

Wholesale Supply Data of Antibiotics in Hong Kong (Year 2018)

Infection Control Branch
Centre for Health Protection
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Background

- The Department of Health (DH) has been collecting antibiotic wholesale supply data through relevant certificate holders / licensed drug wholesalers since 2017
- An activity suggested in the HK Strategy and Action Plan 2017-2022 as a proxy to gauge the overall antibiotic consumption by various sectors in HK
- DH published first-ever territory-wide report of antibiotics supplied to different sectors based on the wholesale supply data in April 2018 and the second report in July 2019 covering the supply data from 2014 - 2017
- It has become an annual surveillance exercise since 2018



Sectors included in the Antimicrobial Use (AMU) Surveillance

Wholesale supply data to the following 8 sectors were included in the surveillance:

1. Department of Health
2. Hospital Authority
3. Private hospitals
4. Private doctors (mutually exclusive with private hospitals)
5. Registered Dentists
6. Veterinary surgeons
7. Community pharmacies
8. Farmers



Classes of Antibiotics Covered

WHO Anatomical Therapeutic Chemical (ATC) under the following groups were covered:

- J01 (Antibacterials For Systemic Use)*;
- A07AA (Antibiotics for Alimentary Tract); and
- P01AB (Nitroimidazole Derivatives for Protozoal Diseases)

* Preparations for external use such as cream and ear/eye drop are excluded



Classification of Antibiotics

| | |
|-------|---|
| J01A | Tetracyclines |
| J01B | Amphenicols |
| J01C | Beta-lactam Antibacterials, Penicillins |
| J01D | Other Beta-lactam Antibacterials |
| J01E | Sulfonamides and Trimethoprim |
| J01F | Macrolides, Lincosamines and Streptogramins |
| J01G | Aminoglycoside Antibacterials |
| J01M | Quinolone Antibacterials |
| J01R | Combinations of Antibacterials |
| J01X | Other Antibacterials |
| A07AA | Antibiotics for Alimentary Tract |
| P01AB | Nitroimidazole Derivatives for Protozoal Diseases |

Source: Anatomical Therapeutic Chemical (ATC) Classification System, World Health Organization



Broad Spectrum Antibiotics

Some broad spectrum antibiotics (i.e., antibiotics with a broad spectrum of coverage) are particularly important to human:

- Reserved for treating infections caused by resistant bacteria in hospitals
- Some are even regarded as last resort antibiotics for treating resistant or life-threatening bacterial infections
 - Examples: carbapenems, colistin



Examples of Broad Spectrum Antibiotics

| ATC Group | Broad spectrum antibiotics with local importance |
|--|--|
| Beta-Lactam Antibacterials, Penicillins (J01C) | Piperacillin/Tazobactam |
| | Cefepime |
| | Cefoperazone/Sulbactam |
| | Ceftaroline Fosamil |
| Other Beta-Lactam Antibacterials (J01D) | Ceftazidime |
| | Ceftolozane/Tazobactam |
| | Ertapenem |
| | Imipenem/Cilastatin |
| | Meropenem |
| Other Antibacterials (J01X) | Colistin |
| | Daptomycin |
| | Linezolid |
| | Teicoplanin |
| | Vancomycin |



Quantification of Antibiotic Usage

Defined Daily Dose (DDD)

- Defined as the assumed average maintenance dose per day for a drug used for its main indication in adults
- Commonly used by many overseas health authorities for comparison of drug usage and research

DDD per 1,000 inhabitants per day (DID)

- A standardised unit used internationally to measure antibiotic use among a definitive population



Limitations

- Self-reporting data by antibiotic product certificate holders/licensed drug wholesalers involving around 1300 products and 130 certificate holders
- Wholesale supply data only provides indirect information to reflect antibiotics use but it is never equal to the actual dispensing or consumption data
- Wholesale supply data contains no information to reflect the appropriateness of use by each sectors
- Whether the use of antibiotics is appropriate depends on the clinical situation



