

ANTIMICROBIAL STEWARDSHIP POLICY IMPLEMENTATION DURING COVID-19 PANDEMIC: A NATIONWIDE SERIAL CROSS-SECTIONAL STUDY

HSD23

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Conflict of interest: Takehiro Ishida is an employee of Daiichi Sankyo Company, Limited. Satoshi Yamaguchi is an employee of Accenture.
This research was conducted independently of these institutions.



INTRODUCTION

【Antimicrobial Resistance (AMR) and Antimicrobial Use】

- AMR occurs in bacteria, fungi, viruses, and parasites according to WHO, and appropriate antimicrobial use is essential for AMR control.
- WHO's AWaRe classifies antibiotics as Access (first-choice), Watch (selective use), or Reserve (use sparingly), with a target of $\geq 60\%$ Access use set in 2019.

【Antimicrobial Stewardship Policies in Japan】

- National Action Plan (2016-2020) targeted a one-third reduction in antimicrobial use from 2013 levels, and the deadline was extended until Mar 2023 in 2022.
- Antimicrobial Stewardship Manual was published by Ministry of Health, Labour and Welfare (MHLW) in Jun 2017.
- Inpatient stewardship incentive of 1,000 JPY was introduced in Apr 2018; outpatient oral antibiotic monitoring and manual reference were added in Apr 2020.

【COVID-19 Pandemic and Government Measures in Japan】

- First state of emergency was declared in Apr 2020, with requests to avoid non-essential outings; COVID-19 was reclassified in May 2023, ending most measures.

AIM

To analyze nationwide trends in antimicrobial use and expenditure in Japan from 2016 to 2022, including changes in antibiotic use by AWaRe category.

METHODS

【Study Design】 Serial cross-sectional study

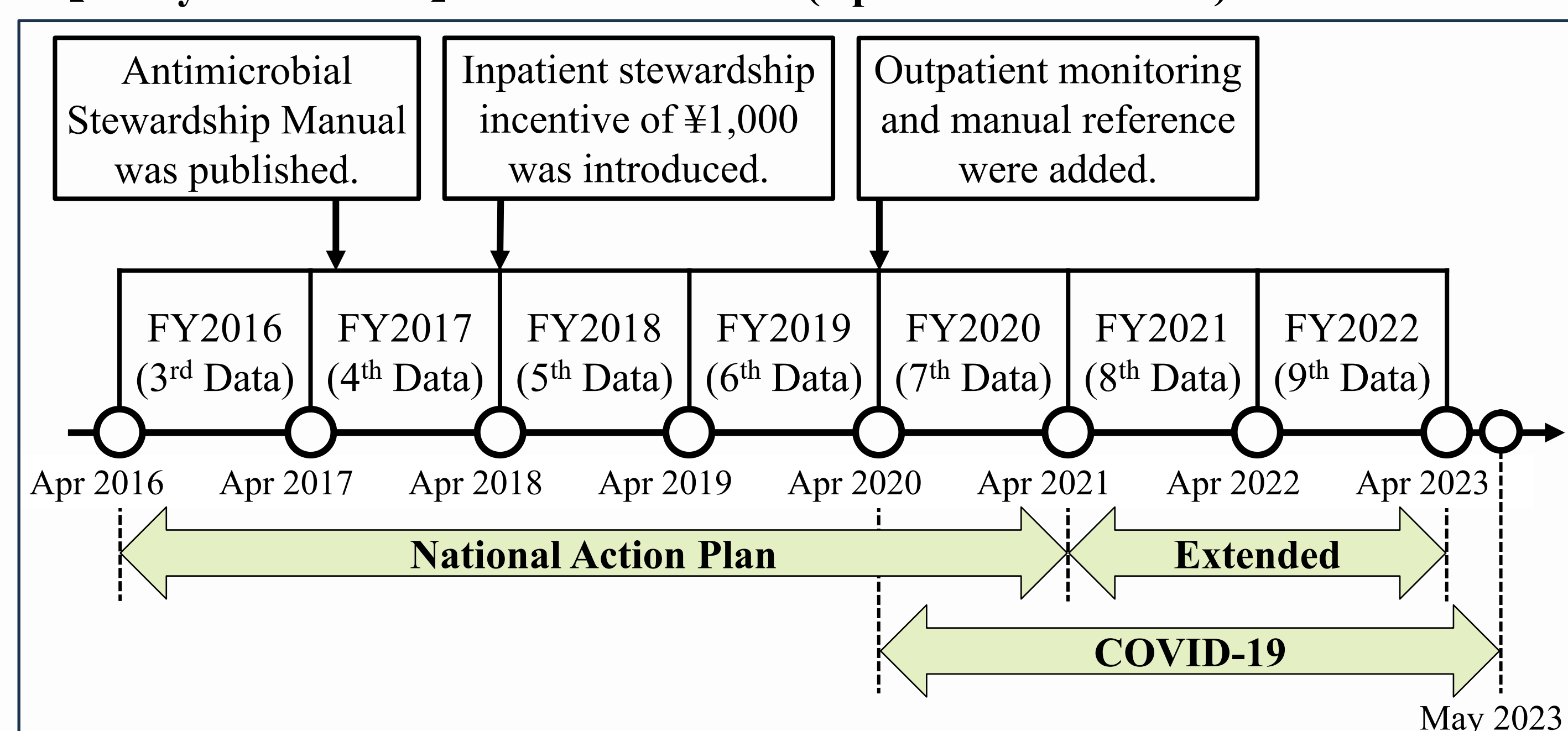
【Data Source】 **NDB Open Data**: Aggregated, nationwide reimbursement claim database published by MHLW, covering nearly all such claims in Japan.

