



10th International Global Virus Network Meeting: Eradication and Control of (Re-)Emerging Viruses

November 28 - 30, 2018 - Les Pensieres Center for Global Health, Veyrier du Lac (France)

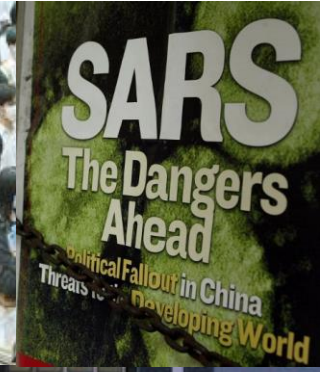
SARS “eradication”

Leo Poon



**HKU
Med**

LKS Faculty of Medicine
School of Public Health
香港大學公共衛生學院



Overview:

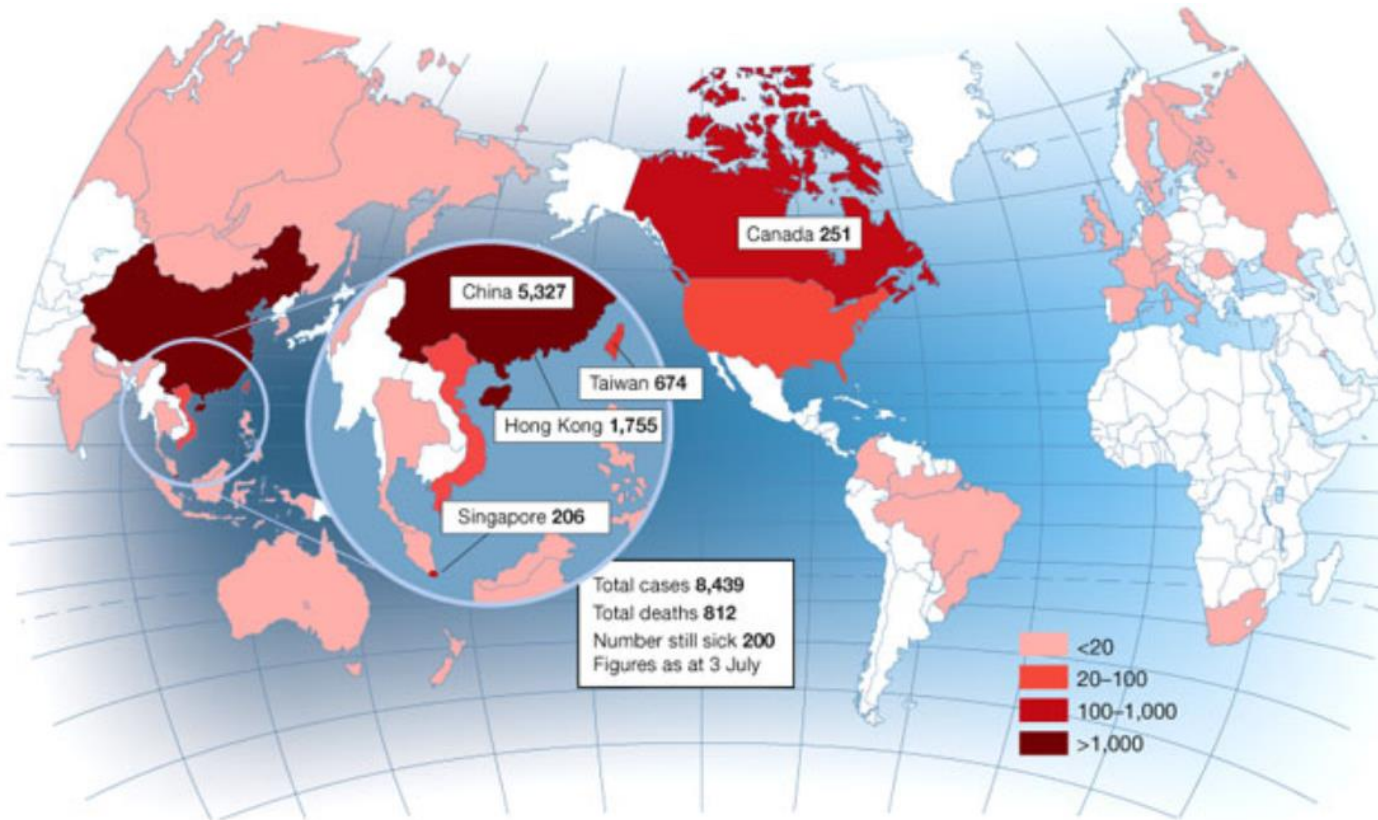
- History
- How did we contain SARS
- Look forward



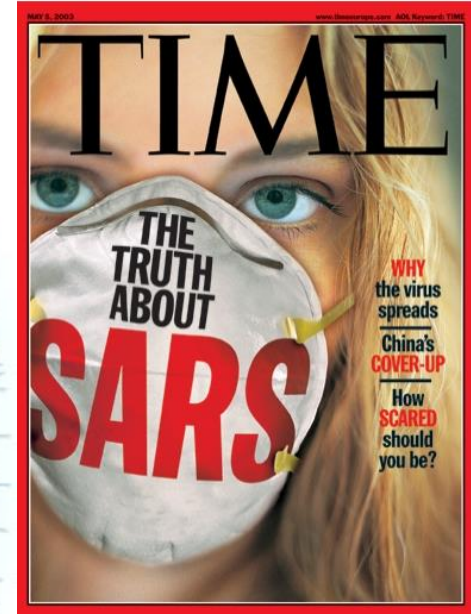
HOW SARS HIT
HONG KONG IN 2003



SARS: the first pandemic of the 21st century



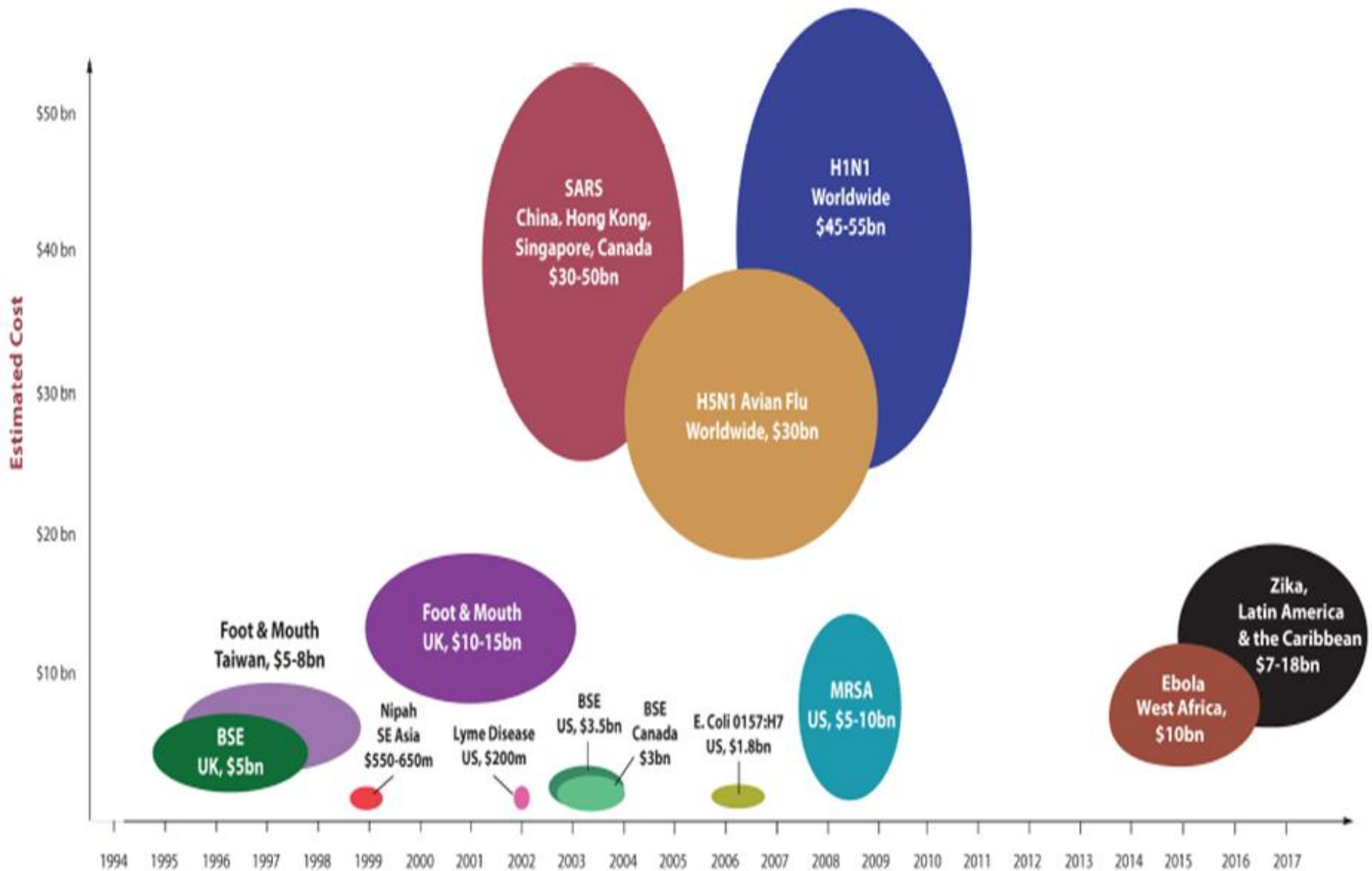
<http://www.nature.com/nature/focus/sars/map.html>