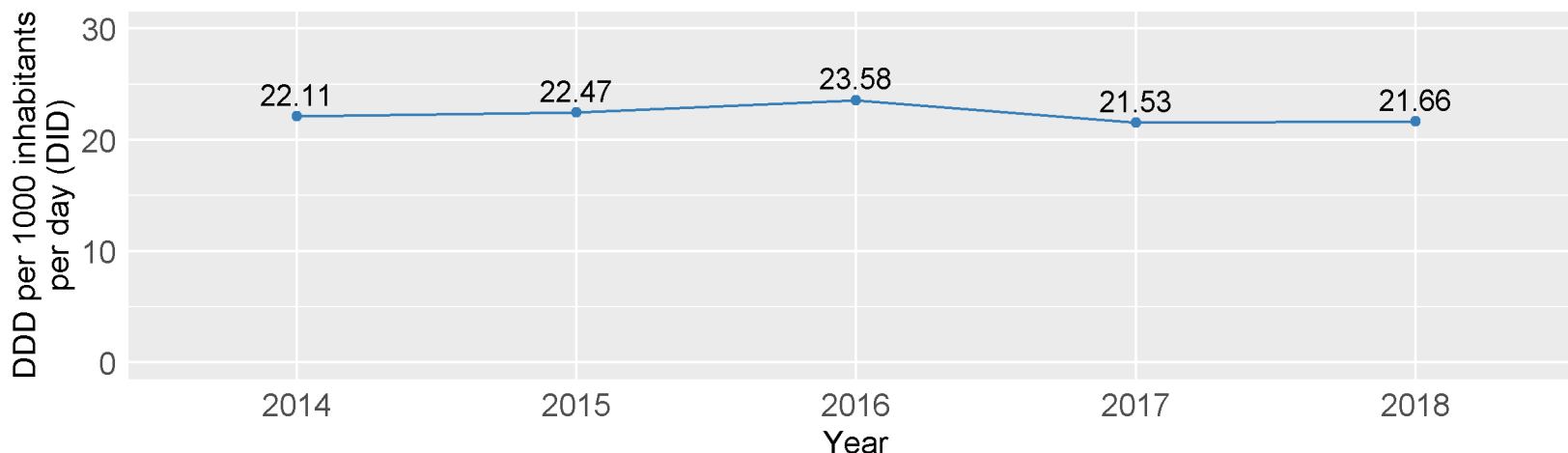
Results - Total Wholesale Supply

| | Year | | | | |
|----------------|-------|-------|-------|-------|-------|
| | 2014 | 2015 | 2016 | 2017 | 2018 |
| DDD in million | 58.52 | 59.94 | 63.49 | 58.27 | 59.18 |
| DID | 22.11 | 22.47 | 23.58 | 21.53 | 21.66 |

*Non-human use antimicrobials supplied to veterinary surgeons and farmers were excluded

- An increase of total supply for human use was seen (by 0.91 million DDD or 0.12 DID) from 2017 to 2018
- When compared with the total supply in 2016 (baseline), a decrease of 4.31 million DDD (1.92 DID) in 2018 was observed

Total volume of antibiotics supplied by wholesalers for human use in Hong Kong (2014 - 2018)



Results - Total Wholesale Supply (by Sector)

| | Year | | | | | |
|--------------------------------|----------|-------|----------|-------|----------|-------|
| | 2016 | | 2017 | | 2018 | |
| | mil. DDD | DID | mil. DDD | DID | mil. DDD | DID |
| Category: Human use | | | | | | |
| Private Doctors | 33.30 | 12.37 | 30.17 | 11.15 | 32.99 | 12.07 |
| Hospital Authority | 13.03 | 4.84 | 13.48 | 4.98 | 13.97 | 5.11 |
| Community Pharmacies | 11.82 | 4.39 | 7.66 | 2.83 | 4.78 | 1.75 |
| Private Hospitals | 3.45 | 1.28 | 4.65 | 1.72 | 4.62 | 1.69 |
| Dentists | 1.34 | 0.50 | 1.82 | 0.67 | 2.16 | 0.79 |
| Department of Health | 0.55 | 0.21 | 0.49 | 0.18 | 0.66 | 0.24 |
| Category: Non-human use | | | | | | |
| Veterinarians* | 0.71 | 0.26 | 0.72 | 0.27 | 0.69 | 0.25 |
| Farmers* | 0.01 | § | 0.02 | 0.01 | 0.01 | 0.01 |

