Disease Burden, Vaccine Coverage and Policy Development in China

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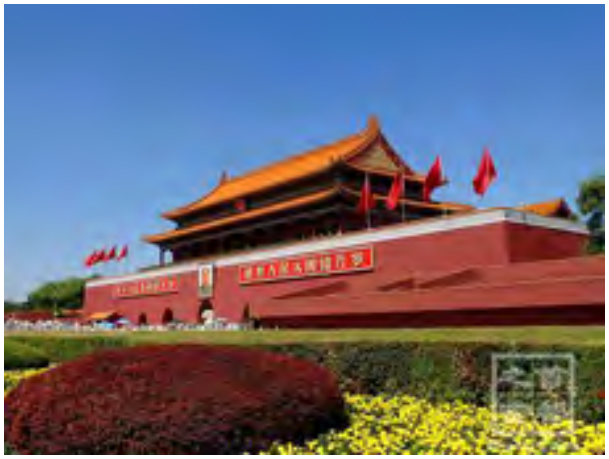
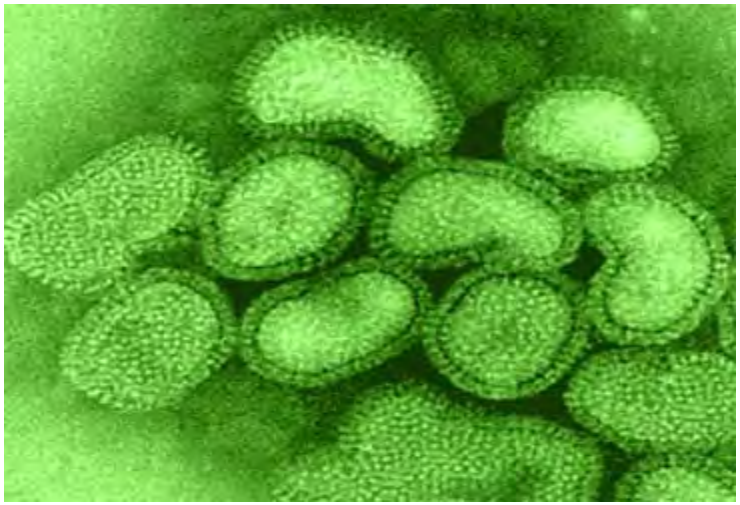
About China

- Total population (2013): 1,393,337,000
- Diverse climate patterns: Temperate Northern region and Subtropical or tropical Southern region
- Difference of urban and rural areas



Seasonal influenza

- Disease burden in China?
- Seasonality and drivers?
- Vaccine supply and demanding?
- Target vaccinated population
- Policy development
- Challenges



Influenza-associated mortality

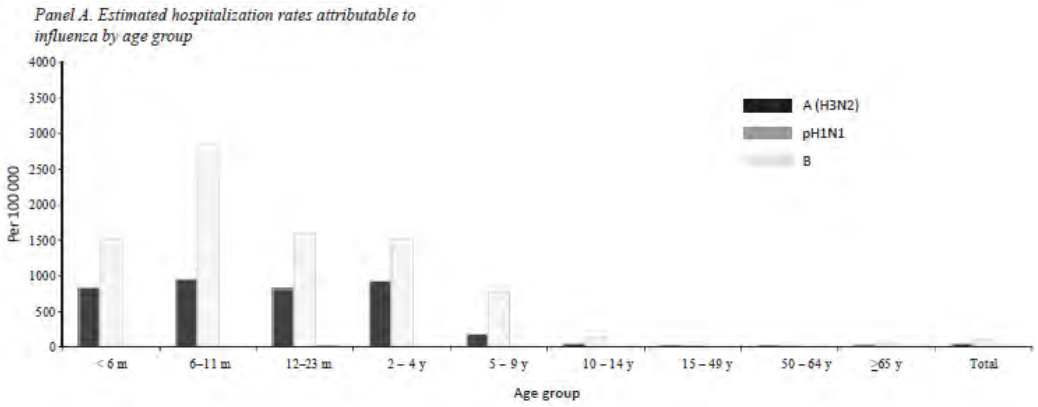
Table 4. **Comparison of estimates of annual influenza-associated excess mortality in China and other selected locations, by age and cause of death as coded[a] or recorded**