5 July

–SARS was contained worldwide

Economic Impact of selected infectious disease outbreaks



Figures are estimates and are presented as relative size. Based upon bio-era, World Bank, and UNDP data. Chart updated by EcoHealth Alliance.

SARS outbreak- emerged from southern China

Official index case: Nov 2002



Lancet, 2004

6 Feb 2003: 218 cases in this province

Rumours of SARS in early 2003.....

Fear factor!



Fujian province in February 11, 2003

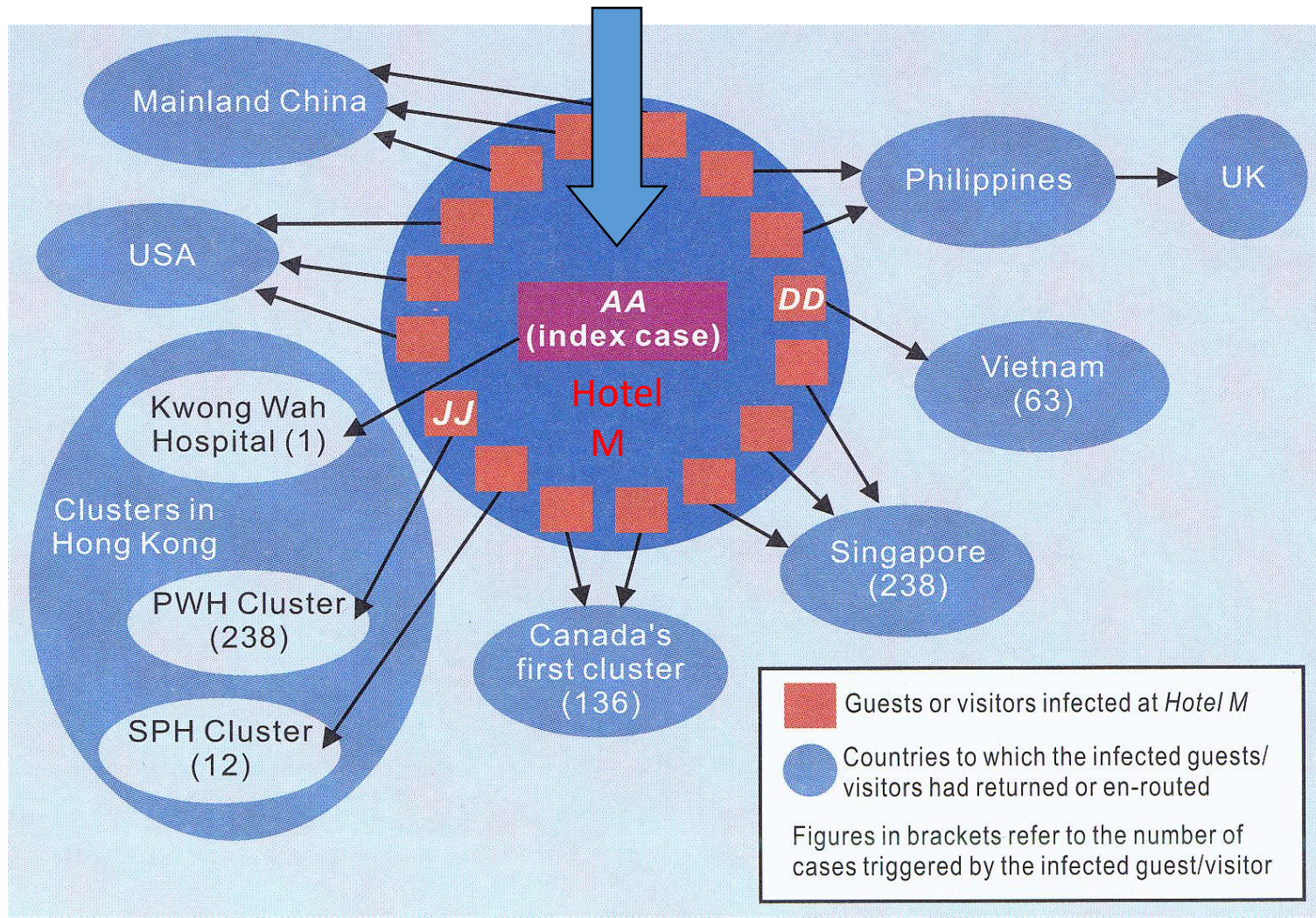
Sale price of a bottle of vinegar:
10 yuan to 1000 yuan



H5N1 pandemic scare:
2 imported H5N1 cases in Hong Kong

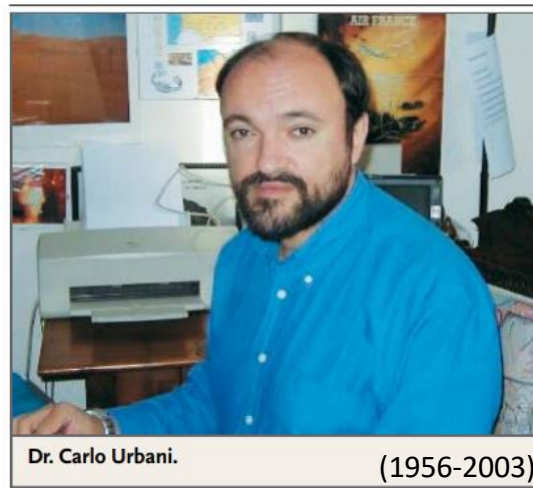
The Hong Kong outbreak

21 Feb 2003 AA: Index case
Guangzhou



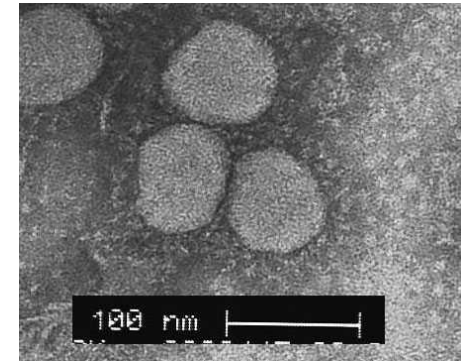
SARS

- 11th March 03:
 - 20 HCW in Hanoi
 - 23 HCW in PWH, Hong Kong
- 12th March 03: WHO Global alert
- 14th March 03: Canada
- 15th March 03: Singapore, Germany
- 15th March 03: WHO Travel advisory
- 17th March 03: WHO Network of SARS Labs



