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Research Article

Antibacterial Medicine Consumption in Private and State Sector Outpatient Settings in Colombo District, Sri Lanka

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ABSTRACT

Introduction: Objective of this study was to determine the quantities and patterns of antibacterial medicine (ABM) consumption in the public and private hospital outpatient settings in Colombo District. **Methods:** A descriptive cross-sectional study was conducted in outpatient settings of selected State and private hospital settings between 2012 and 2013. 2009-WHO methodology was adapted to suit the Sri Lankan healthcare system. Oral systemic aggregated ABM (J01) consumption data was collected and categorized using Anatomical Therapeutic Chemical classification system. It was quantified using Defined Daily Doses (DDDs), and DDDs per 1000 outpatients per day (DID). Results were interpreted using descriptive statistics. **Results:** ABM consumption was 4.21DID and 3.46DID from private and State hospitals respectively. Most common ABM subgroup was penicillin in both private (1.34 DIDs) and State hospitals (2.67 DIDs) followed by macrolides (private hospital = 0.79 DIDs, State hospital = 0.36 DIDs). Five ABMs contributed to 90% drug utilization in State hospitals compared to 12 in private hospitals. Ratio of the consumption of broad spectrum penicillins: narrow spectrum penicillins, cephalosporins and macrolides were 30:1 and 04:1 in private and State hospitals respectively. Amoxicillin (60.3 %) was the predominantly consumed ABM in State hospitals compared to co-amoxiclav (22.9%) in private hospitals. **Conclusion:** Consumption of conventional ABM predominates in State outpatient settings whereas newer broader spectrum ABM in private hospital outpatient settings. The findings highlight the need for antimicrobial stewardship, especially in private hospital outpatient settings. Furthermore, the Ministry of Health, Nutrition and Indigenous Medicine of Sri Lanka should intervene to maintain complete ABM dispensed data of institutionalized ABM consumption surveillance in Sri Lanka.

Key words

Antibacterial medicine consumption; Sri Lanka; Outpatient setting; Private and State sector; Drug utilization

INTRODUCTION

Antibacterial medicines (ABM) are losing their magical power due to emergence of resistance at an alarming rate. Antibacterial resistance (ABR) is identified as a threat to public security.(1) Inappropriate consumption of ABM is one of the major driving forces for the escalation of resistance rates of bacteria. Hence, ABM consumption surveillance is needed to generate data to initiate relevant policies to reduce ABM consumption and ABR, and to preserve lifesaving ABMs.(2) The World Health Organization defines antibacterial consumption data as "estimates derived from aggregated data sources such as import or wholesaler data, or aggregated health insurance data where there is no information available on the patients who are receiving the medicines or why the antimicrobials are being used. These data sources provide a proxy estimate of use of antimicrobials".(3) These consumption data can be collected and presented as total consumption for a country or by settings such as community vs. hospital or State vs. private sectors. In high income countries, ABM consumption surveillances is well established and they publish region and country wise data annually.(4) This helps to direct the policies both at regional as well as national level. The majority of lower middle income countries (LMIC) do not have routine ABM consumption surveillance programmes mainly because of resources limitations and not having computerized data. However, containment of ABR at global or even country level will not succeed only with well-established programmes in high income countries. The WHO plays a pivotal role in assisting LMICs to initiate and sustain activities to combat ABR. In 2009 WHO introduced a method to conduct ABM consumption and ABR surveillances in LMIC.(5) In 2015, at the 68th World Health Assembly, optimum use of ABM was proposed as one of the five priorities in the Global strategic plan to combat ABR.(6) The 2009-methodology recommends using bulk and prescription data which were considered as good attributes for initiating ABM consumption /use surveillances.(5)

While working on reduction of inappropriate consumption of ABR, WHO also recognizes the importance of having universal access to needed ABM. In other words, access to ABM should be ensured while preserving their effectiveness for future. Therefore in 2017, the WHO model list of essential medicines went beyond and categorized ABM as access, watch and reserve medicines.(7) "Access antibiotics, are antibiotics that should be widely available, affordable and quality-assured". Watch group ABMs are "recommended as first or second choice treatments only for a specific, limited number of indications" Reserve group of ABMs are treated as "last resort" options when other alternatives have failed.(7)