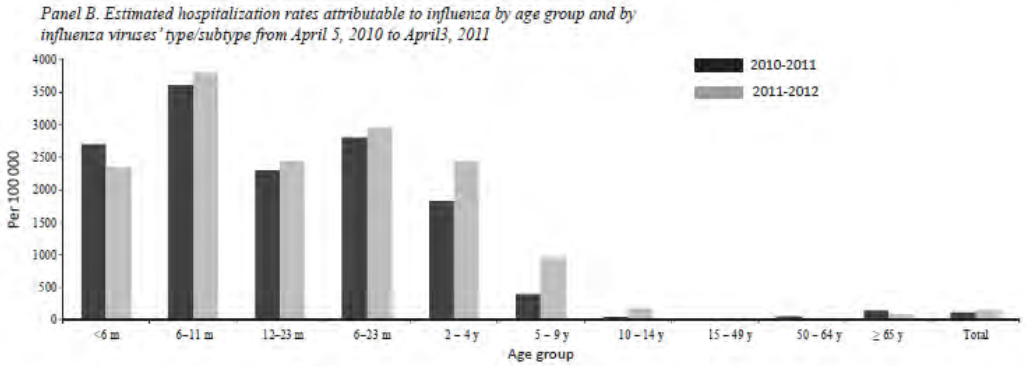
Study area	Model	Study period	Proportion of influenza seasons by:		Excess deaths (per 100 000 people)					
			A(H3N2)	B	All ages			Age ≥ 65 years		
					P&I	R&C	AC	P&I	R&C	AC
Australia[15]	Poisson	1997–2004	NA	NA	NA	NA	NA	15.2	80.4	101.2
China (Guangzhou)[21]	Poisson	2004–2006	2/3	0/3	1.0	9.9	10.6	NA	104.1	111.3
China (northern cities)[b]	Negative binomial	2003–2008	2.5/6	1/6	0.4	12.4	18.0	3.1	106.0	150.8
China (northern cities)[b]	Serfling	2003–2008	2.5/6	1/6	0.4	13.4	17.0	2.6	108.1	131.3
China (southern cities)[b]	Negative binomial	2003–2008	2.5/6	1/6	0.5	8.8	11.3	3.6	64.3	75.4
China (Hong Kong SAR)[19]	Poisson	1996–1999	4/4	0/4	4.1	12.4	16.4	39.3	102.0	136.1
Italy[11,12]	Serfling	1970–2001	21/31	5/31	1.9–2.2	NA	11.6–18.6	12.7–14.2	NA	71.2–115.7
Mexico[16]	Serfling	2000–2008	6/9	1/9	1.5	12.7	15.7	10.4[c]	115.6[c]	147.4[c]
Singapore[22]	Negative binomial	1996–2003	8/8	0/8	2.9	11.9	14.8	46.9	155.4	167.8
United States[4]	Poisson	1990–1999	6/9	2/9	3.1	13.8	19.6	22.1	98.3	132.5
United States[3]	Poisson	1976–2002	14/27	9/27	NA	9.9	NA	NA	72.4	NA
United States[5]	Poisson	1976–2007	17/31	9/31	2.4	9.0	NA	17.0	66.1	NA
United States[10]	Serfling	1980–2001	12/21	6/21	2.9	NA	15.0	22.0	NA	100.0

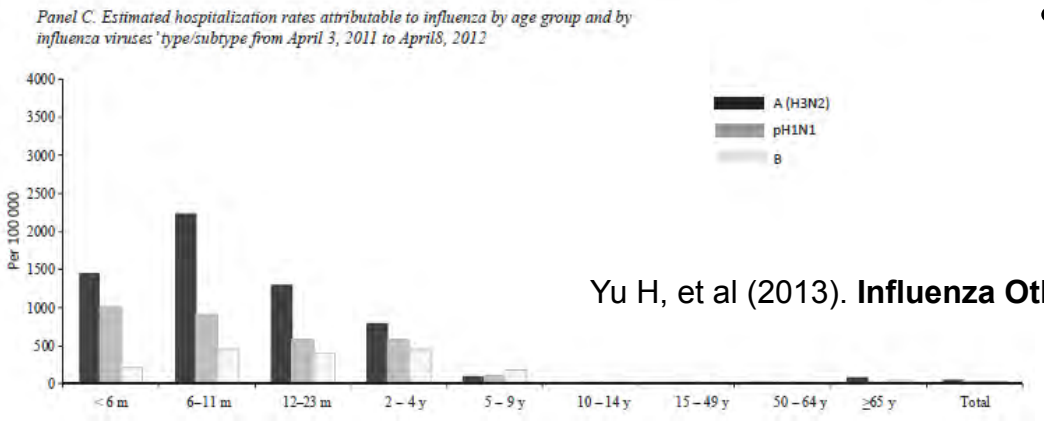
- Excess R&C mortality: 12.4 and 8.8/100,000 in northern and southern
- Most (86%) occurred among people aged >= 65 years
- Higher in B-dominant seasons than H3N2 or H1N1 predominated

Feng L, et al (2012). **Bull World Health Organ** 90(4): 279-288B.

Substantial hospitalization burden







- 13% of SARI cases confirmed influenza, 69% aged <5
- Estimated 115 and 142 SARI hospitalizations per 100,000 during 2010–11 and 2011–12
- Highest rate among children aged 6–11 months

Yu H, et al (2013). **Influenza Other Respiratory Viruses**. DOI:10.1111/irv.12205

Regional variation - mortality impact

Table 2. Influenza-associated excess death rates (per 100 000 people) due to respiratory and circulatory diseases for Northern and Southern Disease Surveillance Point sites

