

## Antimicrobial Usage (AMU) Surveillance in Hong Kong -Wholesale Supply Data (2016-2021)

Dec 2022





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# Background





#### Background

- The Hong Kong Strategy and Action Plan on Antimicrobial Resistance 2017-2022 (Action Plan) was issued in July 2017. New Action Plan was issued in Nov. 2022.
- Activity 3.1.2 suggests collecting antibiotic supply data from different sectors as proxy to reflect the overall usage and trend of antimicrobial usage
- Past summaries published in CHP website in 2018 (Year 2014-16), 2019 (Year 2014-17) and 2020 (Year 2014-18), 2021 (Year 2016-19) and 2022 (Year 2016-20)
- This presentation briefly accounts the surveillance findings for year 2016-2021
- Since the Action Plan was published in July 2017, the situation of 2016 has been chosen as baseline for comparison





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## Method





#### Scope of Data

- Antimicrobials wholesale supply data from licensed drug wholesalers (ever supplied antimicrobials under monitoring) in year 2021 to the following sectors were included:
  - Department of Health (DH)
  - Hospital Authority (HA)
  - Private hospitals
  - Private doctors (mutually exclusive with Private Hospitals)
  - Dentists
  - Veterinary surgeons
  - Community pharmacies
  - Farmers (who had the Antibiotics Permits issued by the Director of Agriculture, Fisheries and Conservation Department)



### Definitions



Department of Health

- Surveillance period is defined by calendar year
- Anatomical Therapeutic Chemical (ATC) classification
  - This system is developed by the World Health Organisation (WHO)
  - It divided drugs into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties
- Defined Daily Dose (DDD)
  - A standardised unit adopted by WHO to facilitate comparison of drug usage
  - Defined as "the assumed average maintenance dose per day for a drug used for its main indication in adults"
  - Each antimicrobial was assigned a DDD constant per route of administration
  - DDD constants are updated by WHO annually<sup>#</sup>
  - The year 2022 version of ATC/DDD was adopted in this report, which is identical as the 2021 version

# https://www.whocc.no/atc\_ddd\_alterations\_\_cumulative/ddd\_alterations/

#### Antimicrobials monitored



- Antimicrobials fall under the following WHO ATC classification were collected from licensed drug wholesalers:
  - J01 Antibacterials for systemic use
  - P01AB Nitroimidazole derivatives, agents against amoebiasis and other protozoal diseases
  - A07AA Antibiotics, intestinal antiinfectives
- Antimicrobials which can be administered by the following routes were included as recommended by WHO
  - Oral
  - Parenteral
  - Rectal
  - Inhalation
- Preparations for topical use were excluded



### WHO AWaRe Categorisation

- WHO introduced the AWaRe categorisation in 2017 for antibiotic stewardship at local, national and global levels with the aim of reducing antimicrobial resistance
- The three categories are:
  - Access

     Indicates the antimicrobials of choice for common infections as first- or second-choice empiric treatment options
  - Watch
    - Includes most of the "highest-priority critically important antimicrobials" for human medicine and veterinary use. These antimicrobials are recommended only for specific, limited indications
  - Reserve - Should only be used as a last resort when all other antimicrobials have failed
- Antimicrobials not listed under WHO AWaRe were grouped as "Others"
- WHO encourages countries or regions to work towards to have 60% or more of the overall AMU under Access and reduce the usage of antimicrobials under Watch and Reserve
- WHO has updated the list of AWaRe classification antibiotics in 2021, which was adopted in this report





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### Broad-spectrum Antimicrobials (Big Guns)

The following broad-spectrum antimicrobials are important on treating resistant infections and being monitored in AMU surveillance with HA Dispensing Data. They are examined separately in this surveillance:

- Piperacillin/tazobactam
- Ceftazidime
- Cefoperazone/sulbactam
- Cefepime
- Ceftaroline fosamil
- Ceftolozane/tazobactam
- Ceftazidime/avibactam

- Meropenem
- Ertapenem
- Imipenem/cilastatin
- Vancomycin
- Linezolid
- Daptomycin
- Colistin
- Teicoplanin