It has been reported that in addition to overall increase in the consumption of ABM (8), broad spectrum ABM are replacing narrow spectrum ABM (9-13). A recent study has shown that prescriptions with ABM for acute respiratory tract infections were common (70%) among outpatient department (OPD) patients.(14)

Sri Lanka is a LMIC with an approximate population of 20 million. Sri Lanka published their strategic plan of combating ABR in accordance with the global action plan in

2017.(15) Sri Lankan government provides health services for free through a network of different levels of healthcare facilities/hospitals. Private sector hospitals also provide health services to a significant proportion of outpatients where patients spend out of pocket. Of the 125 registered private hospitals, 51% are located in the Western province of Sri Lanka.(16) Piloting the methods recommended by WHO for ABM consumption surveillance in LMICs is an important pre-condition before institutionalizing such programs.

Hence, the objective of this study was to determine the quantities and patterns of ABM consumption in the public and private hospital outpatient settings in Colombo District over a period of one year using aggregated ABM data as recommended in 2009-WHO methodology.

METHODS

Study design and duration

This is a part of a large-scale surveillance study of ABM use and resistance carried out between October 2012 and September 2013 in Colombo District. The 2009-WHO methodology was adapted to suit the Sri Lankan healthcare system.(5)

Study settings

Eighteen State sector healthcare facilities and seven private healthcare facilities were identified for this part of the surveillance programme. Of the 18 healthcare facilities in the State sector, 16 were selected using a multistage sampling method. Purposive sampling method was used to select two study settings as ABR data were collected from these two large hospitals (17) (Table 1). Although, all private hospitals in Colombo District listed in the Private Health Services Regulatory Council were invited, only 7 consented.

Table 1: Selection of health facilities from the State sector

Hospital category	Level of care	Number in		Sampling method
		Colombo District	Selected for study	
National hospital	04	01	01	01 (purposive sampling)*
Teaching hospitals	04	08	05	01 (purposive sampling)*, special care institutes excluded
Base hospitals	03	04	01	Simple random sampling method
District hospitals	02	09	03	
Primary medical care units	01	27	08	
Total		56	18	

*The study collected the antibacterial resistance data from two State teaching hospitals and these two settings are intentionally included to collect ABM consumption data.

Ministry of Health, Sri Lanka classifies hospitals depending on the level of care as follows.

Level 1- Primary Medical Care Unit (Primary medical care units, Maternity Home)

Level-2-Divisional Hospitals (District Hospitals, Rural Hospitals, Peripheral units)

Level 3- District Base Hospitals, District General Hospitals

Level 4-Provicinal General Hospitals, Teaching hospitals

Collection of ABM consumption data

Outpatient consumption data for oral ABM for systemic use (J01 group as per Anatomic-Therapeutic- Chemical (ATC) Classification) (18) were obtained from records maintained by pharmacists in State sector hospitals and from inventory movement records in the private sector. Antifungal, anti-tuberculosis and topical ABMs were excluded. First author extracted the details on name, dosage form, strength, and dispensed quantity of ABM (J01) from the above records using a custom-made profoma. Antibacterial medicines were categorized according to the ATC classification.(18)

Analysis of ABM consumption

Antibacterial medicine consumption was quantified using Defined Daily Doses (DDDs) and DDD per 1000 out-patients per day (DID). We used 1000-outpatients instead of 1000 mid year population in calculating DIDs. (19)

$$\text{DDD} = \frac{\text{Strength of the antibiotic X Quantity of supply}}{\text{DDD for the antimicrobial agent}}$$

$$\text{DDD per 1000 out-patients per day (DID)} = \frac{\text{DDDs X 1000}}{\text{Outpatient visits during study period}} \text{ X } 365$$

Following standard indications were used to describe ABM in both settings.(20, 21, and 22)

1. Total consumption of ABM in each study setting using DID.
2. Relative consumptions of ABM by pharmacological sub group.
3. Ratio of the consumption of broad (J01(CR+DC+DD+(F-FA01))) to the consumption of narrow spectrum penicillins, cephalosporins and macrolides (J01(CE+DB+FA01)).(18,20,21)
4. Drug utilization 90%. For drug utilization 90% method, ABMs were ranked according to quantity in DDDs, DU 90% indicates the number of ABM responsible for 90% of DDDs.(22)
5. Relative consumption of ABM with reference to Access, Watch and Reserve WHO grouping. Only core Access antibiotics were included in the Access group.(23)

The data entry, calculation and analysis were performed using Microsoft Excel. Descriptive statistics was used to interpret results.

