Han JW.	Bing Du Xue Bao. 2010 Mar
22	PubMed	2009	Virology	China	Genetic characterization of H1N1 swine influenza A viruses isolated in eastern China.	Qi X, Pang B, Lu CP.	Virus Genes. 2009 Oct
23	PubMed	2009	Both	Indonesia	Avian influenza A H5N1 infections in Bali Province, Indonesia: a behavioral, virological and seroepidemiological study.	Santhia K, Ramy A, Jayaningsih P, Samaan G, Putra AA, Dibia N, Sulaimin C, Joni G, Leung CY, Sriyal J, Peiris M, Wandra T, Kandun N.	Influenza Other Respi Viruses. 2009 May
24	PubMed	2009	Virology	China	Genetic correlation between H3N2 human and swine influenza viruses.	Sun L, Zhang G, Shu Y, Chen X, Zhu Y, Yang L, Ma G, Kitamura Y, Liu W.	J Clin Virol. 2009 Feb
25	PubMed	2009	Virology	China	Isolation and molecular characterization of equine H3N8 influenza viruses from pigs in China.	Tu J, Zhou H, Jiang T, Li C, Zhang A, Guo X, Zou W, Chen H, Jin M.	Arch Virol. 2009

26	PubMed	2009	Virology	China	Two genotypes of H1N2 swine influenza viruses appeared among pigs in China.	Xu C, Zhu Q, Yang H, Zhang X, Qiao C, Chen Y, Xin X, Chen H.	J Clin Virol. 2009 Oct
27	PubMed	2009	Virology	China	Isolation and genetic characterization of avian-like H1N1 and novel ressortant H1N2 influenza viruses from pigs in China.	Yu H, Zhang PC, Zhou YJ, Li GX, Pan J, Yan LP, Shi XX, Liu HL, Tong GZ.	Biochem Biophys Res Commun. 2009 Aug 21
28	PubMed	2009	Both	China	Further evidence for infection of pigs with human-like H1N1 influenza viruses in China.	Yu H, Zhou YJ, Li GX, Zhang GH, Liu HL, Yan LP, Liao M, Tong GZ.	Virus Res. 2009 Mar
29	PubMed	2008	Virology	Thailand	Genetic characterization of H1N1, H1N2 and H3N2 swine influenza virus in Thailand.	Chutinimitkul S, Thippamom N, Damrongwatanapokin S, Payungporn S, Thanawongnuwech R, Amonsin A, Boonsuk P, Sreta D, Bunpong N, Tantilertcharoen R, Chamnanpood P, Parchariyanon S, Theamboonlers A, Poovorawan Y.	Arch Virol. 2008
30	PubMed	2008	Virology	China	Swine infection with H9N2 influenza viruses in China in 2004.	Cong YL, Wang CF, Yan CM, Peng JS, Jiang ZL, Liu JH.	Virus Genes. 2008 Jun
31	PubMed	2008	Virology	Thailand	Occurrence of swine influenza virus infection in swine with porcine respiratory disease complex.	Nakharuthai C, Boonsoongnern A, Poolperm P, Wajjwalku W, Urairong K, Chumsing W, Lertwitcharasarakul P, Lekcharoensuk P.	Southeast Asian J Trop Med Public Health. 2008 Nov
32	PubMed	2008	Virology	China	Genetic analysis of four porcine avian influenza viruses isolated from Shandong, China.	Shi WF, Gibbs MJ, Zhang YZ, Zhang Z, Zhao XM, Jin X, Zhu CD, Yang MF, Yang NN, Cui YJ, Ji L.	Arch Virol. 2008
33	PubMed	2008	Sero- epidemiology	Malaysia	Seroprevalence and risk factors for influenza A viruses in pigs in Peninsular Malaysia.	Suriya R, Hassan L, Omar AR, Aini I, Tan CG, Lim YS, Kamaruddin MI.	Zoonoses Public Health. 2008 Sep

34	PubMed	2008	Virology	Thailand	Genetic diversity of swine influenza viruses isolated from pigs during 2000 to 2005 in Thailand.	Takemae N, Parchariyanon S, Damrongwatanapokin S, Uchida Y, Ruttanapumma R, Watanabe C, Yamaguchi S, Saito T.	Influenza Other Respi Viruses. 2008 Sep
35	PubMed	2008	Virology	China	Isolation and genetic characterization of avian origin H9N2 influenza viruses from pigs in China.	Yu H, Hua RH, Wei TC, Zhou YJ, Tian ZJ, Li GX, Liu TQ, Tong GZ.	Vet Microbiol. 2008 Sep 18
36	PubMed	2008	Virology	China	Genetic evolution of swine influenza A (H3N2) viruses in China from 1970 to 2006.	Yu H, Hua RH, Zhang Q, Liu TQ, Liu HL, Li GX, Tong GZ.	J Clin Microbiol. 2008 Mar
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