A Novel coronavirus is associated with SARS

March 2003, Isolation of SARS CoV



Articles

Lancet

Coronavirus as a possible cause of severe acute respiratory syndrome

*J S M Peiris, S T Lai, L L M Poon, Y Guan, L Y C Yam, W Lim, J Nicholls, W K S Yee, W W Yan, M T Cheung, V C C Cheng, K H Chan, D N C Tsang, R W H Yung, T K Ng, K Y Yuen, and members of the SARS study group**

Tools for
Laboratory diagnosis
Epidemiological studies
Clinical management
etc

The NEW ENGLAND JOURNAL of MEDICINE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome

Christian Drosten, M.D., Stephan Günther, M.D., Wolfgang Preiser, M.D., Sylvie van der Werf, Ph.D., Hans-Reinhard Brodt, M.D., Stephan Becker, Ph.D., Holger Rabenau, Ph.D., Marcus Panning, M.D., Larissa Kolesnikova, Ph.D., Ron A.M. Fouchier, Ph.D., Annemarie Berger, Ph.D., Ana-Maria Burguière, Ph.D., Jindrich Cinatl, Ph.D., Markus Eickmann, Ph.D., Nicolas Escriou, Ph.D., Klaus Grywna, M.Sc., Stefanie Kramme, M.D., Jean-Claude Manuguerra, Ph.D., Stefanie Müller, M.Sc., Volker Rickerts, M.D., Martin Stürmer, Ph.D., Simon Vieth, Hans-Dieter Klenk, M.D., Albert D.M.E. Osterhaus, Ph.D., Herbert Schmitz, M.D., and Hans Wilhelm Doerr, M.D.

ORIGINAL ARTICLE

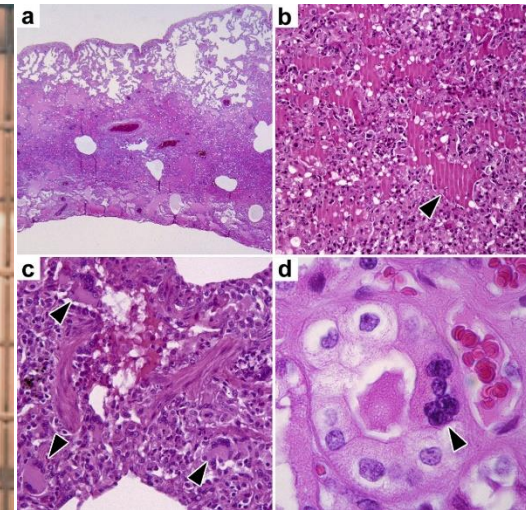
A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome

Thomas G. Ksiazek, D.V.M., Ph.D., Dean Erdman, Dr. P.H., Cynthia Goldsmith, M.S., Sherif R. Zaki, M.D., Ph.D., Teresa Peret, Ph.D., Shannon Emery, Suxiang Tong, Ph.D., Carlo Urbani, M.D.,* James A. Comer, Ph.D., M.P.H., Wilina Lim, Pierre E. Rollin, M.D., Scott Dowell, M.D., M.P.H., Ai-Ee Ling, M.D., Charles Humphrey, Ph.D., Wun-Ju Shieh, M.D., Jeannette Guarner, M.D., Christopher D. Paddock, M.D., Paul Rota, Ph.D., Barry Fields, Ph.D., Joseph DeRisi, Ph.D., Jyh-Yuan Yang, Ph.D., Nancy Cox, Ph.D., James Hughes, M.D., James W. LeDuc, Ph.D., William Bellini, Ph.D., Larry J. Anderson, M.D., and the SARS Working Group†

Koch's postulates fulfilled for SARS coronavirus

- ✓ • The microbe must be present in every case of the disease
- ✓ • The microbe must be isolated from the diseased host and grown in pure culture
- ✓ • The disease must be reproduced when the microbe is introduced into a non-disease susceptible host (animal)
- ✓ • The microbe must be recovered from an experimentally-infected host

Newly discovered coronavirus as the primary cause of SARS!



Nature 2003, 423: 240.

How did we stop the SARS epidemic?

a) Use of highly non-specific case definitions



As more information has become available, WHO-recommended SARS case definitions have been revised as follows:

Suspect Case

A person presenting after 1 February 2003 with history of :

- high fever ($>38^{\circ}\text{C}$)

AND

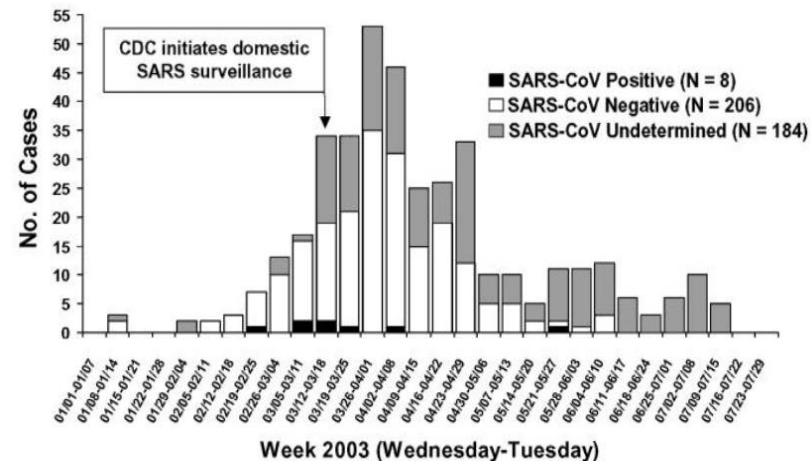
- one or more respiratory symptoms including cough, shortness of breath, difficulty breathing
- close contact* with a person who has been diagnosed with SARS
- recent history of travel to areas reporting cases of SARS

Probable Case

A suspect case with chest x-ray findings of pneumonia or Respiratory Distress Syndrome

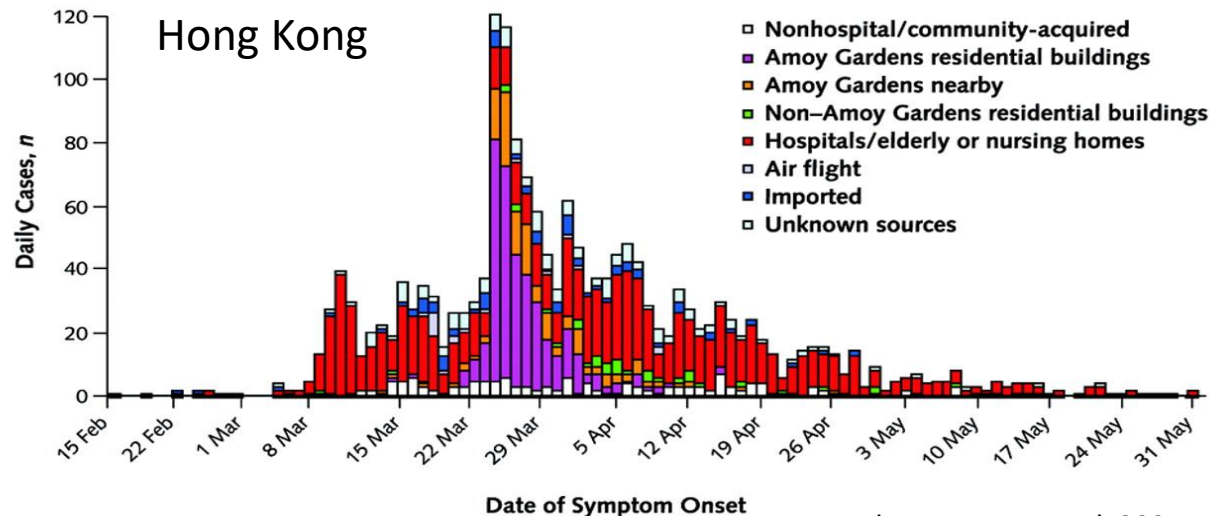
OR

A person with an unexplained respiratory illness resulting in death, with an autopsy examination demonstrating the pathology of Respiratory Distress Syndrome without an identifiable cause.