* Figures for veterinarians and farmers sector should be interpreted with caution, as DDD and DID calculation is only applicable to antimicrobial for human use

§ Less than 0.005



Results - by Classes of Antibiotics (1)

| ATC Pharmacological Subgroup | | Year | | | | | |
|------------------------------|---|-------|-------|-------|-------|-------|-------|
| | | 2016 | | 2017 | | 2018 | |
| Code | Description | DID | % | DID | % | DID | % |
| J01A | Tetracyclines | 2.06 | 8.74 | 1.84 | 8.54 | 1.84 | 8.49 |
| J01B | Amphenicols | § | 0.02 | § | 0.01 | § | § |
| J01C | Beta-Lactam Antibacterials, Penicillins | 11.93 | 50.59 | 11.01 | 51.13 | 11.29 | 52.14 |
| J01D | Other Beta-Lactam Antibacterials | 2.86 | 12.14 | 2.32 | 10.77 | 2.20 | 10.16 |
| J01E | Sulfonamides and Trimethoprim | 0.21 | 0.89 | 0.19 | 0.89 | 0.21 | 0.96 |
| J01F | Macrolides, Lincosamides and Streptogramins | 3.32 | 14.08 | 2.95 | 13.71 | 2.87 | 13.26 |
| J01G | Aminoglycoside Antibacterials | 0.05 | 0.22 | 0.05 | 0.24 | 0.05 | 0.22 |
| J01M | Quinolone Antibacterials | 2.42 | 10.27 | 2.28 | 10.59 | 2.33 | 10.75 |
| J01R | Combinations of Antimicrobials* | - | - | - | - | - | - |
| J01X | Other Antibacterials | 0.29 | 1.24 | 0.32 | 1.48 | 0.32 | 1.46 |
| A07AA | Antibiotics for Alimentary Tract | - | - | 0.10 | 0.46 | 0.12 | 0.54 |
| P01AB | Nitroimidazole Derivatives for Protozoal Diseases | 0.43 | 1.82 | 0.47 | 2.18 | 0.44 | 2.02 |
| Total | | 23.58 | 100 | 21.53 | 100 | 21.66 | 100 |

Note:

Non-human use antimicrobials supplied to veterinary surgeons and farmers were excluded:

* There was no registered product under "Combinations of Antimicrobials" (J01R) in Hong Kong

§ Less than 0.005



Results - by Classes of Antibiotics (2)

- It was observed that the overall increase in DID in 2018 was mainly due to the increase in supply of Beta-Lactam Antibacterials, Penicillins (J01C) (by 0.28 DID)
- Increase of supply was also seen with the groups such as Sulfonamides and Trimethoprim (J01E), Quinolone Antibacterials (J01M) and Antibiotics for Alimentary Tract (A07AA) but the increase was relatively small (from 0.02 to 0.05 DID)
- Other groups were either remained steady or had a slight decrease



