Carbapenemase-producing Enterobacterales (CPE) Surveillance Report

28 February – 7 September 2019

Summary

"Carbapenemase- producing *Enterobacterales* (CPE) infection and colonisation" was added to the list of laboratory notifiable conditions in NSW on 28 February 2019.

This first NSW CPE surveillance report summarises characteristics of patients who were notified with CPE infection or colonisation in NSW by laboratories during the first six months of surveillance (28 February to 7 September 2019). In summary:

Notifications

- 155 unique notifications of carbapenemase- producing *Enterobacterales* (CPE) infection or colonisation in a total of 133 patients were received during this reporting period.

Patients

- 133 patients were identified as having CPE, 27 of whom had more than one notification of CPE identified.
- 9 patients (7%) were under 10 years of age, 72 (54%) were 10-69 years, and 52 (39%) were 70 years or over
- 81 (61%) patients were male and 52 (39%) female

Specimens

Of the 155 notifications, specimens collected included:

- 81 (52%) for screening
- 9 (6%) from sterile sites, consistent with CPE infections
- 42 (27%) from urine
- 23 (15%) from non-sterile sites.

Bacteriology

- 12 different *Enterobacterales* species were detected, mostly:
    - *Enterobacter cloacae* (44, 28%)
    - *Klebsiella pneumoniae* (40, 26%) and
    - *Escherichia coli* (38, 25%).

Genetics

- 5 different carbapenemase genes were detected, including
    - IMP (110, 71%)
    - NDM (27, 17%)
    - OXA-48 like (11, 7%) and
    - KPC (2, 1%).
- 4 (3%) notifications reported a single bacterial species harbouring two different carbapenemases (NDM and Oxa-48 like).

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Introduction

Multi-resistant organisms are a growing threat internationally. Following expert review, NSW Health identified carbapenemase-producing *Enterobacterales* (CPE) as a high priority pathogen.

The NSW Public Health Act 2010 was amended to require laboratory notification of 'carbapenemase-producing *Enterobacterales* infection or colonisation' from 28 February 2019. An aim of implementation of a state wide surveillance program was to assist with identification of cases and increase our understanding of the epidemiology of CPE in NSW. Management of CPE is supported by the NSW Health Guideline for Surveillance and Management of CPE in NSW Health Facilities.

Carbapenemase-producing *Enterobacterales* (CPE)

Enterobacterales are an order of Gram-negative bacilli that occur naturally in the gastro-intestinal tract. They can spread outside the gastro-intestinal tract and cause serious infections such as bacteraemia, pneumonia, urinary tract infections and wound infections.

Carbapenems are an important class of broad spectrum β-lactam antibiotics which are highly effective against most Gram-negative infections. *Enterobacterales* can acquire resistance to carbapenem antibiotics by a number of mechanisms. *Enterobacterales* which are resistant to carbapenem antibiotics, by one of a number of mechanisms, are called carbapenem-resistant *Enterobacterales* (CRE). Carbapenemase-producing *Enterobacterales* (CPE) describe *Enterobacterales* which are resistant to carbapenem antibiotics through production of carbapenemase enzymes encoded by plasmid-mediated carbapenemase genes. The carbapenemase enzymes hydrolyse carbapenems (as well as other β-lactams, such as penicillins and cephalosporins). This means that CPE infections are difficult to treat.

A number of different carbapenemase genes have been reported in *Enterobacterales*. Five of the most important types globally are:

1. Imipenemase (IMP)
2. Klebsiella pneumoniae carbapenemase (KPC)
3. New Delhi metallo-β-lactamase (NDM)
4. Verona integron-encoded metallo-β-lactamase (VIM)
5. Oxacillinases (OXA)

Individuals who have acquired CPE can either carry it harmlessly in their gut, like other *Enterobacterales*, termed colonisation, or may develop an infection with the CPE. A person who is colonised will not have any symptoms.