	Rates (95% CI) for all-age* Age-standardized	Rates (%) by virus subtypes				Rates (95% CI) for age ≥65 years	Age 0–64 years	
		Crude rates	A(H1N1)	A(H3N2)	B	A(H1N1)pdm		Rates (95% CI)	% of all-age
Northern sites									
Rural									
2004–2005	14·8 (10·3–44·8)	13·1 (9·1–39·9)	0·3 (2·3)	0·2 (1·6)	12·6 (96·1)	–	161·9 (114·5–465·5)	1·9 (1·1–7·8)	13·4
2005–2006	17·1 (10·6–47·5)	15·3 (9·4–42·6)	12·2 (80·1)	0 (0·1)	3·0 (19·8)	–	185·4 (116·9–492·5)	2·4 (1·2–8·4)	14·3
2006–2007	12·1 (4·5–41·4)	10·8 (4·0–37·4)	5·6 (51·5)	0·3 (2·9)	4·9 (45·7)	–	131·3 (51·5–425·9)	1·6 (0·4–7·7)	13·8
2007–2008	24·4 (18·8–55·1)	22·1 (17·0–50·2)	0·2 (0·7)	0·2 (0·8)	21·7 (98·5)	–	265·2 (207·7–575·6)	3·2 (2·2–9·4)	13·4
2008–2009	10·1 (5·4–35)	9·4 (4·9–32·5)	7·3 (77·8)	0 (0)	2·1 (22·2)	–	108·7 (59·8–357·0)	1·5 (0·6–6·8)	14·7
Mean	15·7 (9·9–44·8)	14·1 (8·9–40·5)	5·1 (36·2)	0·1 (1·0)	8·9 (62·8)	–	170·2 (109·9–462·5)	2·1 (1·1–8·0)	13·8
2009–2010	24·5 (15·4–61·4)	23·0 (14·5–57·7)	0·1 (0·6)	0·1 (0·5)	10·7 (46·5)	12·1 (52·4)	253·6 (159·9–623·3)	4·4 (2·7–12·1)	17·8
Urban									
2004–2005	11·8 (6·5–35·5)	13·1 (7·3–39·1)	0·2 (1·8)	3·9 (29·7)	8·9 (68·5)	–	125·2 (73·4–346·3)	1·8 (0·7–8·2)	12·5
2005–2006	12·9 (7·7–35·8)	14·5 (8·7–40·1)	11·7 (80·6)	0·7 (4·9)	2·1 (14·6)	–	130·5 (80·1–342·3)	2·6 (1·4–8·9)	16·0
2006–2007	12·7 (5·1–34·9)	14·9 (5·9–40·3)	5·7 (38·1)	5·6 (37·7)	3·6 (24·2)	–	125·7 (50·3–327·1)	2·8 (1·1–9·2)	17·1
2007–2008	14·5 (8·6–36·3)	17·9 (10·7–43·7)	0·1 (0·7)	3·1 (17·4)	14·6 (81·9)	–	155·9 (99·6–353·3)	2·1 (0·6–8·4)	10·7
2008–2009	6·9 (3·6–24·4)	8·4 (4·4–29·4)	6·7 (79·5)	0·2 (2·9)	1·5 (17·6)	–	69·1 (36·9–226·5)	1·4 (0·7–6·7)	14·9
Mean	11·8 (6·3–33·4)	13·6 (7·4–38·4)	4·9 (35·9)	2·7 (19·5)	6·1 (44·6)	–	119·9 (67·3–316·0)	2·1 (0·9–8·3)	14·0
2009–2010	11·6 (5·2–35·5)	14·1 (6·4–42·8)	0·1 (0·7)	1·8 (13·1)	6·7 (47·2)	5·5 (39·0)	113·9 (53·5–330·4)	2·6 (0·9–9·6)	16·7
Southern sites									
Rural									
2004–2005	9·8 (1·1–47·6)	9·7 (1·1–47·4)	0 (0)	3·6 (37·4)	6·1 (62·6)	–	104·0 (13·3–495·4)	1·5 (0–8·3)	14·3
2005–2006	6·9 (1·4–40·1)	6·8 (1·4–39·8)	0 (0)	0·6 (8·5)	6·3 (91·5)	–	75·1 (16·1–420·9)	0·9 (0·1–6·6)	12·1
2006–2007	4·2 (0–36·7)	4·3 (0–37·2)	0 (0)	1·6 (38·3)	2·6 (61·7)	–	44·9 (0–383·3)	0·6 (0–6·2)	13·2
2007–2008	9·5 (1·4–42·2)	9·8 (1·4–43·3)	0 (0)	1·3 (13·7)	8·4 (86·3)	–	103·6 (16·4–444·3)	1·3 (0·1–6·9)	11·7
2008–2009	4·4 (0·1–33)	4·5 (0·1–33·3)	0 (0)	0·5 (10·7)	4·0 (89·3)	–	48·7 (1·4–347·8)	0·6 (0–5·3)	11·4
Mean	7·0 (0·8–39·9)	7·0 (0·8–40·2)	0 (0)	1·5 (21·8)	5·5 (78·2)	–	75·2 (9·4–418·0)	1·0 (0–6·7)	12·6
2009–2010	17·7 (6–62·2)	17·8 (6·0–62·4)	0 (0)	1·1 (6·2)	5·3 (29·7)	11·4 (64·2)	188·7 (63·3–657·3)	2·7 (0·9–10·0)	14·1
Urban									
2004–2005	17·9 (8·1–44·5)	19·7 (9·0–48·8)	0·1 (0·4)	6·7 (34·1)	12·9 (65·4)	–	184·2 (86·2–439·3)	3·3 (1·3–9·8)	15·3
2005–2006	13·4 (7·2–36·1)	14·7 (7·9–39·6)	0·5 (3·5)	1·0 (7·1)	13·2 (89·4)	–	130·2 (73·6–340·8)	3·2 (1·3–9·4)	19·4
2006–2007	7·7 (1·4–30·3)	8·5 (1·5–33·4)	0·2 (2·6)	2·9 (34·4)	5·4 (63·0)	–	76·9 (15·3–290·9)	1·6 (0·1–7·4)	17·5
2007–2008	17·4 (9·8–40·3)	19·8 (11·1–45·4)	0 (0)	2·5 (12·4)	17·3 (87·6)	–	178·3 (101·4–398·3)	3·3 (1·7–8·8)	15·2
2008–2009	8·0 (3·2–26·3)	9·2 (3·7–29·9)	0·3 (3·7)	0·7 (8·1)	8·1 (88·2)	–	78·9 (33·4–247·7)	1·8 (0·6–6·8)	17·6
Mean	12·9 (5·9–35·5)	14·3 (6·6–39·3)	0·2 (1·6)	2·7 (19·1)	11·3 (79·2)	–	128·6 (61·5–341·1)	2·6 (1·0–8·4)	16·7
2009–2010	13·7 (5·4–40·1)	15·8 (6·3–46·2)	0·0 (0·1)	1·9 (11·9)	9·9 (62·3)	4·1 (25·7)	136·0 (54·7–391·0)	2·9 (1·1–9·3)	16·8