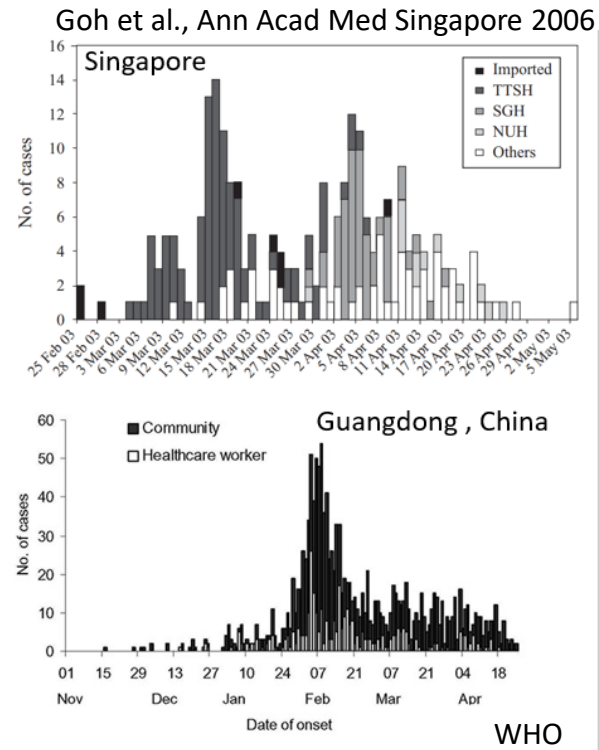


B) Strict Infectious disease control

SARS outbreak in hospital settings



Leung et al. Ann Intern Med. 2004



- Prompt guideline on management of severe acute respiratory syndrome (SARS)
 - PPE
 - Patient management
 - etc

Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS)

W H Seto, D Tsang, R W H Yung, T Y Ching, T K Ng, M Ho, L M Ho, J S M Peiris, and Advisors of Expert SARS group of Hospital Authority*

*Members listed at end of report

Lancet 2003

C) Aggressive contact tracing and quarantine policy

Isolation

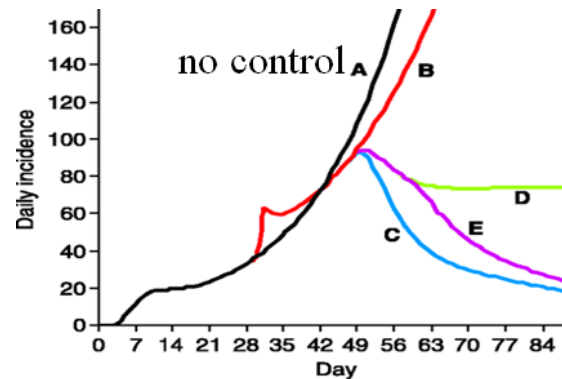


School closure



Cumulative numbers of persons under quarantine during the SARS outbreak, Taiwan, 2003, and the quarantined SARS patients classified by their status*

Level and reason for quarantine	No. quarantined persons	No. quarantined officially confirmed SARS-CoV case-patients	No. quarantined laboratory-confirmed, antibody-positive SARS case-patients
Level A			
Family members	7,921	8	2
Classmates and teachers	16,564	1	0
Healthcare workers	2,409	0	3
Others†	19,224	6‡	1
All others§	9,514	2	1
Subtotal	55,632	17	7
Level B	95,828	0	0
Total	151,460	17	7



50% drop in population contact rates
50% reduction in hospital transmission

70% reduction in total transmission

D) Early travel advisory and intensive updates from WHO

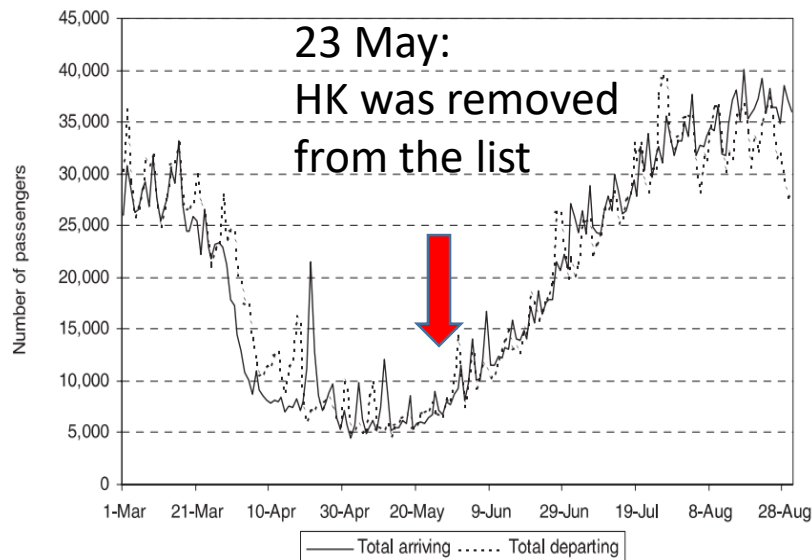


Emergencies preparedness, response

World Health Organization issues emergency travel advisory

15 March 2003

Figure 3. Number of arriving and departing air passengers in Hong Kong (1 March 2003 to 31 August 2003)



Emergencies preparedness, response

Situation Updates - SARS

96 updates within 4 months

Numerous press conferences for general public and teleconferences for expert group meetings

Transparency and accountability!

E) We were lucky in some sense.....

i) SARS patients were not highly infectious in the first week of disease onset.

