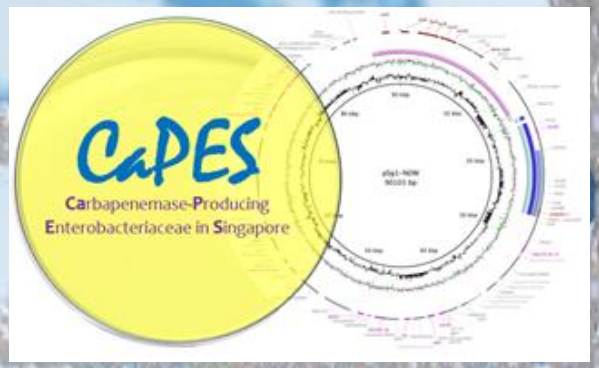
POPULATION WGS FOR CPE TRANSMISSION

Dr Ng Oon Tek
oon_tek_NG@ttsh.com.sg



https://www.google.com.sg/search?q=genomics&source=lnms&tbm=isch&sa=X&ved=0ahUKEwjH3_OJuLTaAhUGR48KHdWUCuoQ_AUICigB&biw=1280&bih=659#imgrc=QMCBNU9uwPRPbM:

Contents

- Bad bugs, no drugs
- Prevention
- Singapore situation
- WGS to uncover CPE transmission
- WGS – international NDM spread

High-level Meeting on Antimicrobial Resistance

September 21 @ 10:00 am - 6:00 pm

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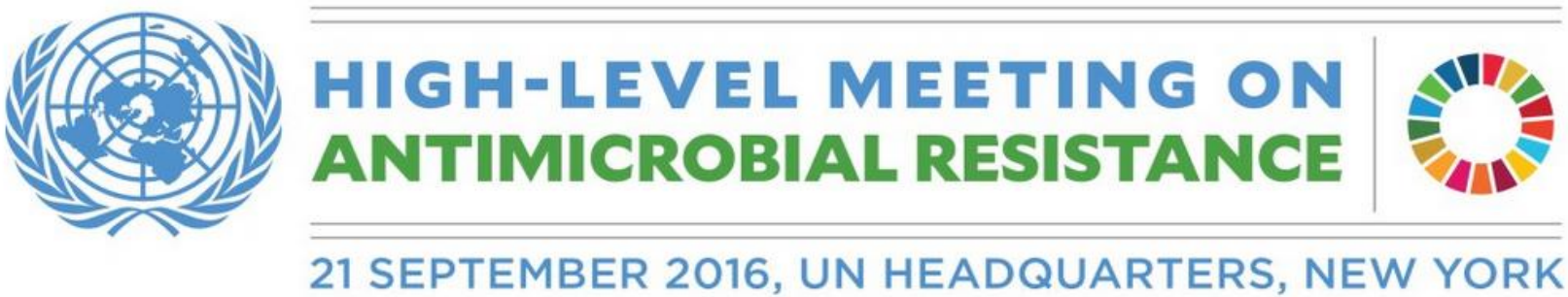


On 21 September 2016, the President of the UN General Assembly convenes an one-day high-level meeting at the UN Headquarters in New York on "Antimicrobial Resistance", with the participation of Member States, non-governmental organizations, civil society, the private sector and academic institutions, in order to provide input.

The primary objective of the meeting is to summon and maintain strong national, regional and international political commitment in addressing antimicrobial resistance comprehensively and multi-sectorally, and to increase and improve awareness of antimicrobial resistance.

The meeting emphasizes the important role and the responsibilities of governments, as well as the role of relevant inter-governmental organizations, particularly the World Health Organization within its mandate and in coordination with FAO and o IE, as appropriate, in responding to the challenges of antimicrobial resistance, and the essential need for multi-sectorial and cross-sectorial efforts and engagement of all relevant sectors of society, -such as human and veterinary medicine, agriculture, finance, environment and consumers- to generate an effective response, including towards a one-health approach.

It further recalls the World Health Assembly Resolution WHA 68.7 entitled "Global Action Plan on antimicrobial resistance" which reflects a global consensus that antimicrobial resistance poses a significant public health challenge, and emphasizing the paramount significance of achieving the five strategic objectives of the WHA Global Action Plan.

http://www.un.org/pga/71/event-latest/high-level-meeting-on-antimicrobial-resistance/

Carbapenem-resistant Enterobacteriaceae (CRE) threat

Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis

Evelina Tacconelli, Elena Carrara, Alessia Savoldi*, Stephan Harbarth, Marc Mendelson, Dominique L Monnet, Céline Pulcini, Gunnar Kahlmeter, Jan Kluytmans, Yehuda Carmeli, Marc Ouellette, Kevin Outterson, Jean Patel, Marco Cavaleri, Edward M Cox, Chris R Houchens, M Lindsay Grayson, Paul Hansen, Nalini Singh, Ursula Theuretzbacher, Nicola Magrini, and the WHO Pathogens Priority List Working Group†*