	NDB	NDB Open Data
Data	Individual-level data	Aggregated data (by drug, prefecture, etc.)
Access	Expert review & approval required	Publicly available; no restriction
Personal info	Included (anonymized)	Individuals cannot be identified; no hospital-level data

【Data Process】

- Prescription claim data of antibiotics and antifungals were extracted, while antivirals and antiparasitics were excluded, considering the MHLW's manual.
- AWaRe category and Defined Daily Dose (DDD; assumed average dose/day of a drug's main indication) were based on AMR Clinical Reference Center in Japan.

【Analysis Duration】 FY2016-FY2022 (Apr 2016 - Mar 2023)



【Outcomes】

- **DID**: Antimicrobial use expressed as DDD per 1,000 inhabitants per day
- Expenditure analysis included three outcomes:
- **Annual expenditure**: $\sum \{(\text{Prescription units}) \times (\text{Official drug price} / \text{unit})\}$
- **Annual DDDs**: Annual antimicrobial use expressed as DDD
- **Expenditure / DDD**: (Annual expenditure) / (Annual DDDs)

【Statistical Analysis】 Prefecture-level means and 95% CIs were calculated across all 47 prefectures. FY2019 and FY2020 values were compared using two-sided paired t-tests; $p < 0.05$ was considered statistically significant.

RESULTS

Table 1: Nationwide DID Trend for FY2016-FY2022 by AWaRe Category

DID (Share)	FY2016	FY2017	FY2018	FY2019	FY2020	FY2021	FY2022	Difference FY16-22
Total	15.40	14.67	14.27	14.15	10.99	11.12	11.40	-4.00 (-26.0%)
Access	1.50 (11.1%)	1.59 (12.4%)	1.73 (14.0%)	1.88 (15.4%)	1.74 (19.1%)	1.88 (20.3%)	1.99 (20.9%)	+0.49 (+32.9%)
Watch	11.86 (87.8%)	11.07 (86.5%)	10.53 (84.9%)	10.18 (83.5%)	7.28 (79.7%)	7.24 (78.5%)	7.40 (78.0%)	-4.45 (-37.6%)
Reserve	0.15 (1.1%)	0.14 (1.1%)	0.13 (1.1%)	0.13 (1.1%)	0.11 (1.2%)	0.11 (1.2%)	0.10 (1.1%)	-0.05 (-30.9%)
Others	1.90 (-)	1.88 (-)	1.88 (-)	1.97 (-)	1.86 (-)	1.89 (-)	1.90 (-)	+0.01 (+0.4%)