#### Measurement

- The following units were used:
  - Overall quantity of antimicrobials supplied to various sectors: DDD\*
  - Supply quantity after considering the annual mid-year population of Hong Kong: DDD per 1,000 inhabitants per day (DID)
- The following measurements were calculated:
  - Overall wholesale supply quantity
  - Antimicrobials wholesale supply by different grouping
    - Distribution by WHO AWaRe categorisation
    - Distribution by Sector
    - ATC Pharmacological Subgroup
    - 10 most supplied antimicrobials
  - Wholesale supply quantity of selected broad-spectrum antimicrobials





### **Statistical Method**

- Year 2016 was chosen as the baseline for comparison as the Hong Kong Strategy and Action Plan on Antimicrobial Resistance 2017-2022 was issued in mid-2017 and such decision was endorsed by the High Level Steering Committee (HLSC)
- Following ECDC, compound annual growth rate (CAGR) were used to illustrate average annual rate of change when comparing antimicrobials dispensed in 2021 with that in 2016.

```
CAGR = (SU_{2021}/SU_{2016})^{(1/5)} - 1
```

In this equation, SU<sub>2021</sub> is the total amount of antimicrobials supplied in year 2021, SU<sub>2016</sub> is the total amount of antimicrobials supplied for year 2016





## Results

#### 1. Overall antimicrobials wholesale supply (2016-2021)



# 1. Overall antimicrobials wholesale supply (2016-2021)



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

- A mild increase in total supply was seen (↑ 0.12 DID, ↑ 0.9%) from 2020 to 2021
- When compared with the total supply in 2016 (baseline), a decrease of 6.63 DID (↓ 32.5%) in 2021 was observed (CAGR:-7.6%)



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## Results

2A. Antimicrobials wholesale supply (2016-2021)Distribution by WHO AWaRe categorisation



# 2A. Antimicrobials wholesale supply (2016-2021)Distribution by WHO AWaRe categorisation



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- WHO target of at least 60% antimicrobial consumption being from medicines in the Access Group

- Antimicrobials under Access constituted 55.8% of all antimicrobials supplied in 2016 and increased to 64.3% in 2021 (Exceeded 60%)
- The proportion of antimicrobials under Watch decreased steadily from 40.3% in 2016 to 31.6% in 2021



#### 2A. Antimicrobials wholesale supply (2016-2021) (伊爾生防護中心 - Distribution by WHO AWaRe categorisation

۸\\/>Re	DDD	per 1,000	inhabitan	Average	n-	Compound			
Categorisation	Year 2016	Year 2017	Year 2018	Year 2019	Year 2020	Year 2021	annual change	value	growth rate (16 to 21)
Access	11.36	10.39	10.55	11.20	8.36	8.83	-0.517	-	-4.9%
Watch	8.20	7.36	7.28	7.07	4.71	4.35	-0.783	<0.01	-11.9%
Reserve	0.02	0.02	0.02	0.02	0.02	0.03	0.002	<0.01	11.6%#
Others	0.79	0.64	0.64	0.68	0.52	0.53	-0.046	<0.05	-7.6%

\* Non-human use antimicrobials supplied in Hong Kong were excluded.

<sup>#</sup> CAGR figure for Reserve antimicrobials has to be interpreted with caution, as number of Reserve antimicrobials increased from 5 in 2016 to 10 in 2021

- The supply of antimicrobials under Access and Watch showed decrease of 4.9% and 11.9% in CAGR from 2016 to 2021 respectively
- As the total number of antimicrobials under Reserve supplied in Hong Kong increased from five in 2016 to ten in 2021, the CAGR figure must be interpreted with caution





## Results

2B. Antimicrobials wholesale supply (2016-2021) - Distribution by Sector



#### 2B. Antimicrobials wholesale supply (2016-2021) 任 简生防護中心 - Distribution by Sector



- In 2021, 49.3% of antimicrobials supplied in Hong Kong went to private doctors, followed by Hospital Authority (30.7%) and private hospitals (6.3%)