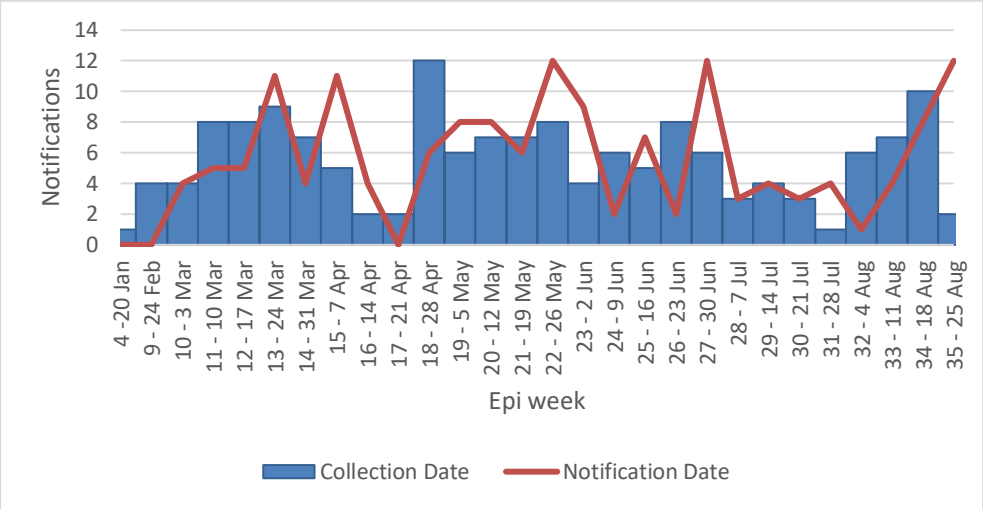
Here we report on the characteristics of patients who were notified in the first 6 months since CPE became notifiable in NSW.

CPE infection or colonisation in NSW: 28 February - 7 September 2019

Notifications

155 unique notifications have been received since 28 February 2019 relating to 133 patients.

Figure 1: Weekly notifications of carbapenemase-producing *Enterobacterales*, by date of collection, NSW 28 February - 7 September 2019



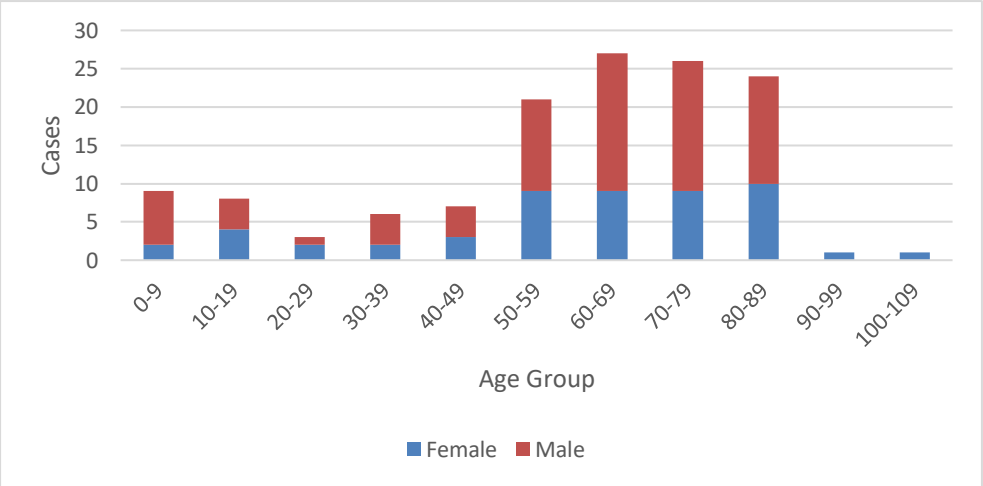
Notes on Figure 1

- Where multiple *Enterobacterales* species are cultured from a single isolate, each species is counted as a separate CPE notification (but a single case).
- Where molecular testing has identified multiple carbapenemase genes from a single *Enterobacterales* species, this will be counted as one notification.

Demographics

Of the 133 patients, 9 (7%) were in children under 10 years of age and 52 (39%) cases were in those aged 70 or above. There was a male preponderance of cases (61% versus 39%).