ii) SARS-CoV is not highly transmissible

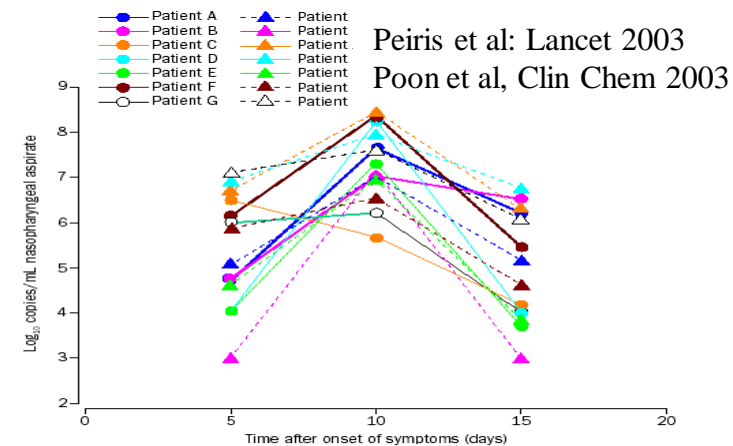
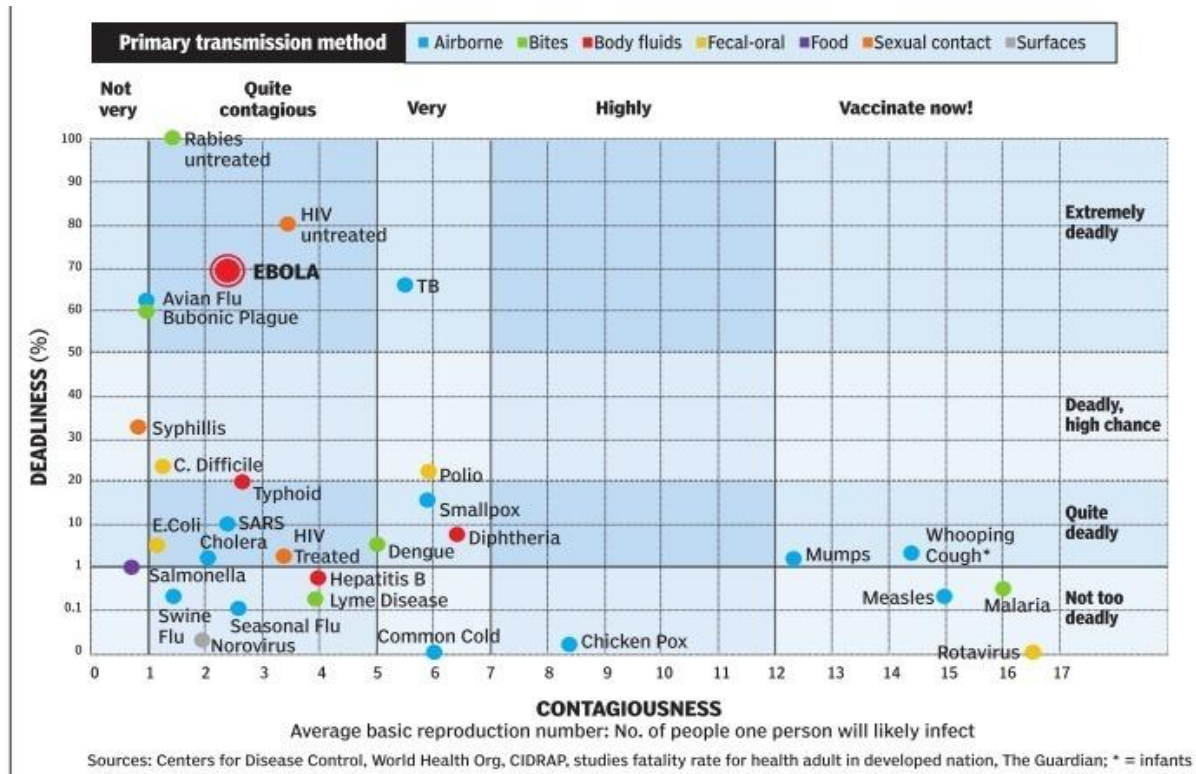
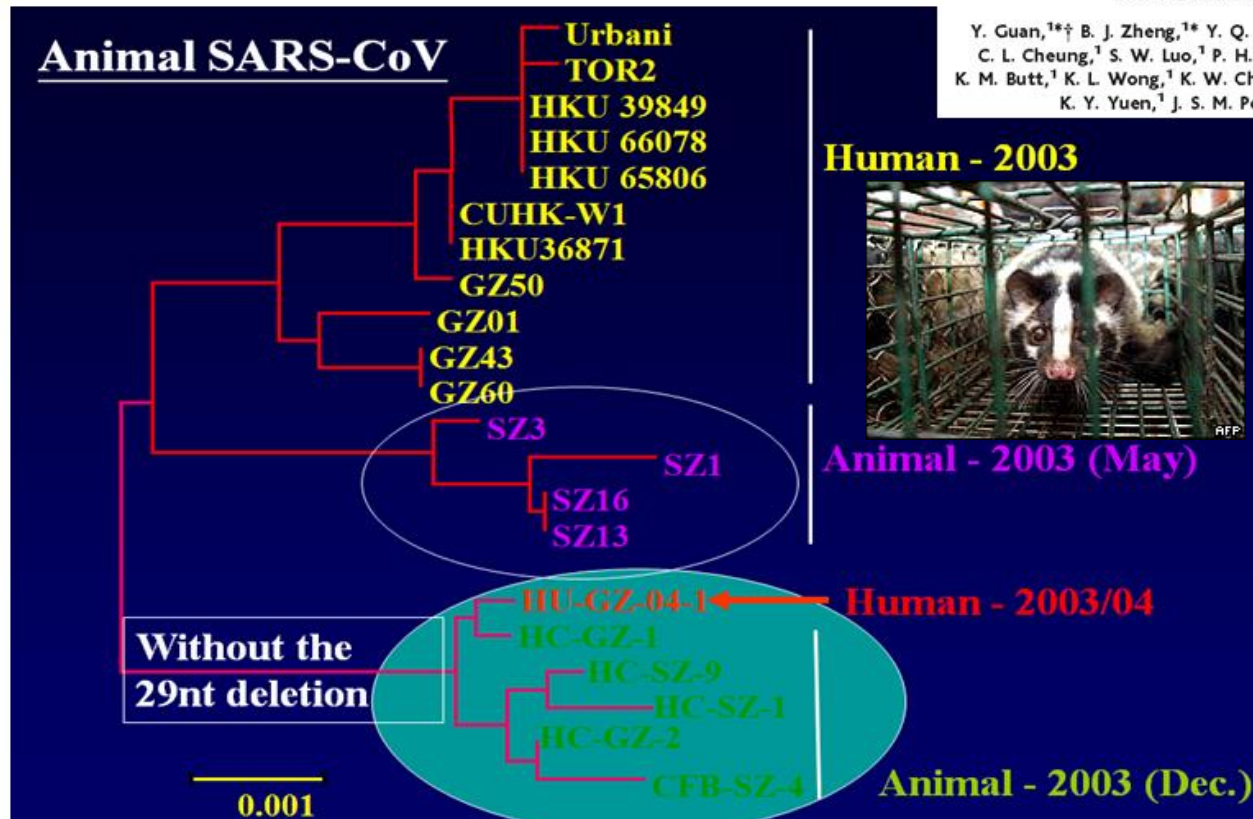


Figure 4: Sequential quantitative RT-PCR for SARS-associated coronavirus in nasopharyngeal aspirates of 14 SARS patients



F) Managed to find the animal source and prompt control measures

SARS is emerged from animals



Science 2003
Isolation and Characterization of
Viruses Related to the SARS
Coronavirus from Animals in
Southern China

Y. Guan,^{1*} B. J. Zheng,^{1*} Y. Q. He,² X. L. Liu,² Z. X. Zhuang,²
C. L. Cheung,¹ S. W. Luo,¹ P. H. Li,¹ L. J. Zhang,¹ Y. J. Guan,¹
K. M. Butt,¹ K. L. Wong,¹ K. W. Chan,³ W. Lim,⁴ K. F. Shortridge,¹
K. Y. Yuen,¹ J. S. M. Peiris,¹ L. L. M. Poon¹



May 2003: Banning of selling masked palm civets in China

Aug 2003: The ban was relaxed

Jan 2004: New human cases, leading to a complete ban of selling masked palm civets

4 laboratory infections in 2003-2004 , one led to a human-to-human transmission.

Will SARS come back?

Chinese Horseshoe bats as the nature reservoir of SARS-like coronaviruses

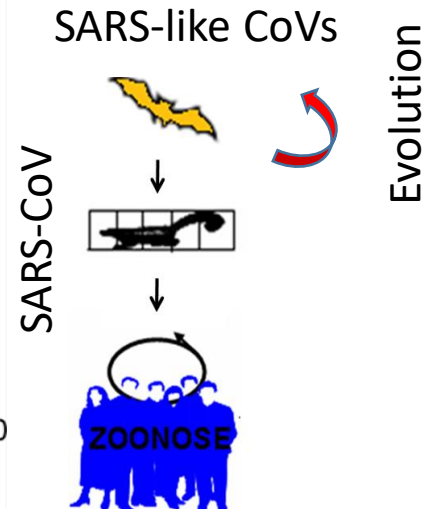
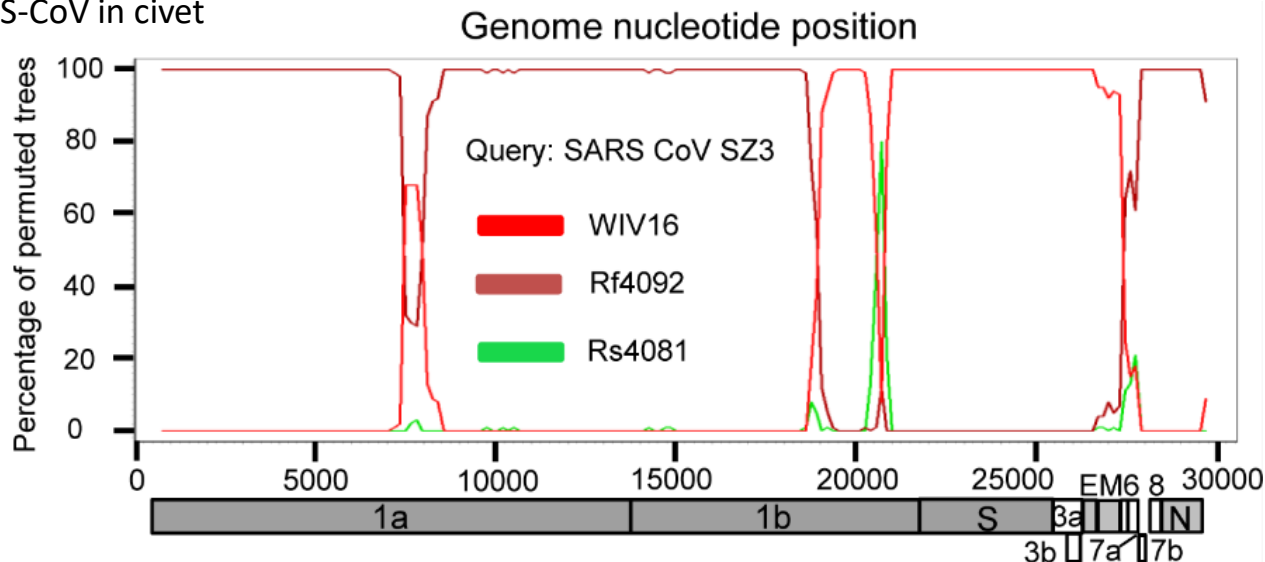
All precursor viruses for SARS-CoV can be found in the same cave at Yunnan (Hu et al., PLoS Path 2017)