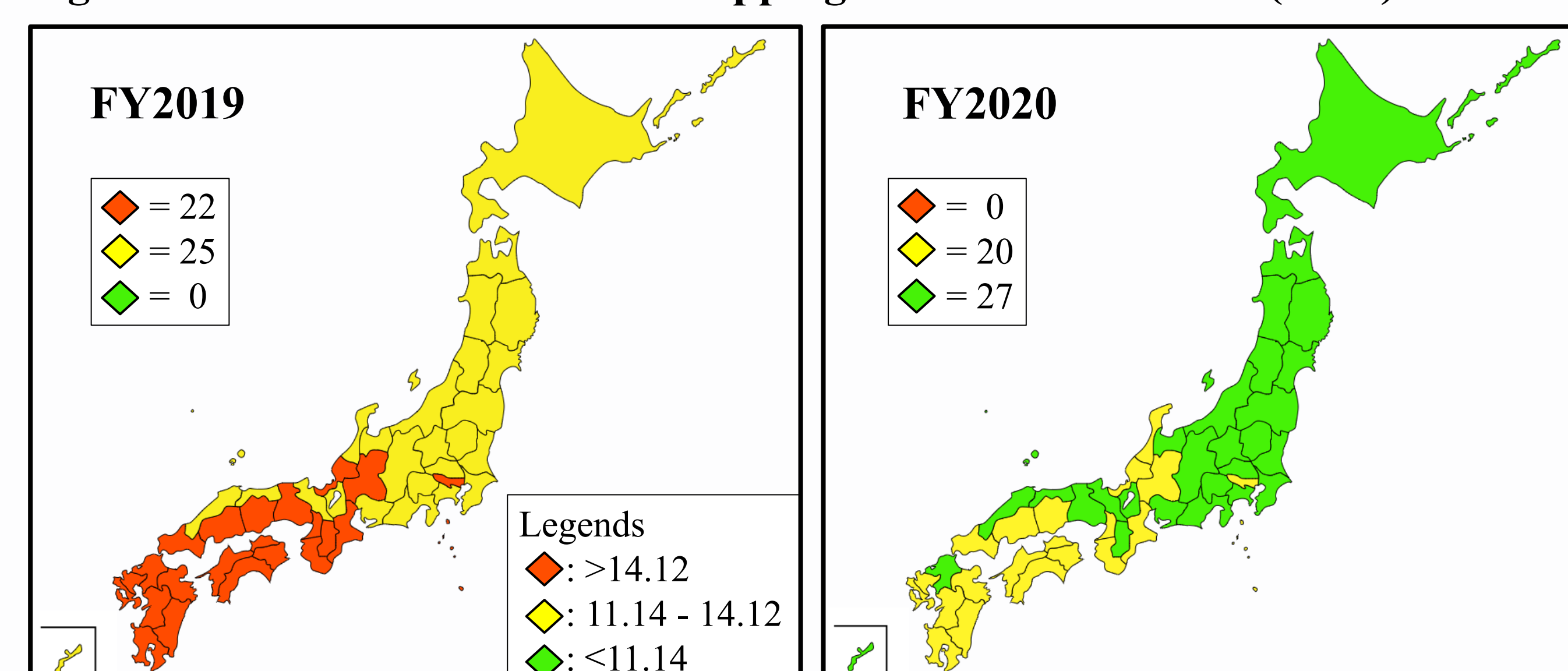
Key finding: Total DID decreased in FY16-22, with marked decline in FY19-20. Watch use decreased; Access share increased but remained below the WHO target.

Table 2: Prefecture-level DID for FY2019-FY2020 by Setting (n=47)

Mean (95% CI)	FY2019	FY2020	Difference FY19-20	p-value	Change FY19-20
Total	14.12 (13.73 - 14.51)	11.14 (10.82 - 11.45)	-2.99 (-3.12 - -2.85)	$p < 0.001$	-21.1% (-21.8 - -20.4)
Outpatient (Oral)	12.78 (12.42 - 13.14)	9.95 (9.67 - 10.23)	-2.83 (-2.96 - -2.70)	$p < 0.001$	-22.1% (-22.9 - -21.4)
Outpatient (Parenteral)	0.10 (0.09 - 0.11)	0.06 (0.06 - 0.07)	-0.04 (-0.04 - -0.03)	$p < 0.001$	-37.0% (-38.6 - -35.5)
Inpatient (Oral)	0.57 (0.53 - 0.60)	0.51 (0.48 - 0.54)	-0.06 (-0.06 - -0.05)	$p < 0.001$	-9.9% (-10.8 - -9.0)
Inpatient (Parenteral)	0.67 (0.65 - 0.69)	0.61 (0.59 - 0.63)	-0.06 (-0.07 - -0.06)	$p < 0.001$	-9.1% (-9.9 - -8.3)

Key finding: DID decreased across all settings and formulations between FY2019 and FY2020, with larger decline in outpatient settings.

Figure 1: DID Prefecture-based Mapping for FY2019-FY2020 (n=47)



Key finding: Nationwide decline in DID was observed between FY2019 and FY2020. DID tended to be higher in western than in eastern Japan.

Table 3: Nationwide Antimicrobial Drug Expenditure for FY2016-FY2022

FY2016 → FY2022 (Change)	Annual Expenditure (billion JPY)	Annual DDDs (million)	Expenditure / DDD (JPY/DDD)
Total	288.2 → 162.1 (-43.8%)	713.5 → 519.9 (-27.1%)	404.0 → 311.7 (-22.8%)
Outpatient (Oral)	157.1 → 79.4 (-49.4%)	651.2 → 470.4 (-27.8%)	241.2 → 168.9 (-30.0%)
Outpatient (Parenteral)	9.7 → 4.7 (-52.0%)	5.6 → 3.0 (-46.6%)	1721.1 → 1545.0 (-10.2%)
Inpatient (Oral)	13.2 → 6.6 (-49.8%)	27.2 → 16.9 (-37.9%)	487.1 → 394.0 (-19.1%)
Inpatient (Parenteral)	108.2 → 71.4 (-34.0%)	29.5 → 29.7 (+0.7%)	3671.1 → 2403.4 (-34.5%)

Key finding: Annual expenditure decreased across all settings, accompanied by decreases in DDDs and expenditure / DDD, except for inpatient parenteral DDDs.

CONCLUSION

Antimicrobial use and expenditure decreased over 2016-2022, with antibiotics shifting from Watch to Access, though Access share remained below the WHO target.



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