- The A(H1N1) pandemic posed a mortality and YLL burden comparable to interpandemic influenza in China

Yu H, et al (2013). **Influenza Other Respir Viruses** 7(6): p 1350-60.

pH1N1 mortality and YLL burden

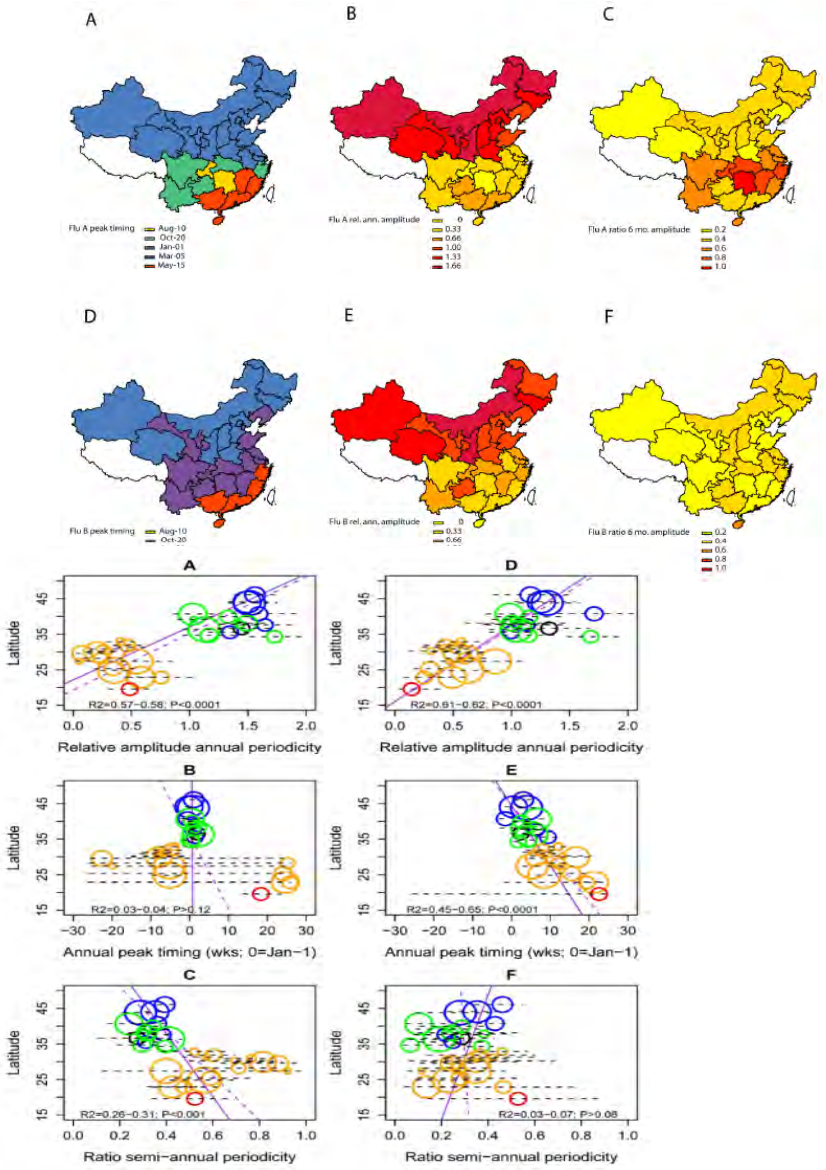
Table 4. Between-country comparison of excess death rates and years of life lost associated with A(H1N1)pdm influenza. Estimates are based on a literature review of studies using an excess mortality modeling approach