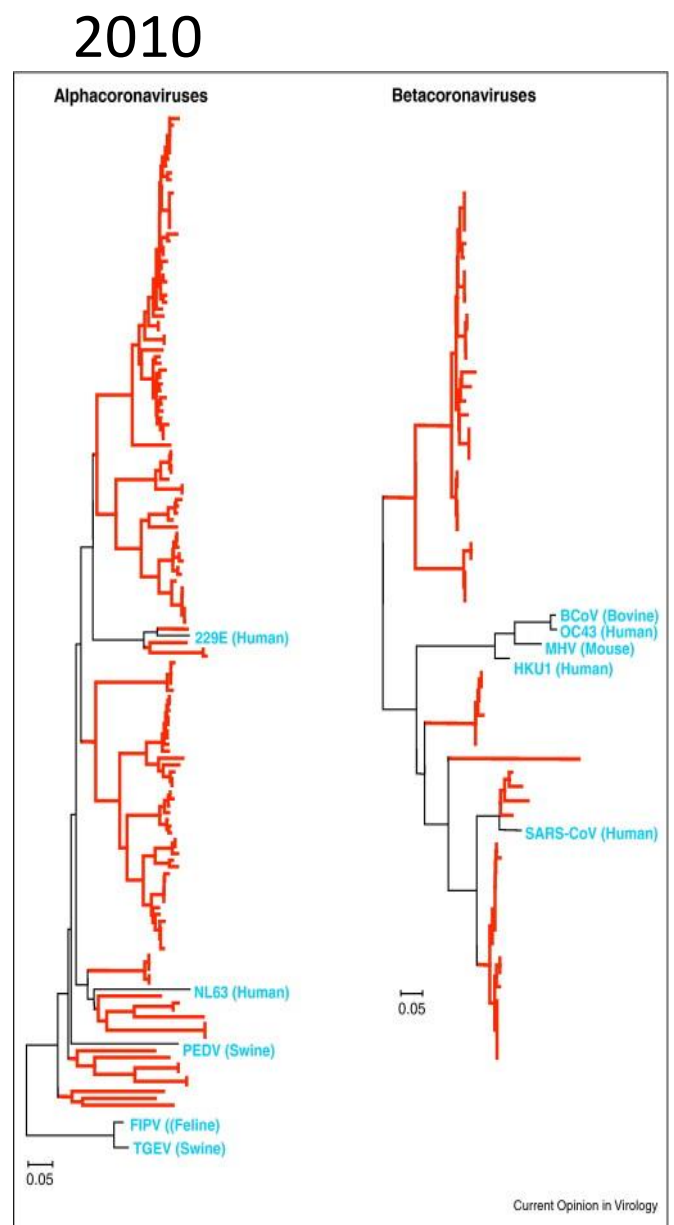
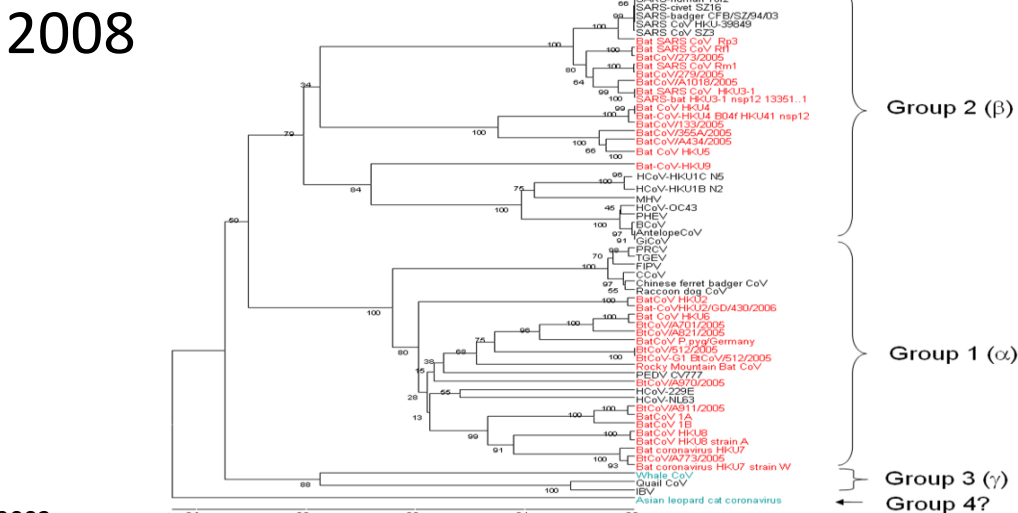
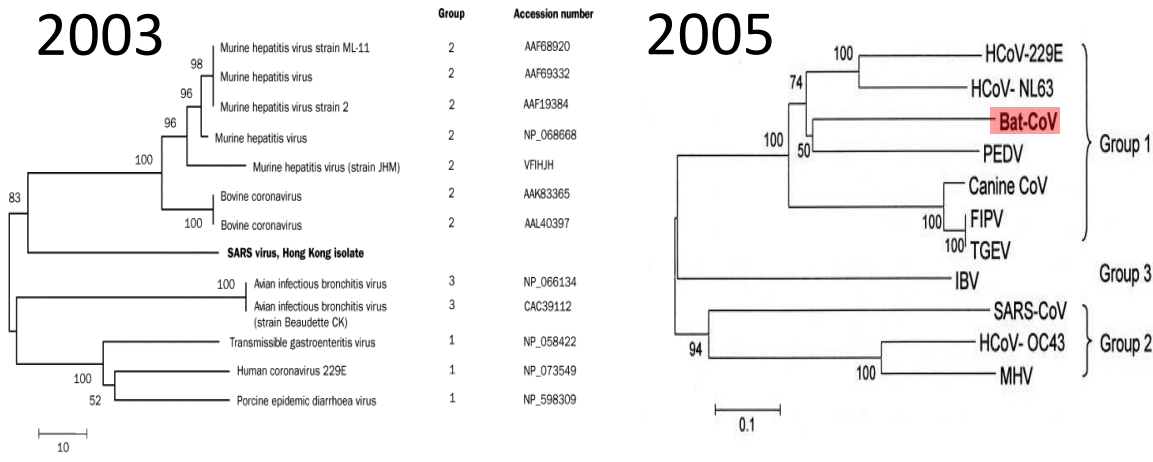
Lau et al., PNAS 2004
Li et al., Science 2005

