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# Japanese antimicrobial consumption surveillance: First report on oral and parenteral antimicrobial consumption in Japan (2009–2013)



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## ABSTRACT

No reliable national antimicrobial consumption data have been available in Japan. The Japanese antimicrobial consumption surveillance (JACS) project started to collect data nationwide on antimicrobial consumption. This paper provides the first sales data from the JACS project on oral and parenteral antimicrobial consumption in Japan as well as the trends for the years from 2009 to 2013. The population-weighted total consumption was expressed as defined daily doses (DDDs) per 1000 inhabitants per day (DID). The value of DID increased from 14.7 in 2009 to 15.8 in 2013. Notably, oral antimicrobials accounted for 92.6% (mean of 2009, 2011 and 2013) of total consumption. Oral third-generation cephalosporins, macrolides and fluoroquinolones accounted for 77.1% (mean of 2009, 2011 and 2013) of oral consumption. Consumption of antimicrobials has increased during the years 2009 and 2013 regardless of the dosage form. This is the first report regarding the population-weighted consumption of oral and parenteral antimicrobials in Japan during the years 2009 and 2013. These results provide useful information for combating the menace of antimicrobial resistance in Japan.

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### 1. Introduction

Antimicrobial use is a main factor responsible for antimicrobial resistance, and the provision of reliable national data regarding antimicrobial consumption is a prerequisite for understanding the epidemiology of antibiotic resistance [1]. The World Health Organization (WHO) has recommended that member nations should develop national plans to combat antimicrobial resistance, and surveillance has been identified as a key component

\* Corresponding author. Present address: Department of Pharmacy, Mie University Hospital, Faculty of Medicine, Mie University, 2-174 Edobashi, Tsu, Mie 514-8507, Japan. Fax: +81 59 232 1201. contributing to the initiation of public health actions and strategy development [2]. Several regions, beginning with the European Union (EU), have reported surveillance data regarding antimicrobial consumption and resistance [3].

In Japan, an online national surveillance programme system [Japan Nosocomial Infections Surveillance (JANIS)] was established by the Ministry of Health, Labour, and Welfare of Japan. Since 2007, this system has been providing basic information regarding the incidence and prevalence of nosocomial infections and antimicrobial-resistant bacteria in Japanese medical settings. However, no surveillance system previously existed for antimicrobial consumption. In 2015, we initiated the Japanese antimicrobial consumption surveillance (JACS) project aimed at collecting data regarding antimicrobial consumption in Japan by two distinct strategies, i.e. collecting sales data regarding oral and parenteral antimicrobials

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prescribed both in hospitals and community settings, and establishing an online system collecting data on the use of parenteral antimicrobials in hospital settings.

In the present study, sales data were collected and analysed successfully reflecting the consumption of oral and parenteral antimicrobials in Japan for the first time and their consumption trends for the years 2009-2013.

# 2. Methods

# 2.1. Data collection and analyses

Sales data for antimicrobials for 2009, 2011 and 2013 were obtained from IMS Japan K.K. (Tokyo, Japan). These data were collected using pharmaceutical sales distribution channels through wholesalers, which accounted for 98% of the total sales in Japan. The data were analysed in accordance with the Anatomical Therapeutic Chemical (ATC) classification using defined daily dose (DDD) as a measurement unit [4]. The 2011 version of the ATC/DDD system was applied to all of the data. Daily doses of some antimicrobials for which DDDs were not defined in the ATC/DDD system were separately defined as JDDD using the approved maintenance dosages in Japan (Table 1). In addition, fluoroquinolones and macrolides were classified into groups based on the reports by Adriaenssens et al. (Table 2) [5,6]. Tosufloxacin and sitafloxacin were added to the table based on their chemical structure and antimicrobial activity.

For normalisation, national data on antimicrobial consumption (antimicrobials for systemic use, ATC 3rd or 4th level) were reported as DDDs per 1000 inhabitants per day (DID). The data for Japan's population were obtained from the results of a population survey report that was published by the Ministry of Health, Labour and Welfare of Japan [7]. Trends were investigated by Spearman's rank correlation analysis.