Country/area	Approach	Mortality outcome	Excess death		Years of life lost	
			Rates per 100 000 (95% CI)	% in 0–64 years	No. per 100 000 (95% CI)	% in 0–64 years
China (this study)	Negative binomial model	R&C	9·4 (4·6–18·6)	19	174 (87–339)	48
United States[14]	Probability model	All-cause	4·1 (2·9–6·0)	87	–	–
United States[15]	Quasi-Poisson model	R&C	4·8 (3·3–6·4)	79	154 (104–204)*	90
Mexico[23]	Serfling model	R&C	15·4 (12·7–18·1)	40**	358 (293–426)*	72**
Brazil[22]	Serfling model***	Respiratory	1·5	–	–	–
United Kingdom[16]	Poisson model	All-cause	7·4	9	–	–
France[18]	Poisson model	Respiratory	0·98 (0·2–1·9)	30	19 (8–33)	–
Denmark[17]	Poisson model	All-cause	9·8 (7·4–12·1)	11	–	–
The Netherlands[19]	Poisson model	All-cause	3·7 (1·6–5·8)	30	–	–
Australia[21]	Serfling model	All-cause	−6·0 (−12; −0·6)	–	–	
Hong Kong SAR, China[20]	Poisson model	R&C	1·6 (0·4–2·9)	15	–	–

- As in other countries, the pandemic was unusually severe in persons 0–64, accounted for 50% YLL burden.

Yu H, et al (2013). **Influenza Other Respir Viruses** 7(6): p 1350-60.

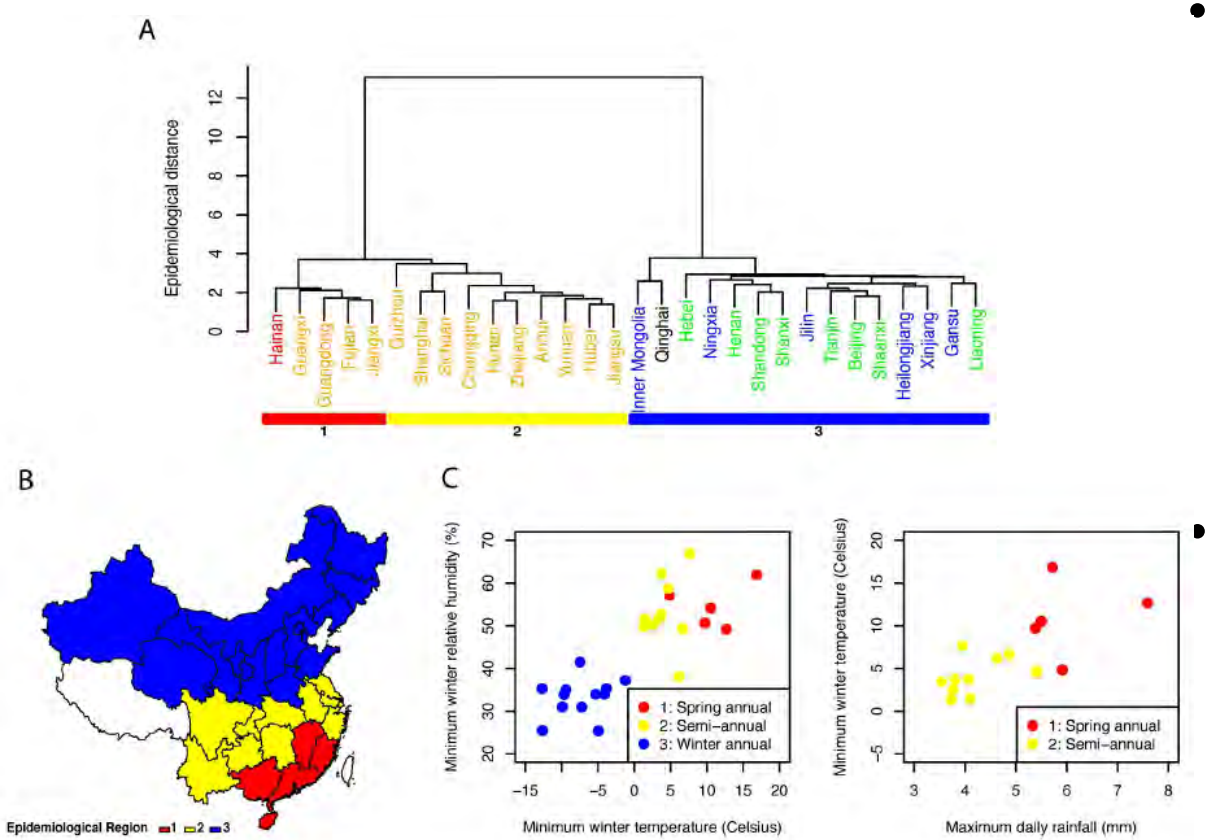
Marked differences - seasonality of A and B



- Annual periodicity of A increased with latitude
  - Nor China (>33^{0}N): in January–February
  - Southernmost regions (<27^{0}N): April–June
  - Intermediate latitudes (27^{0}N-33^{0}N): semi-annual (January–February and June–August)
- B predominated in colder months throughout most of China.

Yu H, et al (2013). **PLoS Med** 10(11): e1001552.

Influenza epidemiological regions and climate predictors



- Regional-specific vaccination strategies would be optimal; annual campaigns initiated 4–6 m apart in Nor and Sou China.
- Climate factors were the strongest predictors of seasonality, minimum temperature, hours of sunshine, and maximum rainfall.