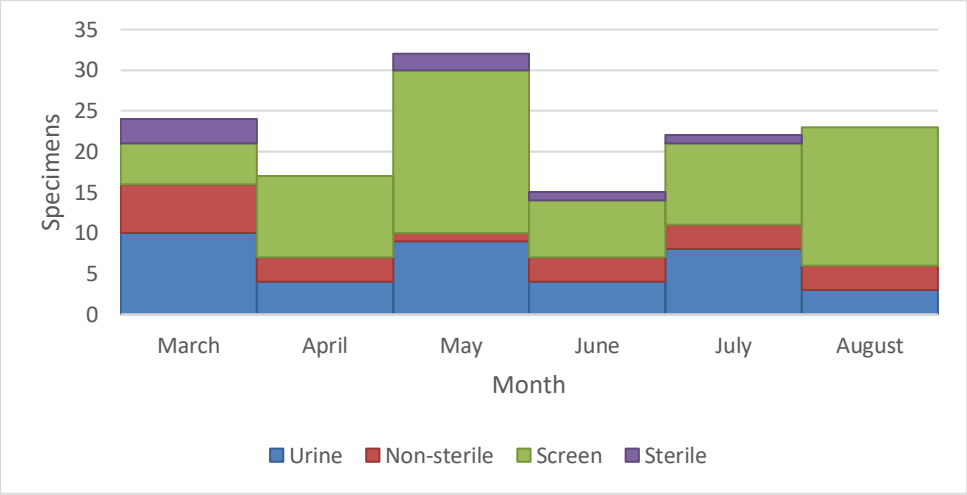
Figure 2: Carbapenemase-producing *Enterobacterales* cases, by sex and age, NSW, 28 February - 7 September 2019



Specimen type

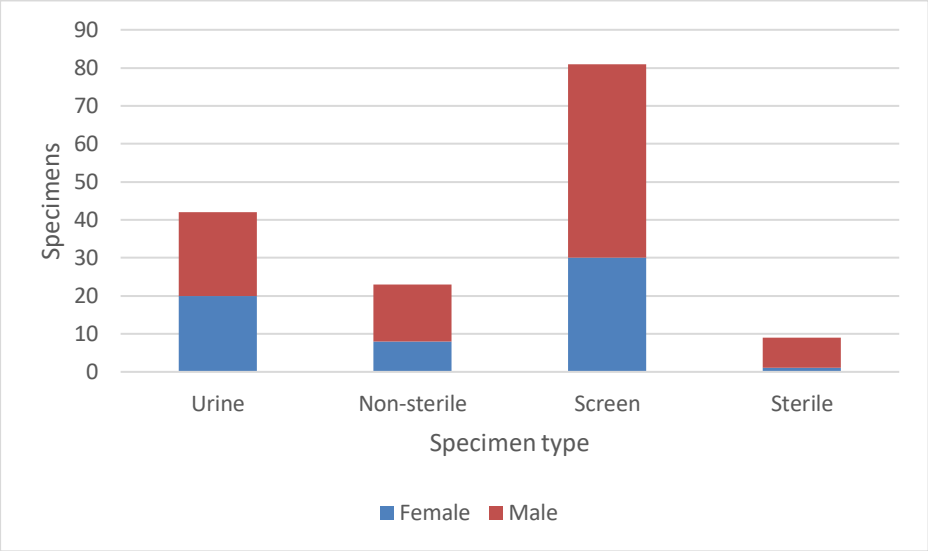
Of the 155 notifications (excluding duplicates and confirmatory testing), 81 (52%) were specimens collected for screening purposes. There were 9 (6%) specimens collected from sterile sites, consistent with CPE infections. The remainder of specimens were collected from non-sterile sites (e.g unspecified swab, faeces, colostomy) or urine, and could represent either infection or colonisation.

Figure 3: Monthly notifications of carbapenemase-producing *Enterobacterales* by specimen type in NSW, 28 February - 7 September 2019



Excluding duplicate notifications and confirmations

Figure 4: Notifications of carbapenemase-producing *Enterobacterales* by specimen type and sex in NSW, 28 February - 7 September 2019