Results - Supply of Broad Spectrum Antibiotics (1)

| ATC Chemical Substance | | Year | | | | | |
|--|--------------------------|-------|-------|-------|-------|-------|-------|
| | | 2016 | | 2017 | | 2018 | |
| Code | Description | DID | %* | DID | %* | DID | %* |
| Beta-Lactam Antibacterials, Penicillins | | | | | | | |
| J01CR05 | Piperacillin/ Tazobactam | 0.114 | 0.483 | 0.127 | 0.591 | 0.137 | 0.633 |
| Other Beta-Lactam Antibacterials | | | | | | | |
| J01DD02 | Ceftazidime | 0.009 | 0.038 | 0.009 | 0.041 | 0.010 | 0.046 |
| J01DD62 | Cefoperazone/ Sulbactam | 0.010 | 0.044 | 0.009 | 0.044 | 0.009 | 0.044 |
| J01DE01 | Cefepime | 0.009 | 0.040 | 0.011 | 0.049 | 0.015 | 0.068 |
| J01DH02 | Meropenem | 0.070 | 0.296 | 0.080 | 0.371 | 0.092 | 0.424 |
| J01DH03 | Ertapenem | 0.024 | 0.104 | 0.026 | 0.123 | 0.029 | 0.134 |
| J01DH51 | Imipenem/ Cilastatin | 0.004 | 0.016 | 0.003 | 0.015 | 0.003 | 0.013 |
| J01DI02 | Ceftaroline Fosamil | 0.001 | 0.005 | 0.002 | 0.008 | 0.002 | 0.008 |
| J01DI54 | Ceftolozane/ Tazobactam | - | - | § | 0.001 | 0.001 | 0.003 |
| Other Antibacterials | | | | | | | |
| J01XA01 | Vancomycin | 0.035 | 0.150 | 0.034 | 0.159 | 0.040 | 0.186 |
| J01XA02 | Teicoplanin | § | 0.001 | - | - | - | - |
| J01XB01 | Colistin | 0.006 | 0.026 | 0.006 | 0.029 | 0.005 | 0.022 |
| J01XX08 | Linezolid | 0.002 | 0.009 | 0.008 | 0.036 | 0.008 | 0.038 |
| J01XX09 | Daptomycin | 0.003 | 0.012 | 0.004 | 0.017 | 0.004 | 0.019 |
| Total Broad Spectrum Antibiotics | | | | | | | |
| Total | | 0.289 | 1.224 | 0.319 | 1.483 | 0.354 | 1.637 |

* Percentage of antimicrobials supplied in Hong Kong, those supplied to registered veterinarian surgeons were not included