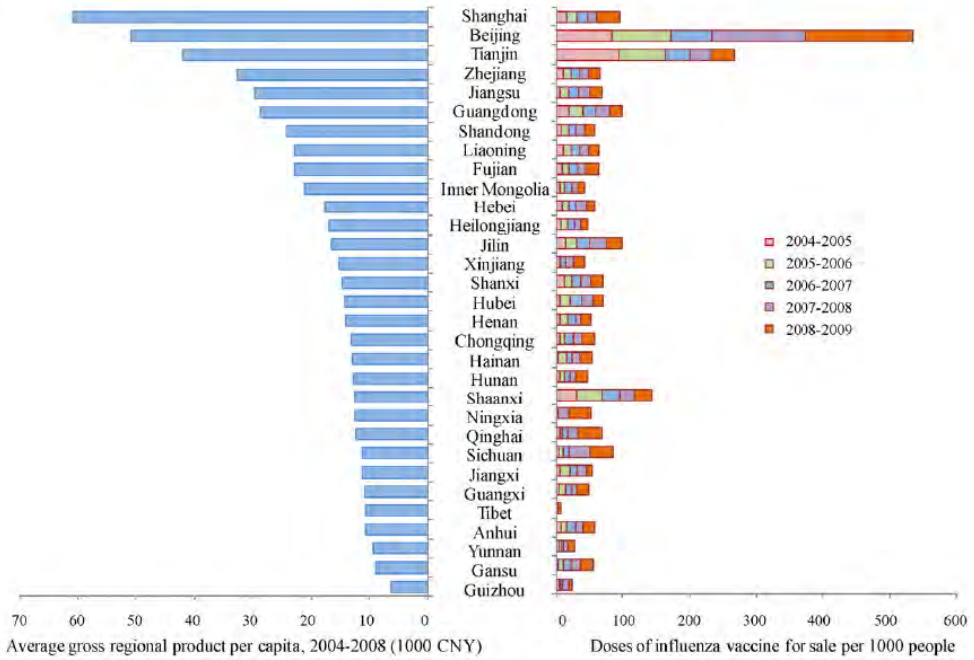
Yu H, et al (2013). **PLoS Med** 10(11): e1001552.

Types and specifications of influenza vaccines marketed in China (by 2014)

Manufacturers	Vaccine Type	Specification
Tasly skinner biological technology (Tianjin) co., LTD	subunit	0.5 ml
Lanzhou institute of biological products co. LTD	split	0.5 ml, 0.25 ml
	wholevirus	1.0 ml
Beijing Tiantan Biological products co., LTD	wholevirus	1.0 ml, 0.5 ml
	split	0.5 ml
Changchun Changsheng biotechnology co., LTD	wholevirus	0.5 ml
Jiangsu Xiansheng WeiKe biological pharmaceutical co., LT	split	0.5 ml, 0.25 ml
Zhejiang Tianyuan Biological pharmaceutical co., LTD	split	0.5 ml, 0.25 ml
Dalian Hissen biological pharmaceutical co., LTD	split	0.5 ml
Shanghai institute of biological products co., LTD	split	0.5 ml, 0.25 ml
Changchun institute of biological products co., LTD	split	0.5 ml, 0.25 ml
Hualan biological product co., LTD	split	0.5 ml, 0.25 ml
Dalian Aleph biological pharmaceutical co., LTD	split	0.5 ml, 0.25 ml
Beijing Sinovac biotech co., LTD	split	0.5 ml, 0.25 ml
Abbott Trading (Shanghai) co., LTD	subunit	0.5 ml
Shenzhen Sanofi Pasteur biological products co., LTD	split	0.5 ml, 0.25 ml
Glaxosmithkline (China) investment co., LTD	split	0.5 ml, 0.25 ml
The Swiss Crucell co., LTD	subunit (virus particle)	0.5 ml

Feng L et al. (2015) **Human Vaccines & Immunotherapeutics** 11:6, 1--25;