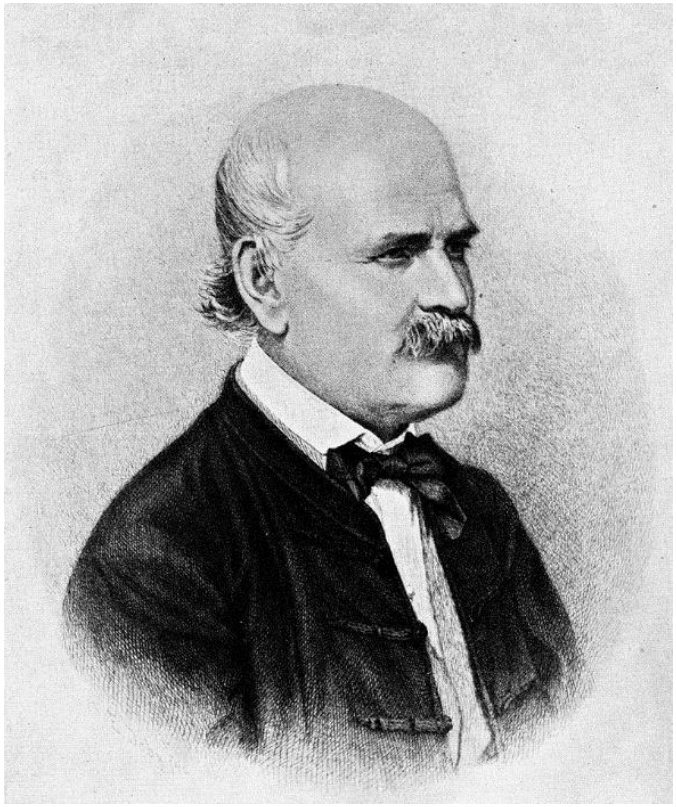
1. Falagas ME, Tansarli GS, Karageorgopoulos DE, Vardakas KZ. Deaths attributable to carbapenem-resistant Enterobacteriaceae infections. Emerg Infect Dis. 2014 Jul;20(7):1170-5. doi: 10.3201/eid2007.121004.
2. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2009;48(1):1–12.

what can we do?

… Especially when there is no cure

https://www.123rf.com/photo_63390268_women-hand-writing-prevention-is-better-than-cure-with-black-marker-on-visual-screen-isolated-on-whi.html

The good news…



Multi-modal strategy (structural factors)

- ✓ Hand hygiene

Surveillance

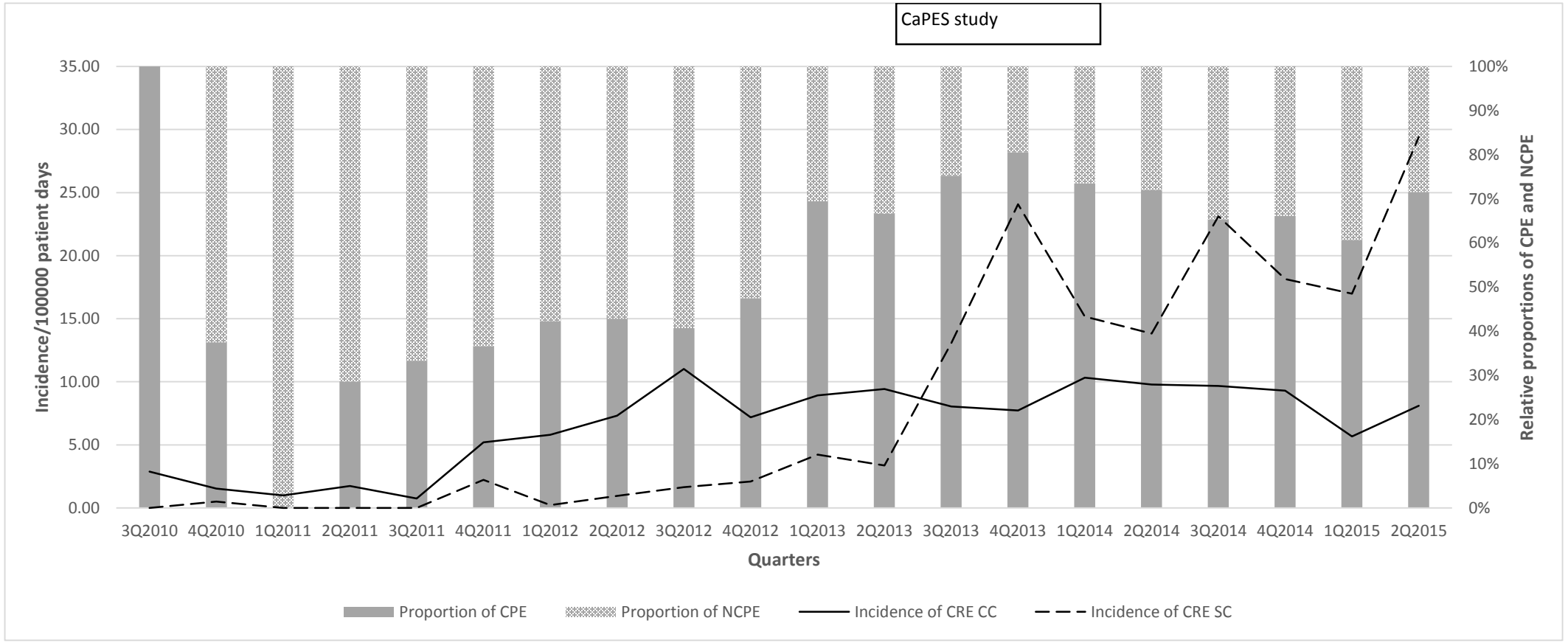
- ✓ Contact precautions
- ✓ Patient isolation
- ✓ Environmental cleaning