# 2B. Antimicrobials wholesale supply (2016-2021) 任 (1995) (Entre for Health Protection - Distribution by Sector

		Average		CAGP					
	Year	Year	Year	Year	Year	Year	annual	p- valuo	$(16 \pm 0.21)$
	2016	2017	2018	2019	2020	2021	change	value	(10 to 21)
Human-use sectors									
Private Doctors	10.82	9.69	10.44	10.91	6.81	6.90	-0.793	-	-8.6%
Hospital Authority	4.07	4.17	4.27	4.47	4.01	4.29	0.024	-	1.1%
Community Pharmacies	3.82	2.51	1.61	1.46	1.05	0.78	-0.563	<0.01	-27.2%
Private Hospitals	1.09	1.38	1.38	1.31	0.93	0.88	-0.071	-	-4.3%
Dentists	0.38	0.50	0.58	0.64	0.61	0.72	0.060	<0.01	13.6%
Department of Health	0.19	0.17	0.21	0.17	0.19	0.17	-0.002	-	-2.3%

- After the significant drop from 2019-20 in private doctors, private hospitals and community pharmacies, mild decrease in 2021 for private hospitals and community pharmacies while a mild increase for private doctors
- Supply to dentists showed an obvious increase of 13.6% although the absolute amount was small (0.38 to 0.72 DID)
- Supply to community pharmacies showed the most obvious decrease of 27.2% in CAGR from 2016 to 2021



#### Antimicrobials wholesale supply for Community Pharmacies (by ATC Pharmacological Subgroup)



- When further analysed by sectors, an obvious decrease could be seen with community pharmacies from 2016 to 2021 (from 3.82 to 0.78 DID, ↓79.6%) and contributed by almost all ATC pharmacological subgroups, especially beta-lactam antibacterials, penicillins (J01C) (↓91.2%)
- Smaller magnitudes of decrease could be seen with tetracyclines (J01A) and quinolones (J01M)



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# Antimicrobials wholesale supply for Private Doctors (by ATC Pharmacological Subgroup)



ATC Pharmacological Subgroup
 Beta-Lactam Antibacterials, Penicillins (J01C)
 Tetracyclines (J01A)
 Macrolides, Lincosamides and Streptogramins (J01F)
 Quinolone Antibacterials (J01M)
 Other Beta-Lactam Antibacterials (J01D)
 Others

Note: Text inside bar chart refers to: DID (Annual percentage)

- For private doctors, mild increases were observed from 2020 to 2021 for Betalactam antibacterials, penicillins (J01C) (<sup>1</sup>0.32DID, 11.8%), and Tetracyclines (J01A) (<sup>1</sup>0.11DID, 11.1%)
- Mild decease were observed for macrolides, lincosamides and stregtogramins (J01F) (↓0.15DID, 12.6%), quinolones (J01M) (↓0.13DID, 14.3%), and other betalactam antibacterials (J01D) (↓0.08DID, 9.3%)



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#### Antimicrobials wholesale supply for Hospital Authority (by ATC Pharmacological Subgroup)

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2 -

0 -

DDD per 1,000 inhabitant days (DID)

0.36 (8.9%)

0.39 (9.6%)

0.30 (7.4%)

0.40 (9.8%)

0.34 (8.5%)

2016

2017

2018

2019

Year



For Hospital Authority, most obvious increases were observed in • beta-lactam antibacterials, penicillins (J01C) (<sup>10.11DID</sup>, 5.4%), while other groups remained rather stable in 2021

2020

2021



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#### Antimicrobials wholesale supply for Private Hospitals (by ATC Pharmacological Subgroup)





 For private hospitals, most obvious decrease was beta-lactam antibacterials, penicillins (J01C) (↓ 0.07DID, 15%), while other groups remained rather stable in 2021



#### Antimicrobials wholesale supply for Dentists (by ATC Pharmacological Subgroup)



2020

2021

2018

Year

2019

2016

2017



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#### Antimicrobials wholesale supply for Department of Health (by ATC Pharmacological Subgroup)





For DH, a mild decrease was observed from 2020 to 2021 ( $\downarrow$  0.0233 DID,  $\downarrow$  11.9%). The results should be interpreted with caution as the absolute change for each group is very small



## Results

2C. Antimicrobials wholesale supply in Hong Kong (by ATC Pharmacological Subgroup)



#### 2C. Antimicrobials wholesale supply (2016-2021) 任意 生防護中心 - by ATC Pharmacological Subgroup



In 2021, beta-lactam antibacterial, penicillins (J01C) was the most commonly supplied antimicrobial group (46.0%) by wholesale, followed by tetracyclines (J01A) (14.6%), macrolides, lincosamides and streptogramins (J01F) (10.9%), quinolone antibacterials (J01M) (10.4%), and other beta-lactam antibacterials (J01D) (9.0%)