SARS-CoV might be generated by recombination events:

SARS-CoV in civet

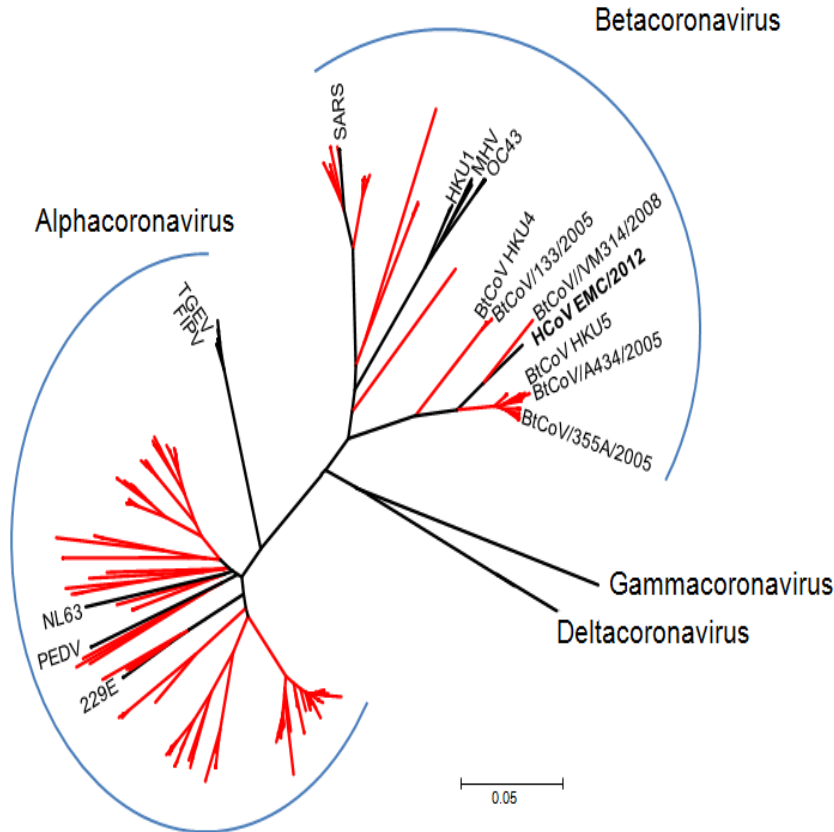


Explosion on coronaviruses of bat origins since 2003



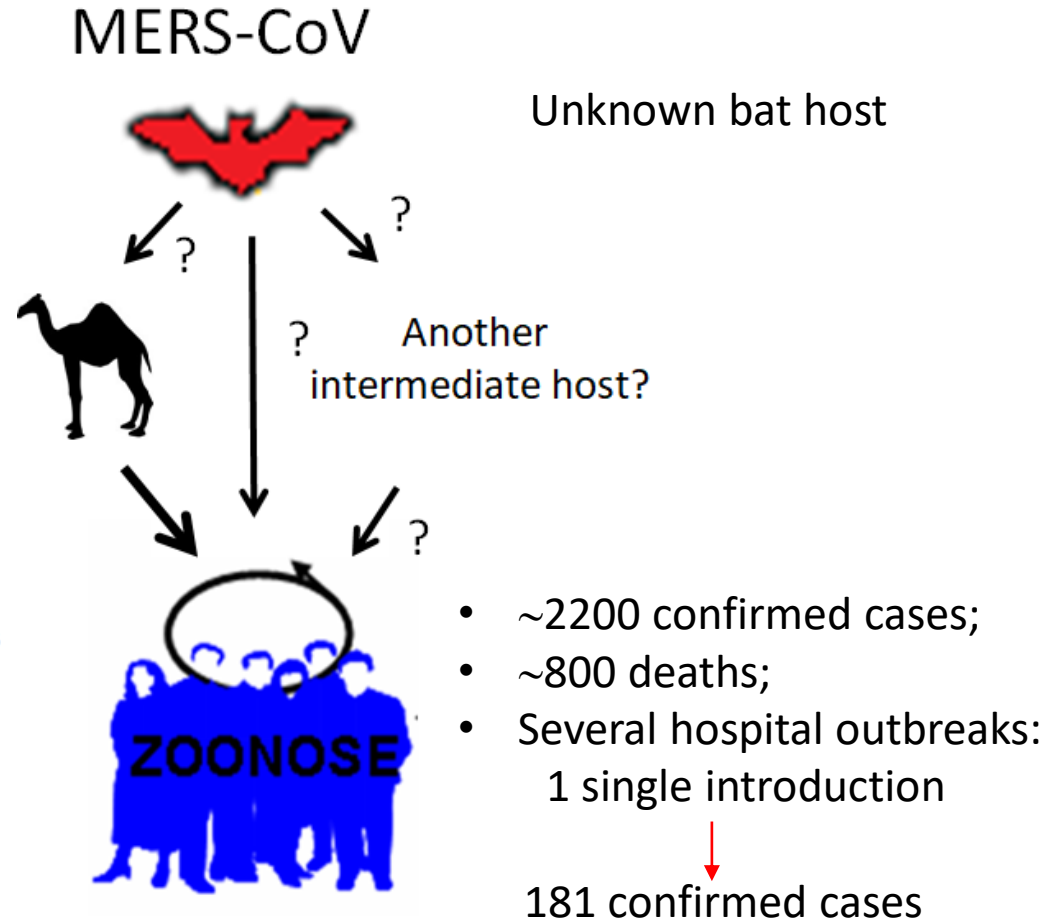
Lancet 2003
Science 2003
J Virol 2005
J Virol 2006
J Gen Virol 2006
J Gen Virol 2008
Studies from other groups at different geographical regions

Emergence of MERS-CoV



Bat coronavirus	Host	Location	Accession number
BtCoV/VM314/2008	<i>Pipistrellus</i> bat	Netherlands	GQ259977
BtCoV/133/2005	<i>Tylonycteris</i> bat	China	DQ648794.1
BtCoV/355A/2005	<i>Pipistrellus</i> bat	China	DQ648809.1
BtCoV/A434/2005	<i>Pipistrellus</i> bat	China	DQ648819.1
HKU4	<i>Pipistrellus</i> bat	China (HK)	DQ249214.1
HKU5	<i>Tylonycteris</i> bat	China (HK)	DQ249217.1

