Since the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) into the childhood immunization program in Hong Kong in September 2009, and replacement of higher valent PCV10 and PCV13 in 2010 and 2011, a local epidemiological study conducted in 2010-2013 revealed changes in carriage prevalence and serotype distribution in young children in the post-PCV7 era (Ho et al., 2015). Our study aimed to provide a high-resolution picture of the changes in the pre- and post-vaccine era by whole genome sequencing (WGS) of pneumococci collected in Hong Kong.

### Methodology

A total of 525 isolates collected during 1995-2017 from Hong Kong were selected and sent for WGS to represent the pre- (1995-2008) and post-PCV7 (2009-2015) implementation eras for both carriage Invasive Pneumococcal Disease (IPD, n=227) population as presented in Figure 1.

### Results

#### Population structure

Ten sequence clusters (SCs) were identified amongst 525 sequenced isolates from Hong Kong. Of which, SC4 (serotype 3), SC5 (serotype 15A), SC7 (serotype 19A/F), SC8 (serotype 19A/F) and SC9 (serotype 15A) were predominantly associated with post-PCV7 collection as presented in Figure 2. SC1 (serotype 14) and SC4 (serotype 3) had the highest invasive odds ratio (OR) of 3.56 and 6.57 respectively. Other characteristics are presented in Table 1.

#### Capsular switching events

A total of 8 capsular switching events were detected, represented as black dots (●). Three of which resulted in a clonal expansion in SC4, SC7 and SC10, indicated with red arrows (→). Two of these expansions were observed in the post-PCV7 era, these are SC4 (serotype 9V → 3) and SC7 (serotype 19F → 19A). The capsular switching region of them were estimated to be 18.8kb and 29.6kb in length, switching all genes involved in the production of capsular polysaccharides.

### Conclusion

We observed changes in the prevalence of lineages in the pre- and post-PCV7 collections. Two of the capsular switching variants from PCV7 serotypes to non-PCV7 serotypes were followed by clonal expansions in the post-PCV7 era. The expansion of capsular switched variant in SC4 is particularly worrisome owing to the lineage's highly invasive OR.