### 

	ATC Pharmacological Subgroup	DD	D per 1,00	0 inhabita	Average		CACD			
Cada	Description	Year	Year	Year	Year	Year	Year	annual	р-	
Code	Description	2016	2017	2018	2019	2020	2021	change	value	(16 to 21)
J01C	Beta-Lactam Antibacterials, Penicillins	8.68	7.89	8.09	8.52	5.97	6.32	-0.490	-	-6.1%
J01A	Tetracyclines	2.07	1.85	1.87	2.05	1.91	2.00	0.001	-	-0.7%
J01F	Macrolides, Lincosamides and Streptogramins	3.34	2.96	2.89	2.82	1.66	1.50	-0.375	<0.01	-14.8%
J01M	Quinolone Antibacterials	2.43	2.29	2.34	2.19	1.61	1.42	-0.206	<0.05	-10.2%
J01D	Other Beta-Lactam Antibacterials	2.85	2.30	2.17	2.19	1.36	1.24	-0.309	<0.01	-15.3%
	Nitroimidazole Derivatives, Agents									
P01AB	Against Amoebiasis and Other Protozoal	0.43	0.47	0.44	0.46	0.44	0.50	0.007	-	2.8%
	Diseases									
J01X	Other Antibacterials	0.29	0.32	0.32	0.34	0.32	0.31	0.004	-	1.3%
J01E	Sulfonamides and Trimethoprim	0.21	0.19	0.22	0.21	0.18	0.20	-0.002	-	-0.8%
A07AA	Antibiotics, Intestinal Antiinfectives	<0.005	0.10	0.12	0.12	0.14	0.20	0.032	<0.01	#
J01G	Aminoglycoside Antibacterials	0.05	0.05	0.05	0.05	0.03	0.04	-0.004	<0.05	-7.1%
J01B	Amphenicols	<0.005	<0.005	<0.005	<0.005	-	-	-0.002	<0.05	-
J01R	Combinations of Antimicrobials*	-	-	-	-	-	-	-	-	-
	Total	20.37	18.41	18.49	18.96	13.62	13.74	-1.345	<0.05	-7.6%

Note:

Antimicrobials supplied for non-human use in Hong Kong (e.g. veterinary surgeons and farmers) were not included \* There was no registered product under "Combinations of Antimicrobials" (J01R) in Hong Kong # The CAGR for antimicrobials under A07AA is not applicable as the 2016 figure was not complete

- Antimicrobials under P01AB (Nitroimidazole Derivatives) increased most (2.8% in CAGR)
- Antimicrobials under J01D (Other Beta-Lactam Antibacterials) and J01F (Macrolides, Lincosamides and Streptogramins) decreased most (-15.3% and -14.8% in CAGR respectively)





## Results

2D. Antimicrobials wholesale supply in Hong Kong (10 most supplied antimicrobials)



# 2D. Antimicrobials wholesale supply (2016-2021) 任意 10 most supplied antimicrobials



- The 10 most supplied antimicrobials contributed >80% of all antimicrobials supplied from 2016 to 2021
- In 2021, amoxicillin and beta-lactamase inhibitor (J01CR02) continued to be the most commonly supplied antimicrobial (26.3%) by wholesale, followed by amoxicillin (J01CA04) (13.0%), and doxycycline (J01AA02) (12.6%)