Seasonal influenza vaccine supply and target population

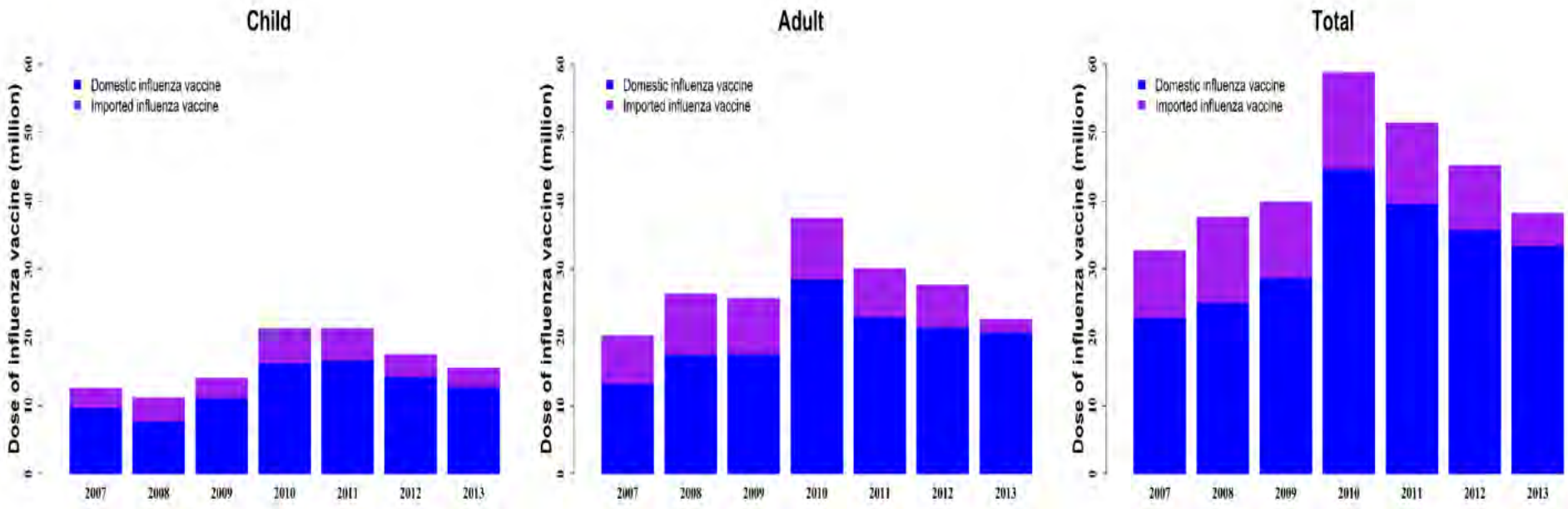


Feng L, et al (2010). **Vaccine** 28(41): 6778-6782.

Table 3
Estimation of target population for influenza vaccination in China.

	Population (in millions)
Chinese population by age group [9]	
0–4 years	68.1
5–9 years	72.6
10–19 years	193.9
20–59 years	807.4
≥60 years	186.1
Total	1328.0
Target population for seasonal influenza vaccination	
Children aged 6–59 months	61.3 [9]
Persons aged ≥60 years	186.1 [9]
Persons aged 5–59 years who have medical conditions that put them at higher risk for influenza-related complications[a]	84.0 [9–19]
Pregnant women[b]	11.6 [19–21]
Health care personnel	6.2 [9]
Household contacts and caregivers of children aged <5 years and adults aged ≥60 years[c]	136.1
Household contacts and caregivers of persons aged 5–59 years with chronic medical conditions[c]	84.0
Staff of kindergartens and nursery	1.4 [9]
Total	570.6

Vaccine supply and estimated coverage, 2007-2013



- The annual supply for both children and adults: 32.8 million in 2007, 58.9 million in 2010, 38.2 million in 2013
- An average coverage of 2.0% and 1.1% (with maximum of 2.7% and 1.8% in 2010) of total target population
- 25% and 50% wastage

Timeline of China's Seasonal Influenza Vaccination Recommendation

- 2003 **MoH**
- 2005 **MoH**
- 2007 **China CDC**
- 2008 **China CDC**
- 2009 **China CDC**
- 2010 **China CDC**
- 2014 **China CDC**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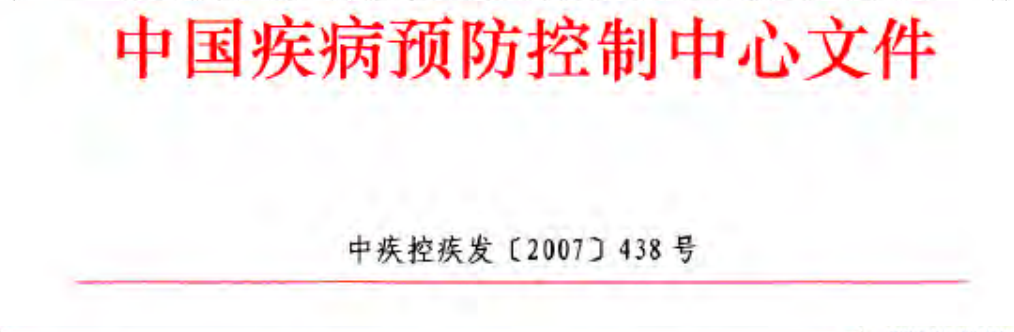
各省、自治区、直辖市卫生厅局，新疆生产建设兵团卫生局：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PRODUCT REVIEW

Human Vaccines & Immunotherapeutics 11:6, 1–25; April 1, 2015; Copyright © 2015 Taylor & Francis Group, LLC

Technical guidelines for the application of seasonal influenza vaccine in China (2014–2015)