#### 3. Results

#### 3.1. Antimicrobial consumption in Japan from 2009 to 2013

Trends in antimicrobial consumption (in DID) from 2009 to 2013 are presented in Fig. 1 (total), Table 3 (oral) and Table 4 (parenteral). The population-weighted total consumption in Japan (in DID) revealed an increase from 14.7 in 2009 to 15.8 in 2013 (Fig. 1). Notably, oral antimicrobials accounted for 92.6% (mean of

#### Table 2

First-generation FQs

Classification of available fluoroquinolones (FOs) and macrolides in Japan (ATC classification, 2011 version)

ATC level	Name	Route	ATC level	Name	Route	ATC level	Name	Route
J01MA06	Norfloxacin	0	J01MA01	Ofloxacin	0	J01MA05	Moxifloxacin	0
-			J01MA02	Ciprofloxacin	O/P	J01MA16	Gatifloxacin	0
			J01MA04	Enoxacin	0	J01MA17	Prulifloxacin	0
			J01MA07	Lomefloxacin	0	J01MA18	Pazufloxacin	Р
			J01MA08	Fleroxacin	0	J01MA19	Garenoxacin	0
			J01MA09	Sparfloxacin	0	J01MA21	Sitafloxacin	0
			J01MA12	Levofloxacin	O/P			
			_a	Tosufloxacin	0			
Short-acting macrolide			Intermediate-acting macrolide			Long-acting macrolide		
ATC level	Name	Route	ATC level	Name	Route	ATC level	Name	Route
J01FA01	Erythromycin	0	J01FA06	Roxithromycin	0	J01FA10	Azithromycin	0
J01FA02	Spiramycin	0	J01FA07	Josamycin	0		•	
J01FA03	Midecamycin	0	J01FA09	Clarithromycin	0			
J01FA12	Rokitamycin	0	J01FA15	Telithromycin	0			

Second-generation FQs

ATC, Anatomical Therapeutic Chemical; O, oral; P, parenteral.

<sup>a</sup> ATC level was not determined.

#### Table 1

Daily doses of Japanese antimicrobials for which DDDs were not defined in the ATC/ DDD classification system separately defined as JDDD.<sup>a</sup>

	-	
ATC group/chemical substance	Administration route	JDDD
J01CA		
Ampicillin/cloxacillin	Oral	2
<b>x</b> ,	Parenteral	4
Ciclacillin	Oral	2
Lenampicillin	Oral	1
J01CE		
Benzylpenicillin benzathine	Oral	0.96
J01DB		
Cefroxadine	Oral	2.1
J01DD		
Cefteram pivoxil	Oral	0.6
J01DI		
Faropenem	Oral	0.9
Tebipenem pivoxil	Oral	0.84
J01EE		
Trimethoprim/sulfamethoxazole	Oral	0.48
	Parenteral	0.48
J01FA		
Midecamycin	Oral	0.6
J01GB		
Astromicin	Parenteral	0.4
J01MA		
Garenoxacin	Oral	0.4
Lomefloxacin	Oral	0.6
Tosufloxacin	Oral	0.6
J01XB		
Polymyxin B	Oral	0.387
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DDD, defined daily dose; ATC, Anatomical Therapeutic Chemical.

<sup>a</sup> JDDD was separately defined using the approved maintenance dosage in Japan.

2009, 2011 and 2013) of total consumption, of which oral thirdgeneration cephalosporins (J01DD), macrolides (J01FA) and fluoroquinolones (J01MA) accounted for 77.1% (mean of 2009, 2011 and 2013) of oral consumption.

Table 3 shows the trends in oral antimicrobial consumption between 2009 and 2013. Total use of oral antimicrobials increased by 1.07-fold from 13.62 in 2009 to 14.61 in 2013. Based on Spearman's rank correlation analysis, oral consumption of secondgeneration cephalosporins significantly decreased in 2013 compared 2009.

Use of parenteral antimicrobials increased by 1.14-fold from 1.070 in 2009 to 1.225 in 2013 (Table 4). Notably, based on Spearman's rank correlation analysis, parenteral consumption of combinations of penicillins including *β*-lactamase inhibitors

Third-generation FQs

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