Ethics review committee approval was obtained from the Ethics Review Committee of Faculty of Medicine, University of Colombo (EC-11-121). Administrative approval was obtained from all relevant Authorities.

RESULTS

ABM consumption was 4.21 and 3.46 DIDs respectively for private and State sectors (Table 2). Although seven private hospitals consented, only three of them had complete data to calculate DIDs. Beta lactam penicillin (J01C) was the most common ABM subgroup in both private (1.34 DIDs) and State hospital outpatient settings (2.67 DIDs) followed by macrolides (private sector = 0.79 DIDs, State sector = 0.36 DIDs). The ratio of broad: narrow spectrum penicillins, cephalosporins and macrolides, was 30:1 in private hospital outpatient settings where as it was 0.4: 1 in State hospitals outpatient settings.

Antibacterial medicine consumption with reference to the WHO grouping of Access, Watch and Reserve is illustrated in Figure 1. In private hospital outpatient settings, Watch group ABM agents accounted for 41% whereas

Table 2: Total consumption and relative consumption of J01 antibacterial medicine (ABM) pharmacological subgroup dispensed from State sector outpatient settings and Private sector outpatient settings

ATC code	ABM according to the Pharmacological subgroup	DDD/1000 outpatients per day		Consumption as a proportion of total J01 consumption (%)	
		Private	Sate	Private	State
J01A	Tetracyclines	0.40	0.08	9.44	2.38
J01C	Beta lactam antibacterial, penicillin	1.34	2.67	31.95	77.36
J01D	Other beta lactam antibiotics	0.73	0.14	17.46	4.02
J01E	Sulfonamides and trimethoprim	0.02	0.02	0.40	0.60
J01F	Macrolide and lincosamides and streptogramins	0.79	0.36	18.85	10.35
J01M	Quinolone antibiotics	0.76	0.05	18.16	1.54
J01X	Other	0.16	0.13	3.73	3.75
	Total	4.21	3.46	100	100

ATC, Anatomic-Therapeutic- Chemical (ATC); ABM, Antibacterial medicine; DDD, Daily Defined Dose

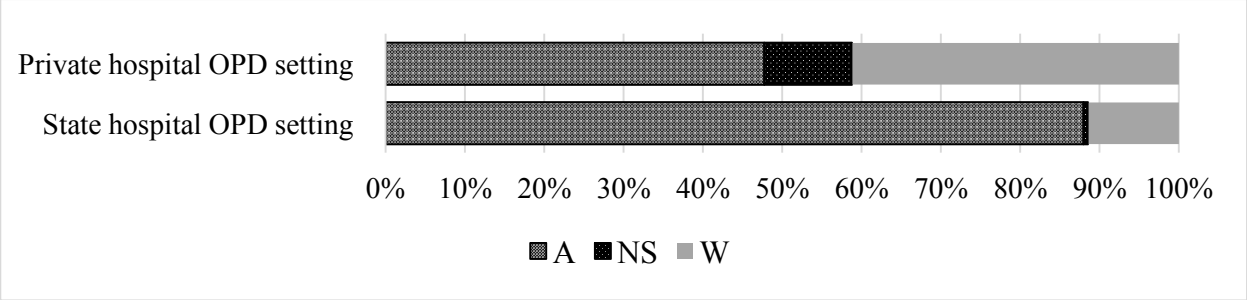

Figure 1: Percentage of ABM use in DDD/1000 inhabitant per day according to WHO Access, Watch, Reserve grouping (A- Access, W- Watch, NS- Not specified)

in State hospital outpatient settings Access group accounted for 88%.

Penicillins accounted for 2.67 DIDs (77%) of ABM dispensed in the State hospital settings compared to 1.34 DIDs (32%) dispensed in the private hospital settings. Within this group, amoxicillin was the most popular in the State sector (2.09 DIDs, 78%) compared to co-amoxiclav (0.96 DIDs, 72%) in the private sector.