Surveillance cultures of the environment

Monitoring, audit and feedback

https://fr.wikipedia.org/wiki/Ignace_Philippe_Semmelweis#/media/File:Ignaz_Semmelweis.jpg

Singapore



Clinical cultures/ Surveillance cultures

- **2010:** 2.9 per 100,000 patient-days/ 0.8 per 100,000 patient-days
- **2012:** 7.7 per 100,000 patient-days/ 16.0 per 100,000 patient-days

Main questions

- What are the sources of ongoing transmission of CPE in Singapore?
- What are the sources of CPE bacterial transmission in Singapore?
- What are the sources of CPE plasmid transmission in Singapore?

Pilot analysis (n=33)

Genetically-Linked Bacterial Transmission	
Classification	Number of Isolates
Genetically Distinct	18
Genetically linked to previous cases	15
- Hospital contact	6
- Ward contact	4
Genetically linked but no known ward or hospital contact	5

- Of 15 genetically-linked bacterial transmissions, 5 (33%) had no apparent ward or hospital contact
- 2 predominant plasmids found (pEC-S01 and pNDM-Sg1)

J Antimicrob Chemother 2016; **71**: 3081–3089
doi:10.1093/jac/dkw277 Advance Access publication 2 August 2016

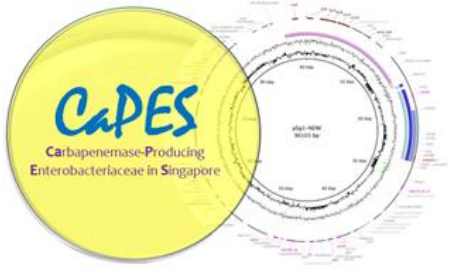
CaPES WGS transmission study

- Determine the sources of CPE transmission at a population level

- **Sub-groups:**

➢ Determine the sources of genomically-linked ***bacterial transmission*** at a population level

➢ Determine the sources of genomically-linked ***plasmid transmission*** at a population level



International NDM study

AIMS:

1) Determine the main genomic pathways of NDM spread across borders.

2) Will NDM mimic the successful global genomic spread of the previous Extended-Spectrum-beta-lactamases ?

    e.g. CTX-M-15 – E. coli ST 131 pairing ?

Other ongoing studies…

- Outbreak genomics (Singapore, East Malaysia)
- Community household CPE transmission
- Long-term care facility CPE transmission
- Hospital environmental microbiome
- Bench studies (Type VI secretion system, Glycosylated cationic *β*-peptide block copolymers)

Summary (Epidemiologic)

- Genomically-linked plasmid transmission accounts for a significant amount of CP gene transmission.

- Features of genomically-linked bacterial transmission:
  - Significant proportion no known epidemiologic contact (30%).
  - Close to a third have direct ward contact.
  - A further third have indirect ward contact (suggesting ongoing sources in wards e.g. sinks/ inanimate objects as a source).

- Genomically-linked plasmid transmission different:
  - Majority have direct ward contact.

- WGS can help uncover ongoing transmission routes and help focus/ augment infection prevention efforts.

Summary (Genomic)

- 5 NDM-positive cassette types found in analysis.
- These cassette-types (and associated plasmids) facilitate genomic spread of the NDM gene into multiple bacterial species and STs.
- NDM is prevalent in high-risk clones (with high prevalence of ESBL genes e.g. CTX-M-15 in *E. coli* ST131).
- Overall, understanding plasmid transmission and hidden sources of CP gene and developing agents and strategies to address them may help in reducing CPE transmission.

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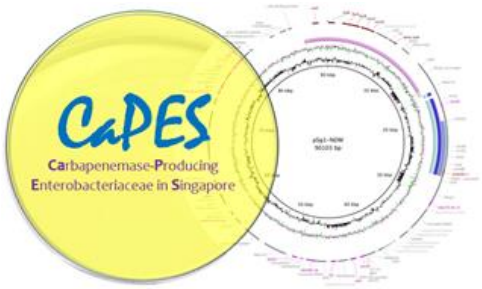
Teo Yik Yng (NUS School of Public Health)

WGS Analysis team:
Xu Weizhen (TTSH)
Prakki Sai Rama Sridatta (TTSH)
Natascha May Thevasagayam (TTSH)
Victor Lee (TTSH)
Liang De (TTSH)
Amanda Chua (TTSH)

(Note: Hospitals and academic institution noted in brackets.)



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Dr David Wareham, Dr Lynette Minyu Phee

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