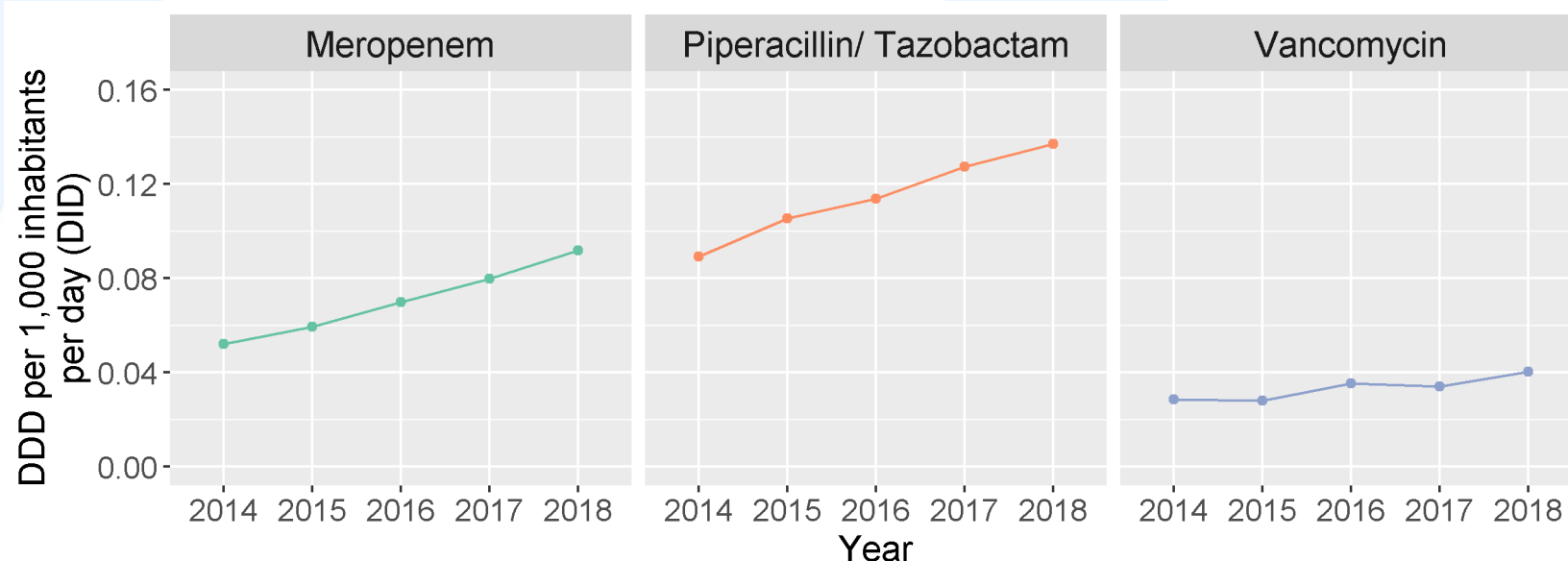
§ Less than 0.0005

Results - Supply of Broad Spectrum Antibiotics (2018)

- The 14 locally-important broad spectrum antibiotics though only accounted for 1.64% of the total wholesale supply in 2018 but the supply trend was increasing for the past 3 years
- Majority of them (99.46%) were supplied to hospitals
- The top 3 broad spectrum antibiotics with the highest volume of wholesale supply were:
 - Piperacillin/ Tazobactam (0.137 DID)
 - Meropenem (0.092 DID)
 - Vancomycin (0.040 DID)
- These 3 antibiotics accounted for 1.24% of the total wholesale supply in 2018 while the rest only accounted for 0.39%