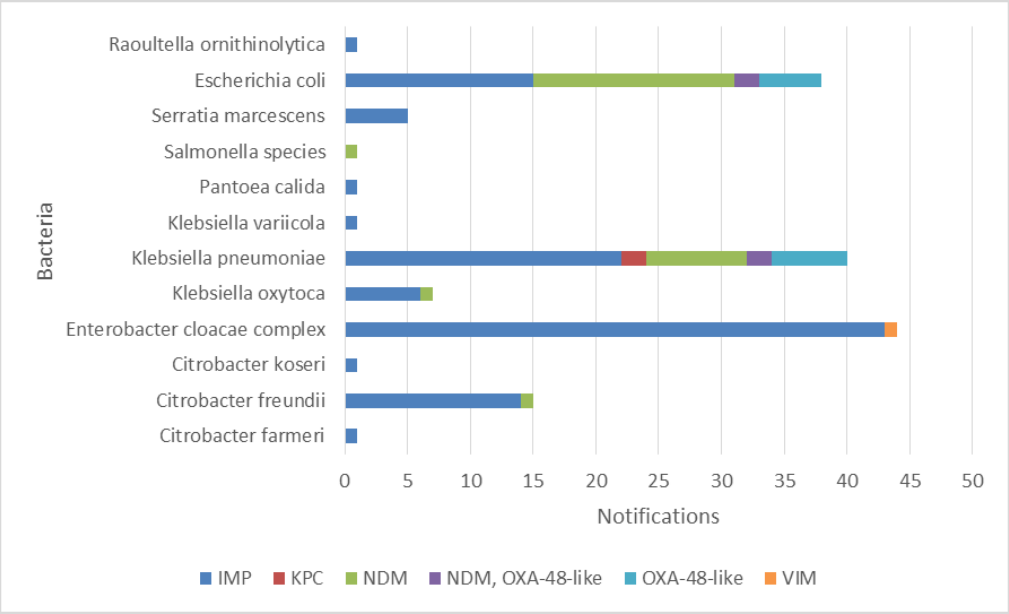
Excluding duplicate notifications and confirmations

* A specimen marked "screening" or some variation is considered to be part of a deliberate screen for CPE. The two remaining categories, non-sterile site and urine, could represent either an infection or colonisation.

Bacteriology

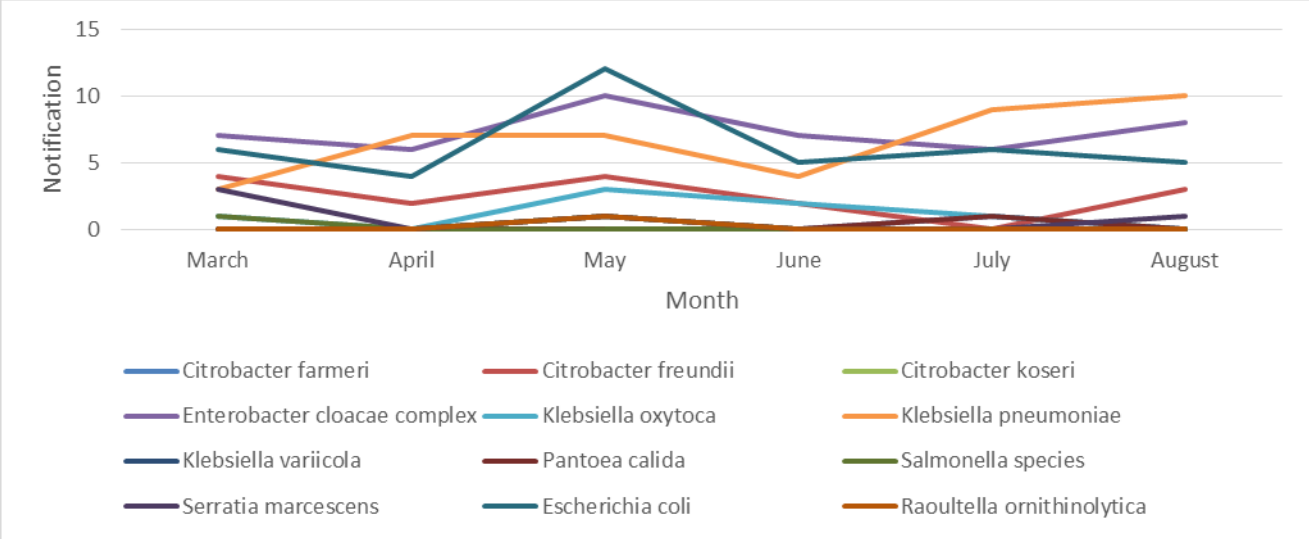
12 different *Enterobacterales* species were detected in the notified cases. The majority of notifications comprised of *Enterobacter cloacae* (44, 28%), *Klebsiella pneumonia*e (40, 26%), and *Escherichia coli* (38, 25%).