Chan and Poon mBio, 2013



Camel is an important reservoir for MERS-CoV

Chu et al., EID 2014

Hemida et al., EID 2014

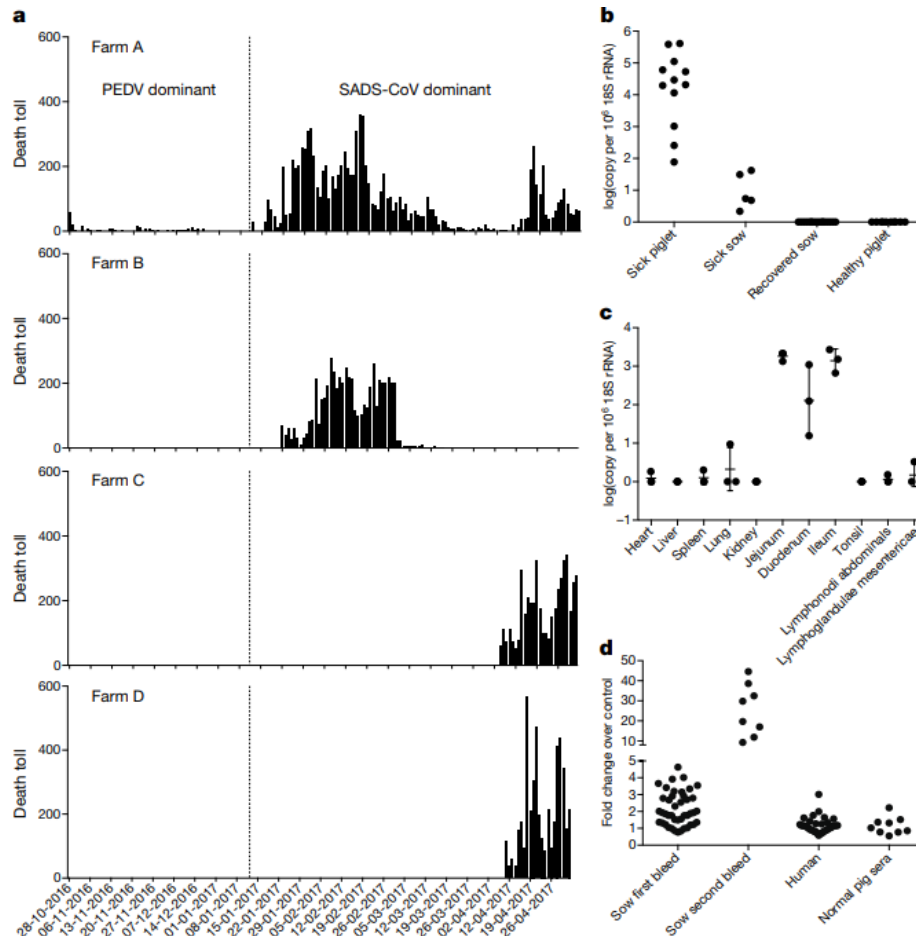
Chu et al., Eurosurveillance 2015

Chu et al., PNAS 2018

Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin

Peng Zhou^{1,12}, Hang Fan^{2,12}, Tian Lan^{3,4,12}, Xing-Lou Yang¹, Wei-Feng Shi⁵, Wei Zhang¹, Yan Zhu¹, Ya-Wei Zhang², Qing-Mei Xie^{3,4}, Shailendra Mani⁶, Xiao-Shuang Zheng¹, Bei Li¹, Jin-Man Li², Hua Guo¹, Guang-Qian Pei², Xiao-Ping An², Jun-Wei Chen^{3,4}, Ling Zhou^{3,4}, Kai-Jie Mai^{3,4}, Zi-Xian Wu^{3,4}, Di Li^{3,4}, Danielle E. Anderson⁶, Li-Biao Zhang⁷, Shi-Yue Li⁸, Zhi-Qiang Mi², Tong-Tong He², Feng Cong⁹, Peng-Ju Guo⁹, Ren Huang⁹, Yun Luo¹, Xiang-Ling Liu¹, Jing Chen¹, Yong Huang², Qiang Sun², Xiang-Li-Lan Zhang², Yuan-Yuan Wang², Shao-Zhen Xing², Yan-Shan Chen^{3,4}, Yuan Sun^{3,4}, Juan Li⁵, Peter Daszak^{10*}, Lin-Fa Wang^{6*}, Zheng-Li Shi^{1*}, Yi-Gang Tong^{2,11*} & Jing-Yun Ma^{3,4*}

Nature 2018



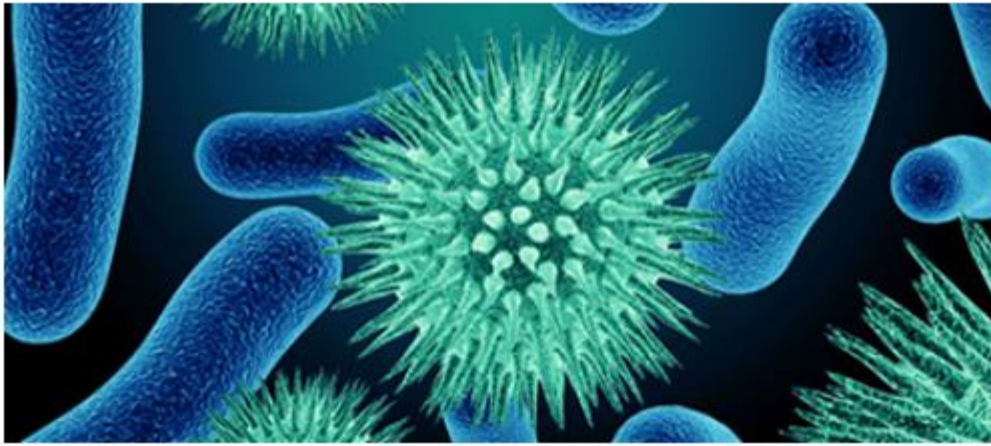
- An outbreak killed 24,693 piglets in four farms at Guangdong
- The virus is genetically similar to HKU2-like bat coronaviruses
- A highly similar virus can also be detected in bats in Guangdong Province

Implications:

- Food security?
- Trading?
- Facility host switching?

WHO R&D Blueprint

List of Blueprint priority diseases



- Crimean-Congo haemorrhagic fever (CCHF)
- Ebola virus disease and Marburg virus disease
- Lassa fever
- Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)
- Nipah and henipaviral diseases
- Rift Valley fever (RVF)
- Zika
- Disease X

The One Health Triad



Lesson learned by Hong Kong

- Preparedness Plan
- Early Case Detection, Surveillance, and Notification
- Infection Control Preparedness
- Laboratory Preparedness
- Clinical Management Preparedness
- Development of Surge Capacity
- Effective Communication Preparedness Plans
- Interdisciplinary/Multidisciplinary Approach

H5N1, 2009 H1N1 pandemic and H7N9

Conclusion

- SARS in 2003 was caused by a zoonotic virus;
- Aggressive measures were used to contain SARS;
- There was a huge investment in pandemic preparedness in the SARS aftermath;
- The precursor viruses of SARS-CoV still circulate in bats;
- CoVs in bats and other animals continuous pose threats to human (health and food security);
- The current MERS outbreak highlights the strengths and weaknesses of preparedness plan.

WHO Network of Laboratories

SARS

- Federal Laboratories for Health Canada, Winnipeg, Canada
- Health Canada, Ottawa, Canada
- Public Health Laboratory Centre, Hongkong SAR China
- Prince of Wales Hospital, Hongkong SAR China
- The University of Hongkong, Hong Kong SAR, China
- Institut Pasteur, Paris, France
- Bernhard-Nocht Institute, Hamburg and Johann Wolfgang Goethe Universitat, Frankfurt, Germany
- National Institute of Infectious Disease, Tokyo, Japan
- Erasmus MC, Rotterdam, The Netherlands
- Singapore General Hospital, Singapore
- Central Public Health Laboratory, London, UK
- Centers for Disease Control & Prevention, Atlanta, USA

AFDC, Hong Kong



SARS-D.T.V.

Research Grants Council
of Hong Kong
香港 研究資助局





Food and Agriculture Organization
of the United Nations



World Health
Organization



The University of Hong Kong: School of Public Health: Malik Peiris, Daniel Chu, Mahen Perera, M Chan, Chris Mok, Renee Chan, Eric Lau, Y Guan, John Nicholls, P Wang

National Research Centre, Giza, Egypt: G Kayali, MA Ali

King Faisal University, KSA: MG Hemida, A Al Naeem

King Fahad Medical City, KSA: S Fagbo, A Hakawi

Seoul National University College of Medicine, Myoung-don Oh, SW Park, WB Park, PG Choe, SJ Choi, JY Chun, HS Oh, KH Song et al

Guangzhou Medical University, 1st Affiliated Hospital: NS Zhong, Ling Chen et al.

CIRAD: Eve Miguel, V Chevalier, F Roger;

Institut Pasteur: Maria van Kerkhove

Abu Dhabi Food Control Authority: Z Al Hammadi, YM Yassir, SS Al Muhairi

University of Iowa: S Perlman, J Zhao

Transboundary State Central Veterinary Laboratory, Mongolia: B Damdinjav, B Khisgee

University of Queensland: Rafat Al Jassim

R Fouchier, B Haagmans, M Koopmans (Erasmus MC), C Drosten, M Muller (U Bonn), Aron Hall (US CDC); Bernard Faye



Research Fund Secretariat
Food and Health Bureau
Hong Kong Special Administrative Region