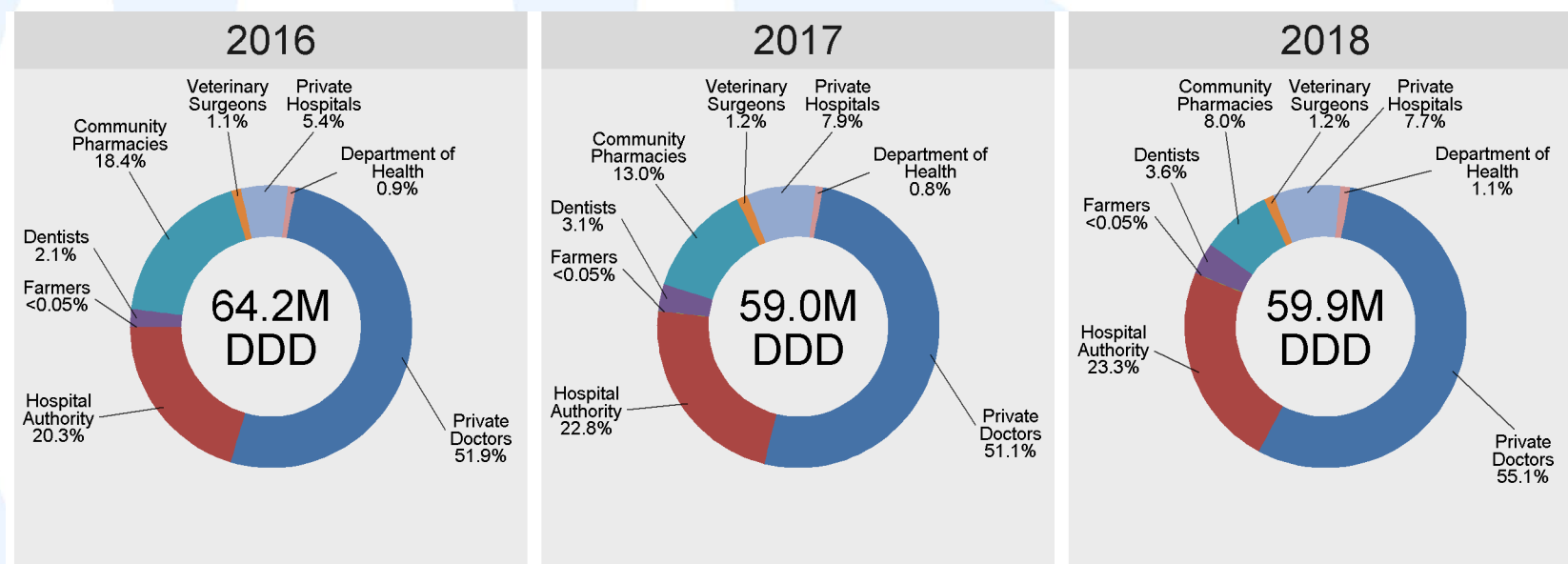


Results - Supply of Broad Spectrum Antibiotics (Top 3)



- A steady increase was observed with the top 3 broad spectrum antibiotics
- Piperacillin/ Tazobactam increased by about 7.6% and Meropenem increased by about 15.0% when compared with the 2017 figures
- Annual increase of vancomycin was about 18.0% but the absolute amount of increase was only 0.006 DID

Results - Among Different Sectors (1)



The figures included the supply of antibiotics to both human and animals sectors



Results - Among Different Sectors (2)

- The top 3 sectors supplied with the largest proportion of overall antibiotics in 2018 were:
 - Private Doctors (55.1%)
 - Hospital Authority (23.3%)
 - Community Pharmacies (8.0%)
- These 3 sectors accounted for 86.4% of the overall supply to all sectors by wholesaling
- The supply of antibiotics to community pharmacies decreased sharply in two consecutive years from 18.4% in 2016 to 13.0% in 2017 and was 8.0% in 2018
- Then followed by private hospitals (7.7%), registered dentists (3.6%) and registered veterinarian surgeons (1.2%)
- Same pattern of ranking was observed for the past 3 years



WHO “AWaRe” Classification (1)

- WHO in 2017 introduced the Access, Watch, Reserve (“AWaRe”) classification of antibiotics in its Essential Medicines List
- A tool for antibiotic stewardship at local, national and global levels with the aim of reducing antimicrobial resistance but also ensuring appropriate treatment are readily available
- AWaRe classifies antibiotics into three stewardship groups: **Access**, **Watch** and **Reserve**, to emphasize the importance of their optimal uses and potential for developing antimicrobial resistance.



WHO “AWaRe” Classification (2)

- Antibiotics in the **ACCESS** group should be available at all times as 1st line treatments for a wide range of common infections
- The **WATCH** group includes antibiotics that are recommended as first- or second-choice treatments for a small number of infections. Their use should be dramatically reduced to avoid further development of resistance.
- The third group, **RESERVE** should be considered as last-resort options and used only in the most severe circumstances when all other alternatives have failed, such as for life-threatening infections due to multidrug-resistant bacteria.

<https://www.who.int/news-room/detail/06-06-2017-who-updates-essential-medicines-list-with-new-advice-on-use-of-antibiotics-and-adds-medicines-for-hepatitis-c-hiv-tuberculosis-and-cancer>



Examples of Antibiotics Under WHO “AWaRe”

AWaRe Categorization

| Access | Watch | Reserve | Others [^] |
|----------------------------------|----------------|------------|-----------------------------|
| Amoxicillin and Enzyme Inhibitor | Azithromycin | Cefepime | Cefuroxime |
| Amoxicillin | Levofloxacin | Linezolid | Combinations of Penicillins |
| Doxycycline | Clarithromycin | Colistin | Lymecycline |
| Metronidazole | Ciprofloxacin | Daptomycin | Cefaclor |
| Cefalexin | Ofloxacin | Fosfomycin | Tetracycline |

[^]Antibiotics that are not included in the WHO Model List of Essential Medicines have not yet been categorized, and are reported as “Others”