Figure 5: Notifications of carbapenemase-producing *Enterobacterales* by host bacterial species and carbapenemase gene type in NSW, 28 February -7 September 2019



Excluding duplicate notifications and confirmations

Figure 6: Monthly carbapenemase-producing *Enterobacterales* notifications by organism in NSW, 28 February - 7 September 2019

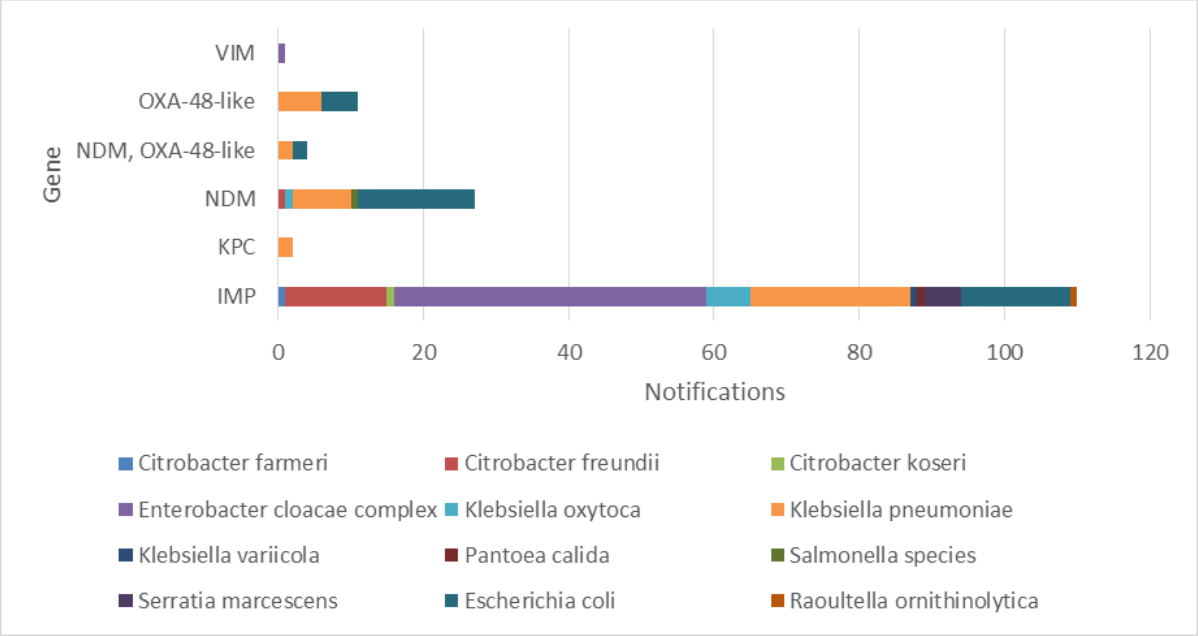


Excluding duplicate notifications and confirmations

Genetics

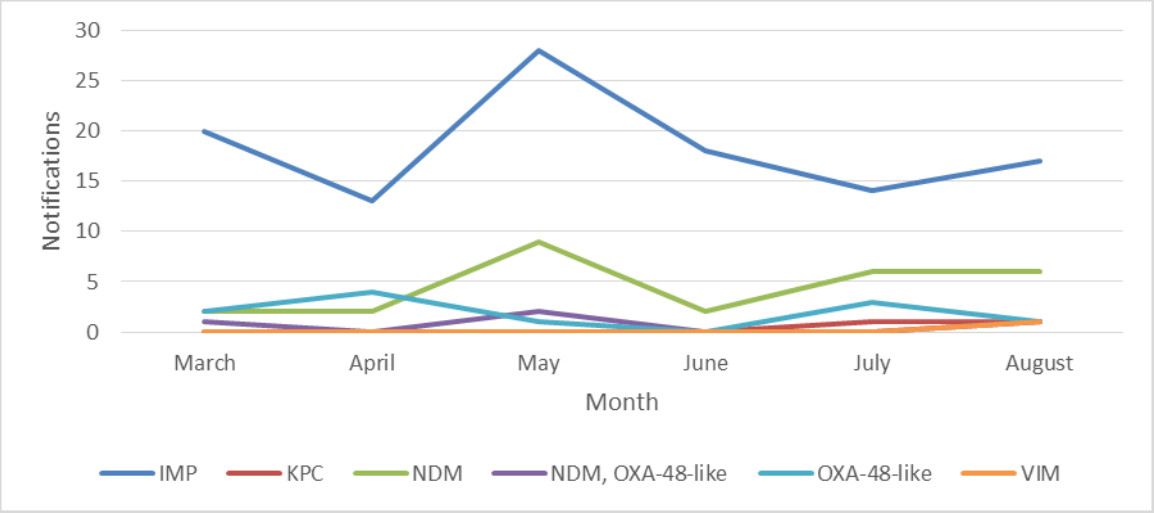
During the surveillance period, the most commonly reported carbapenemase genes were IMP (110 notifications), NDM gene (27 notifications) and OXA-48 like (11 notifications). There were two notifications of a KPC-producing *Klebsiella pneumoniae*. Four notifications reported a single bacterial species harbouring two different carbapenemases (NDM and OXA-48 like).