Macrolides accounted for 0.36 DIDs (10%) in the State hospital setting compared to the 0.79 DID (19%) dispensed in private hospital settings. Erythromycin was the main macrolide available in the State sector, which accounted for 0.35DID (97%), whereas clarithromycin

and azithromycin accounted for 0.39 DIDs (50%) and 0.33 DIDs (42%) respectively in the private sector. Relative consumption of cephalosporins is summarized in Table 3. Cephalexin (0.14 DID) was the main cephalosporin consumed in the State sector. In the private sector, cephalexin (0.14 DID 95%), cefuroxime (0.38 DID 96%) and cefixime (0.20 DID 99.7%) were the main cephalosporins belonging to 1st, 2nd and 3rd generations respectively.

Table 3: Relative consumption of cephalosporins by generation

Generation of cephalosporins	DDD/1000 inhabitants per day (% of total)	
	Private	State
First generation (J01DB)	0.15 (19.90)	0.14 (100.00)
Second generation (J01DC)	0.39 (53.38)	0.00
Third generation (J01DD)	0.20 (26.72)	0.00
Total (J01D)	0.73	0.14

DDD, Daily Defined Dose

The relative consumption of fluoroquinolones in State sector and private sector were 0.04 DID (71%) and 0.74 DID (97%) respectively. Ciprofloxacin (State = 0.03 DIDs, private = 0.39 DIDs) was the leading quinolone dispensed in both outpatient settings. In State outpatient settings ciprofloxacin (65%) and norfloxacin (6%) were the only fluoroquinolones dispensed compared to ciprofloxacin (51%) and levofloxacin (35%) in private outpatient settings. Within the tetracyclines pharmacological subgroup, doxycycline was the main ABM dispensed in both State (0.08 DID, 96%) and private (0.34, 100%) outpatient settings.

90%DU

Five ABMs contributed to 90%DU in State outpatient settings (Amoxicillin 60.3%, cloxacillin 13.4%, erythromycin 10.0%, cephalexin 4.0% and metronidazole 2.5%). Twelve ABMs contributed to 90% DU in private outpatient settings (co-amoxiclav 22.9%, doxycycline 9.4%, clarithromycin 9.3%, ciprofloxacin 9.2%, cefuroxime 9%, azithromycin 7.9%, amoxicillin 6.7%, levofloxacin 6.3%, cefixime 4.7%, cephalexin 3.3%, and metronidazole 2.8%)

Monthly variation of ABM consumption by pharmacological subgroups during October 2012-September 2013 is shown in Figure 2.

Comparison of antibiotics dispensed at each level of healthcare in the State sector

Table 4 compares the ABMs dispensed in DDDs per 1000 outpatients per day at the different levels of State sector hospital outpatient settings.

DISCUSSION

The aim of this study was to determine the quantities and patterns of ABMs in the State and private hospital outpatient settings in Colombo district from 2012 to 2013. During the study period, ABM consumption in private hospital outpatient settings were greater (4.21DID) than the State hospital outpatient settings (3.46 DID).

Penicillin, macrolide, and cephalosporins were three major subgroups of ABMs consumed in both settings. However, penicillin was the

main ABM subgroup consumed as reported by initial studies carried out in Sri Lanka.(24) The ABM consumption pattern of Colombo District is similar to other countries as well.(25) The remarkable variation seen in consumption of antibiotic subgroups between State and private sectors were most probably due to policy regulations in the State sector and profit margins in the private sector: This explains the predominant use of narrow spectrum ABMs in the State outpatient facilities and broad-spectrum ABMs in the private hospital outpatient settings. (5, 26)

In State sector, supply of ABMs are limited to those listed in the Essential Medicines List (EML) and the Hospital Formulary (HF) explains the pattern observed. Since medicines being given free of charge is the major contributing factor for patients coming to State sector OPD (14), prescribers tend to prescribe ABMs which are available in the OPD pharmacy. This explains the predominant use of amoxicillin (60% of consumption) and old, narrow spectrum ABMs accounting for 90% of DU. This old, narrow-spectrum ABM consumption pattern is same in the State hospital outpatient settings in India as well.(26)

During the study period ABM consumption in Level 2 State hospital outpatient settings was three times higher than the Level 4 State hospital outpatient settings.