Results - by WHO "AWaRe" Classification

| Year | AWaRe Categorization | | | | | | | | | |
|------|----------------------|------|-------|------|---------|-----|---------------------|------|-------|-----|
| | Access | | Watch | | Reserve | | Others [^] | | Total | |
| | DID | % | DID | % | DID | % | DID | % | DID | % |
| 2014 | 13.83 | 62.6 | 5.45 | 24.7 | 0.02 | 0.1 | 2.80 | 12.7 | 22.11 | 100 |
| 2015 | 14.05 | 62.6 | 5.56 | 24.7 | 0.03 | 0.1 | 2.83 | 12.6 | 22.47 | 100 |
| 2016 | 14.47 | 61.4 | 6.12 | 26.0 | 0.03 | 0.1 | 2.96 | 12.5 | 23.58 | 100 |
| 2017 | 13.39 | 62.2 | 5.63 | 26.1 | 0.03 | 0.2 | 2.48 | 11.5 | 21.53 | 100 |
| 2018 | 13.64 | 63.0 | 5.63 | 26.0 | 0.04 | 0.2 | 2.34 | 10.8 | 21.66 | 100 |

[^]Antibiotics that are not included in the WHO Model List of Essential Medicines have not yet been categorized, and are reported as "Other"

- WHO advised to have over 60% of the overall use of all antibiotics under the class of Access^{*}
- From 2014 to 2018, the overall wholesale supply of antibiotics in HK had over 60% fell under the group Access



Summary 1: Overall Supply

- Totaled 59.9 million DDD in 2018
 - + 0.91 million DDD or 0.12 DID vs 2017
 - - 4.31 million DDD (or 1.92 DID) vs 2016 baseline
- Top 3 most supplied antibiotic
 - Beta-lactam Antibacterials, Penicillins (52.14%)
 - Macrolides, Lincosamides and Streptogramins (13.26%)
 - Quinolone Antibacterials (10.75%)
 - These groups (accounting for about 76%) are usually prescribed as 1st-line treatment for suspected bacterial infections in community and hospital settings
- Comparison of data with overseas countries must be interpreted with caution



Summary 2: Broad Spectrum Antibiotics

- 14 locally-important broad spectrum antibiotics accounted for 1.64% of the total supply in Hong Kong
- More than 99% supplied to HA and private hospitals
- Top 3 most supplied broad spectrum antibiotics in past 5 years
 - These antibiotics are namely
 - Piperacillin / Tazobactam
 - Meropenem
 - Vancomycin
 - They accounted for 76% of the 14 locally-important broad spectrum antibiotics in 2018
 - Steady increase of supply was observed with these 3 antibiotics over the past few years



Summary 3 – Supplying Sector

- Top 4 sectors in terms of wholesale supply volume:
 - Private doctors (55.1%)
 - Hospital Authority (23.3%)
 - Community pharmacies (8.0%)
 - Private hospitals (7.7%)
- Supplied with the largest amount is not unexpected as these 2 sectors are the major healthcare service providers
- Sharp decrease in supply to community pharmacies for 2 years

| Year | DDD (change compared with last year) | % total volume |
|------|--------------------------------------|----------------|
| 2016 | 11.82 M | 18.4% |
| 2017 | 7.66 M (- 4.16M) | 13.0% |
| 2018 | 4.78M (- 2.88M) | 8.0% |



Summary 4 – WHO “AWaRe”

- More than 60% of the overall wholesale supply of antibiotics in HK under the class of "Access" for the past 5 years
- Compared with the WHO recommendation
 - As a whole
 - HK have met the WHO recommendation



Way Forward

- Dissemination of results
 - Upload on CHP website for public information
 - Inform relevant stakeholders
- Health education and promotion making use of the data
 - Continue to promote judicious use of antibiotics to the public
 - Advocacy to healthcare workers through additional channels
e.g. HK College of Family Physicians, medical publications
- Continue enhanced regulation and enforcement
- Continue on-going surveillance activities with enhancement
via the development of One Health Antimicrobial Resistance
Information System (AMRIS)



End of Presentation

Thank you