# 2D. Antimicrobials wholesale supply (2016-2021) 任意 10 most supplied antimicrobials

Ą		DDD p	er 1,000 in	Average		CACD				
Codo	Description	Year	Year	Year	Year	Year	Year	annual	p-value	$(16 \pm 0.21)$
Coue	Description	2016	2017	2018	2019	2020	2021	change		(10 to 21)
J01CR02	Amoxicillin and Beta- Lactamase Inhibitor	4.16	4.31	4.59	4.91	3.33	3.62	-0.153	-	-2.8%
J01CA04	Amoxicillin	2.95	2.34	2.33	2.45	1.72	1.79	-0.215	<0.05	-9.5%
J01AA02	Doxycycline	1.69	1.54	1.58	1.77	1.63	1.73	0.019	-	0.5%
J01MA12	Levofloxacin	1.29	1.26	1.39	1.30	0.99	0.89	-0.083	-	-7.2%
J01FA09	Clarithromycin	1.50	1.32	1.19	1.21	0.76	0.80	-0.148	< 0.01	-11.8%
J01DC02	Cefuroxime	1.63	1.39	1.31	1.27	0.73	0.64	-0.199	<0.01	-17.0%
J01FA10	Azithromycin	1.54	1.39	1.48	1.38	0.74	0.56	-0.198	<0.05	-18.2%
J01XD01/ P01AB01	Metronidazole	0.47	0.51	0.48	0.50	0.47	0.53	0.005	-	2.2%
J01CR50	Combinations of Penicillins	0.78	0.56	0.54	0.59	0.42	0.41	-0.063	<0.05	-12.1%
J01MA02	Ciprofloxacin	0.74	0.63	0.62	0.59	0.40	0.38	-0.072	<0.01	-12.5%
	Others	3.61	3.15	2.98	2.98	2.41	2.39	-0.238	<0.01	-7.9%
	Total	20.37	18.41	18.49	18.96	13.62	13.74	-1.345	<0.05	-7.6%

Note:

Antimicrobials supplied to veterinarians, and non-human use antimicrobials (i.e. ATC code starts with Q) were not included

\* Metronidazole was classified as J01XD01 if for parenteral use and P01AB01 if for oral/rectal use

- Metronidazole (J01XD01/P01AB01) and doxycycline with positive CAGR of 2.2% and 0.5% respectively, others of the top ten have –ve CAGR
- Supply of cefuroxime (J01DC02) and azithromycin (J01FA10) decreased most (-17.0% and -18.2% respectively in CAGR) from 2016 to 2021





## Results

3. Wholesale supply of selected broad-spectrum antimicrobials



#### 3. Wholesale supply of selected broadspectrum antimicrobials





Ceftolozane/ tazobactam (J01DI54)

- In 2021, piperacillin/tazobactam was the most commonly supplied (42.1%) broadspectrum antimicrobial, followed by meropenem (21.8%) and vancomycin (14.2%)
- Majority of these broad spectrum antimicrobials were supplied to HA and private hospitals from 2016 to 2021 (about 99%)

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#### 3. Wholesale supply of selected broadspectrum antimicrobials



ATC Chemical Substance			DDD per 1,0	Average	n	CAGR				
Code	Description	Year 2016	Year 2017	Year 2018	Year 2019	Year 2020	Year 2021	annual change	value	(16 to 21)
Beta-Lactam Antibacterials, Penicillins										
J01CR05	Piperacillin/tazobactam	0.114	0.128	0.138	0.149	0.152	0.166	0.010	< 0.01	7.7%
Other Beta-Lactam Antibacterials										
J01DH02	Meropenem	0.047	0.053	0.062	0.069	0.075	0.086	0.008	<0.01	12.9%
J01DH03	Ertapenem	0.025	0.027	0.029	0.029	0.029	0.034	0.002	< 0.01	6.6%
J01DD02	Ceftazidime	0.009	0.009	0.010	0.012	0.011	0.013	0.001	<0.05	8.3%
J01DD62	Cefoperazone/sulbactam	0.011	0.009	0.010	0.009	0.008	0.008	§	< 0.01	-5.6%
J01DE01	Cefepime	0.005	0.005	0.007	0.007	0.008	0.009	0.001	<0.01	13.8%
J01DH51	Imipenem/cilastatin	0.004	0.003	0.003	0.003	0.002	0.002	§	< 0.01	-10.2%
J01DI02	Ceftaroline fosamil	0.001	0.002	0.002	0.002	0.002	0.002	§	-	6.1%
J01DD52	Ceftazidime/avibactam	-	§	-	0.001	0.001	0.002	§	-	*
J01DI54	Ceftolozane/tazobactam	-	§	0.001	0.001	0.001	-	§	-	*
<b>Other Ant</b>	ibacterials									
J01XA01	Vancomycin	0.036	0.034	0.041	0.044	0.047	0.056	0.004	< 0.01	9.5%
J01XX08	Linezolid	0.008	0.008	0.009	0.009	0.008	0.009	§	-	3.7%
J01XX09	Daptomycin	0.003	0.004	0.004	0.005	0.004	0.005	§	-	10.6%
J01XB01	Colistin	0.002	0.002	0.002	0.002	0.002	0.002	§	-	-3.1%
J01XA02	Teicoplanin	§	-	§	-	-	-	§	-	-
Total Broa	d Spectrum Antibiotics									
	Total	0.263	0.284	0.315	0.341	0.350	0.393	0.025	< 0.01	8.3%