Figure 7: Notifications of carbapenemase-producing *Enterobacterales* by gene type and bacterial species in NSW, 28 February - 7 September 2019



Excluding duplicate notifications and confirmations

Figure 8: Monthly carbapenemase notifications by gene in NSW, 28 February - 7 September 2019



Excluding duplicate notifications and confirmations

Notifications by Local Health District and Speciality Networks

Notifications were received from patients in 12 of 15 NSW Local Health Districts (LHD), as well as private hospitals and speciality networks. Notifications relates to the location of the patient at the time the sample was taken not the location of acquisition.

Table 1: Notifications by Local Health District in NSW, 28 February - 7 September 2019

LHD/SHN	Notifications
Central Coast	1
Hunter New England	13
Murrumbidgee	1
Nepean Blue Mountains	5
North Sydney	26
South East Sydney	16
Sydney	15
Southern NSW	2
South Western Sydney	8
Sydney Children's	10
Western NSW	2
Western Sydney	31
Illawarra Shoalhaven	5
Other	20
Grand Total	**155**

Excluding duplicate notifications

Note: Other represents samples with unspecified location, private hospitals and St Vincent's Health Network

Glossary

Term	*Definition*
Carbapenemase-producing *Enterobacterales* (CPE)	*Enterobacterales* which produce a carbapenemase, by means of an acquired carbapenemase gene.
Carbapenem-resistant *Enterobacterales* (CRE)	*Enterobacterales* which are resistant to carbapenem antibiotics, by a number of means, including carbapenemase gene acquisition.
Carbapenemase enzyme	Beta-lactamase which hydrolyses carbapenems, usually along with other beta-lactams
CPE colonisation	The presence of the CPE bacteria in or on a body surface without signs of invasive infection. The primary site of CPE colonisation is usually the lower gastro-intestinal tract.
CPE infection	The invasion of a person's bodily tissues by the CPE bacteria and their subsequent multiplication, typically resulting in disease-causing symptoms and the reaction of host tissues to these organisms and the toxins they produce.
Enterobacterales	Gram-negative bacilli that occur naturally in the gastro-intestinal tract
MRO	Multi-Resistant Organism

Appendices

Appendix 1: Methods

Surveillance data were collected and analysed as part of routine public health action.

Notifications were received in the form of "doctor's reports" of the genetic test for carbapenemase genes. The data available on these reports was limited to details of the organism and gene and basic demographic information on the patient.

Diagnosis of CPE required identification of a CPE gene through genotypic testing in a species of *Enterobacterales*, following a laboratory's standard diagnostic protocol.

Notifications were included in this report if they were received by the NSW Ministry of Health (notification date) between 28 of February and 7 September, represented a NSW case, and met the case definition.

Notifications are counted as NSW cases where the address of residence:

- is in NSW or
- is overseas, and the diagnosis was made in NSW (therefore likely representing a visitor to NSW) or
- is recorded as unknown

Notifications are defined as any laboratory result that diagnosed CPE. Patients are individuals with a diagnosis of CPE colonisation or infection. Due to the natural history of CPE individual patients may generate multiple notifications representing different organism or genes.

- Each patient is counted once regardless of how many notifications received
- For notifications, each separate organism with a CPE gene is counted as a new notification. (Excluding for duplicate notifications).
- Organisms with more than one gene are counted as one notification

Demographic data is based on patient count.

Time series data is based on date of notification.

The total number of notifications received is reported, however duplicate notifications (i.e. repeat sending or confirmation from second lab for the same specimen) are excluded from further analysis.

Data were analysed by organism, genotype, specimen type, age, and sex where information was available.

Notifications were defined as screening if the sample was reported as "screening", "MRO screen" or "swab, screening", sterile specimens were defined as isolation of CPE from normally sterile sites. The category of non-sterile included specimens from sites that would not be sterile, such as wound swabs. The category "urine" included any variation of mid-stream urine, urine, catheter urine.

Analysis was undertaken using basic statistical software.

Surveillance of CPE is a collaboration between health care providers, Local Health Districts, Specialist Health Networks, laboratories, the Clinical Excellence Commission and Health Protection NSW.