Table 4: The volume of antibiotics dispensed in DDDs per 1000 outpatients per day in different levels of institutes in the State sector

ATC code	Antibiotic	DDDs per 1000 outpatient per day			
		Level 1 (N=8)	Level 2 (N=3)	Level 3 (N=1)	Level 4 (N=4)
J01CA04	Amoxicillin	1.75	6.82	1.99	2.00
J01FA01	Erythromycin	0.27	0.97	0.24	0.36
J01AA02	Doxycycline	0.82	0.25	0.02	0.00
J01CF02	Cloxacillin	0.24	0.81	0.71	0.46
J01DB01	Cephalexin	0.30	0.48	0.37	0.07
J01CR02	Co-amoxiclav	0.08	0.11	0.05	0.07
J01MA02	Ciprofloxacin	0.01	0.18	0.17	0.00
J01XD01	Metronidazole	0.07	0.15	0.01	0.10
J01FA09	Clarithromycin	0.00	0.23	0.00	0.00
J01XE01	Nitrofurantoin	0.09	0.09	0.03	0.04
	Total	3.74	10.28	3.64	3.23

DDD, Daily Defined Dose; Ministry of Health, Sri Lanka classifies hospitals depending on the level of care as follows.
Level 1- Primary Medical Care Unit (Primary medical care units, Maternity Home)
Level-2-Divisional Hospitals (District Hospitals, Rural Hospitals, Peripheral units)
Level 3- District Base Hospital, District general Hospital
Level 4-Provicinal General Hospital, Teaching hospital

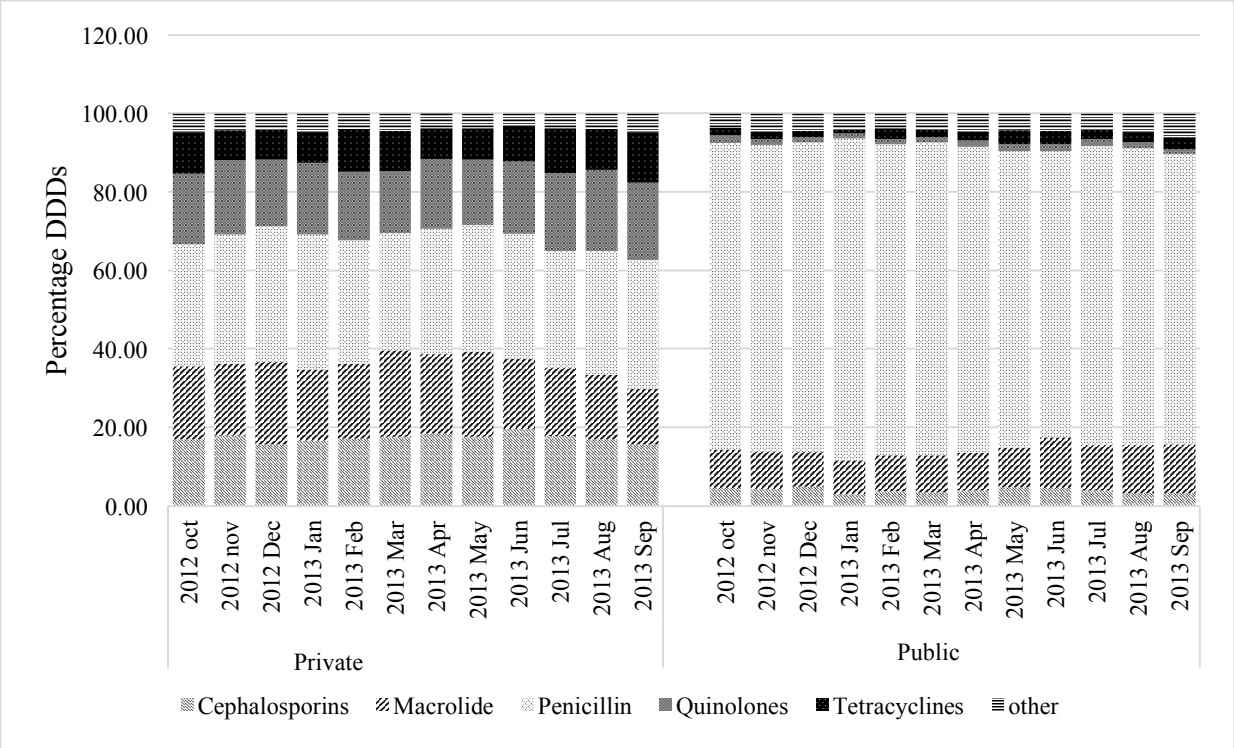

Figure 2: Monthly variation of Antibacterial medicine (ABM) consumption classified according to Anatomical Therapeutic Chemical Classification 3rd level during October 2012-September 2013 in three private sector outpatient settings and one State sector outpatient setting