Antimicrobials supplied for non-human use in Hong Kong (e.g. veterinary surgeons and farmers) were not included \* The CAGR for the supply of antimicrobial is not applicable as it is a newly introduced antimicrobial which was not available in 2016 & Less than 0.0005

§ Less than 0.0005

- Total wholesale supply of selected broad-spectrum antimicrobials reported an average annual increase of 0.025 DID (or 8.3% in CAGR) with statistical significance
- Piperacillin/ tazobactam, meropenem and vancomycin have been the 3 most supplied selected broad-spectrum antimicrobials from 2016 to 2021. They accounted for about 78% of all selected broad-spectrum antimicrobials under monitoring in 2021





### Remarks on interpretation of results (1)

- DDD is a technical unit of use that does not necessarily reflect the recommended or average prescribed dose
- There are no separate DDDs for children which makes the DDD estimates for paediatric formulations more difficult to interpret





### Remarks on interpretation of results (2)

- The surveillance of antimicrobials by wholesale supply in Hong Kong is a voluntary self-reporting by licensed drug wholesalers and could have reporting errors
- Wholesale supply data is used as a proxy for the amount of antimicrobials supplied to each sector, therefore the figures are not equivalent to dispensing figures
- Wholesale supply data could be affected by marketing strategies, e.g. discount offers
- Readers are cautioned not to use the Hong Kong figures to make direct comparison with that of other countries as the health care services provision system and the methodology in collecting the surveillance data may not be the same



### Summary (1)



- The overall wholesale supply of antimicrobials decreased from 20.37 DID in 2016 to 13.74 DID 2021 (Slide 14)
- The overall wholesale supply of antimicrobials remained similar to 2020 (13.62 vs 13.74 DID) during the pandemic of COVID-19 (Slide 14)
- With 64.3% of the overall antimicrobial supply under the Access group of WHO AWaRe categorization, Hong Kong has exceeded the overall 60% benchmark under Access as recommended by WHO (Slide 16)
- Majority of antimicrobials supplied in Hong Kong went to private doctors (49.3%), the major primary healthcare service providers, followed by Hospital Authority (30.7%) and private hospitals (6.3%) in 2021 (Slide 19)





### Summary (2)

- Among the supply for human use, supply to community pharmacies showed a significant decrease of 27.2 % in CAGR
- from 2016 to 2021 while supply to dentists showed an obvious increase of 13.6% (Slide 20)
- Among the ten most supplied antimicrobials, the two most significant decreased in supply volume were cefuroxime and azithromycin (\$\sqrt{17.0%}\$ and \$\sqrt{18.2%}\$ respectively in CAGR) from 2016 to 2021 (Slide 32)
- When compared with 2020, Amoxicillin and beta-lactamase inhibitor continued to be the most supplied antimicrobial with a mild rebound (个8.6%) (Slide 32)
- Overall data of wholesale supply of broad-spectrum antimicrobials showed an average annual increase of 0.025
   DID (or 8.3% in CAGR) from 2016 to 2021 (slide 35)





#### Recommendations

- The 2021 results should be read with caution as the pandemic of Covid-19 might have changed the regular practice and arrangement of medical services in Hong Kong. Close monitoring of the antimicrobial supply data is required in subsequent years to further assess its impact of COVID-19.
- As the majority of antimicrobials were supplied to private doctors (49.3%) and Hospital Authority (30.7%), strengthening the implementation of antibiotic stewardship programme in primary care and public hospitals are recommended
- Majority of the broad spectrum antimicrobials were supplied to HA or private hospitals. The continuous rising supply trend of these broad spectrum antimicrobials warrants to further enhance the promulgation of antibiotic stewardship programme at hospital setting





# THE END

Thank you