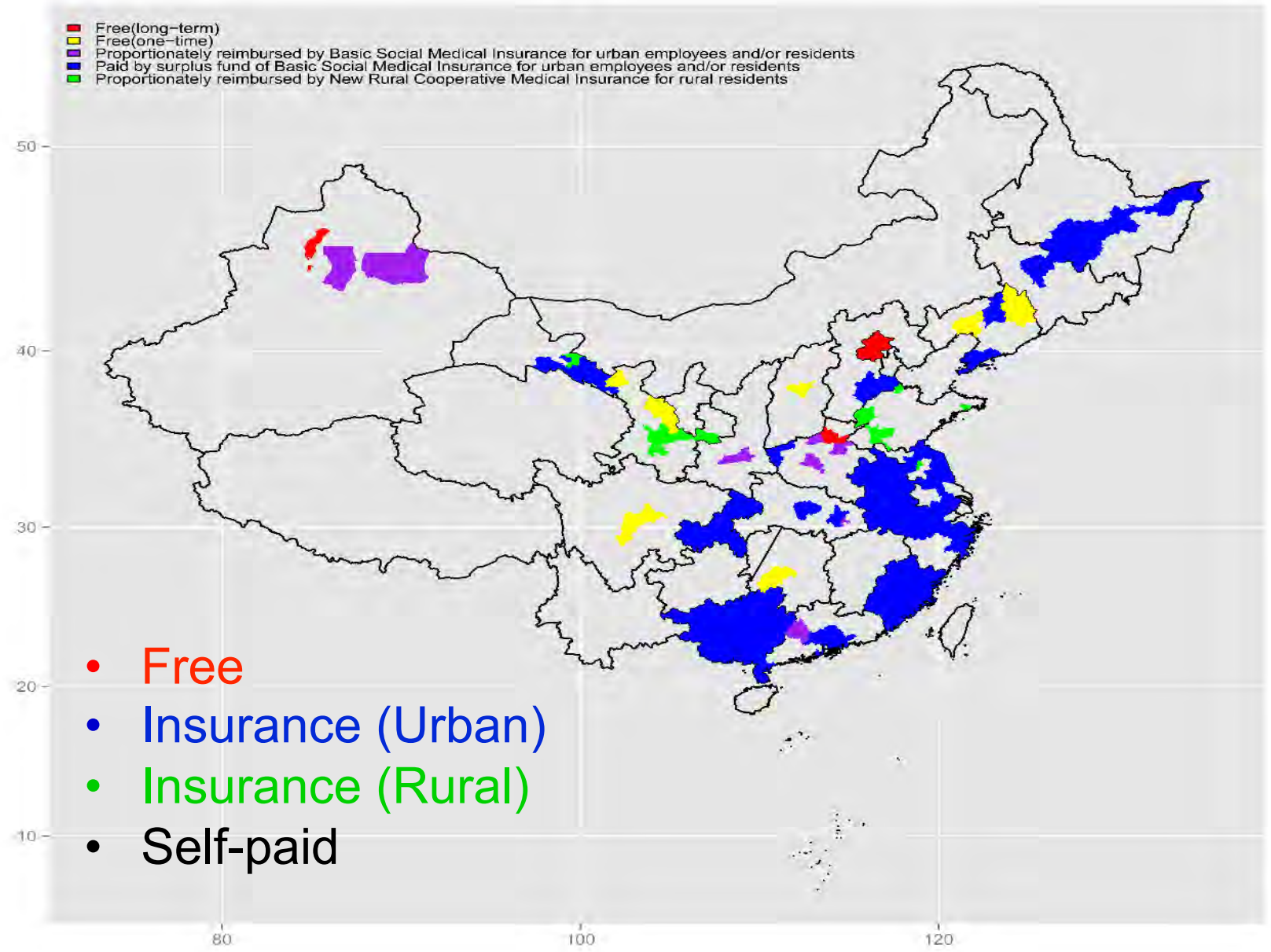
Luzhao Feng[1], Peng Yang[2], Tao Zhang[3], Juan Yang[1], Chuanxi Fu[4], Ying Qin[1], Yi Zhang[2], Chunna Ma[2], Zhaoqiu Liu[5], Quanyi Wang[2], Genming Zhao[3], and Hongjie Yu[1,*]

[1]Key Laboratory of Surveillance and Early-warning on Infectious Disease; Division of Infectious Disease; Chinese Center for Disease Control and Prevention; Beijing, China; [2]Beijing Center for Disease Control and Prevention; Beijing, China; [3]School of Public Health; Fudan University; Shanghai, China; [4]Guangzhou Center for Disease Control and Prevention; Guangzhou, China; [5]Hua Xin Hospital; First Hospital of Tsinghua University; Beijing, China

Recommended priority groups for influenza vaccination

- Pregnant women
- The family members and caregivers of infants <6 months
- Infants and children aged 6–23 months old
- Children aged 2–5 y
- Elderly ≥60 y of age
- Persons with specific chronic underlying diseases
- Healthcare workers

Diverse Reimbursement Policy for influenza vaccination in 2013



GAP Analysis for China

- Lack of scientific evidence for recommendation
  - ✓ Health and economic burden
  - ✓ Vaccine Effectiveness and Cost-effectiveness
  - ✓ Cost and efficiency analysis of different strategy
- Perception of public, government and health-care providers on influenza and vaccination
- Coverage rates were rather low, and most vaccination concentrated on school age children and young adults
- Vaccination services patterns

Challenges

- Strengthen vaccination strategy related research
  - ✓ Health and social impact (epidemiology and disease burden)
  - ✓ Protection effectiveness and economic evaluation of influenza vaccination by sub-population
  - ✓ Novel vaccine R&D
- Encourage local government to establish public reimbursement policy for high-risk population
- Strengthen collaboration with health-care faculties and community, and improve perception on flu and vaccine
- Improve the vaccination services (Adult immunization, and immunization services by health-care faculties)
- ……

Thank you for your attention