Prescribers working in Level 1 and 2 are very junior in service and may not have sufficient diagnostic skills. Furthermore, there is limited facilities for laboratory tests to support their diagnosis. This problem needs urgent reconciliation otherwise will lead to inappropriate prescribing of antibiotics leading to ABR.

Consumption of ABMs in private hospital outpatient settings reflects the free prescribing pattern of prescribers. Prescribers preferred broad spectrum ABM over old and narrow spectrum ABM. This pattern has been evident in other studies as well.(27) Coamoxiclav (22%) has become the popular penicillin in the private sector. Prescribers feel amoxicillin is ineffective and therefore they tend to select co-amoxiclav.(14) Studies have documented high resistance rates to amoxicillin in the same settings.(17, 28)

ABM prescribing pattern is influenced by diverse reasons such as (i) diagnostic uncertainty and concern for bacterial super infection, (ii) perceived expectations from patient, (iii) competition to retain patients and, (iv) influence by the pharmaceutical industry. (14, 29). The WHO classification of AWaRe (Access, Watch, Reserve) has helped us to understand the pattern of ABM consumption in both these settings. Data had been collected before WHO introduced this classification, however the consumption in State sector has

reflected this classification where 4 of the 5 ABM that contributed to 90% of DU were from the Access group, compared to only 5 out of 12 in the private sector. In State sector ABM supply is limited to EML and HF whereas in private sector profit dictates the supply of ABM.

Despite studies reporting high rates of resistance to both amoxicillin and co-amoxiclav, (17, 28) the prescribing pattern in both settings have not been guided by these resistance data. Usefulness of surveillance data of ABM consumption and resistance rely on the fact that both should be linked and influence the prescribing pattern and antibiotic prescribing policy. We have provided the evidence that it is possible. It is now in the hands of a focal point for combating ABR in the Ministry of Health, Nutrition and Indigenous Medicine of Sri Lanka to take up the lead and institutionalize this pilot project into a routing programme.

There are minor changes seen in the monthly ABM consumption pattern (Figure 2) and this may be due to the daily variation in number of patients visiting OPD facilities, prevailing disease conditions, and out of stock situation of ABM occasionally seen in the State sector. Some countries describe a clear seasonal variation with antibiotic use but this was not evident in our study. (8, 30, 31,)

To the best of our knowledge, no studies have reported ABM consumption surveillance data from both State and private sector settings in Sri Lanka using the WHO methodology recommended for LMIC. This is a major strength of our study. However, there are some limitations. Private sector data may not be representative as only three hospitals who voluntarily consented and had the required data were included in the surveillance. Since this was an investigator initiated surveillance study we did not have the mandate to get the consent as well as to request the private hospitals to maintain complete data. Focal point for combating ABR in the Ministry of Healthcare and Nutrition probably can do both if this surveillance is going to be institutionalized.

CONCLUSION

This study provides a snapshot of oral systemic ABM consumption in the private sector and State sector outpatient settings in the Colombo District. The consumption of conventional ABM predominates in State outpatient settings, and newer, broader spectrum ABMs in private hospital outpatient settings. The findings highlight the need for antimicrobial stewardship, especially in private hospital outpatient settings. Furthermore, the Ministry of Healthcare and Nutrition of Sri Lanka should intervene to maintain complete ABM dispensed data in order to institutionalize ABM consumption surveillance in Sri Lanka. This will help in monitoring the effectiveness of future interventions to curtail the inappropriate ABM consumption as well.

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Author's Declaration

The authors declare that all persons listed as authors have read and given approval for the submission of this manuscript.

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Competing Interests

The authors declare that they have no competing interests to disclose.

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